

# Pain Assessment in 21st-Century Neuropsychiatry.

Introducing Plural, Perspective, Situated  
Epistemic Frames for the Epidiagnostic  
Characterisation of Pain Experiences.

Alejandro Cardeña Martínez

Doctoral Thesis



—  
**Thesis Director**

Prof. Dr. Ángel Luis Peña Melián  
Dpt. Anatomy & Embryology  
School of Medicine — UCM

—  
**Research Lines**

*Clinical Epistemology*  
*Clinical Ergonomics*  
*Neuro-Psychiatry*  
*Diagnostics*  
*H-CI*

—  
**PhD Programme**

'Logics & Philosophy of Science'  
University of Salamanca || ECyT

—  
**2019**



—  
**To the people in pain**



# Index

*Acknowledgements (i)*

*Director's Introduction (iii)*

## **Q I — Presentation, Focus & Scope of this Work:**

§1 Introduction & Justification of the Thesis: The Value of Epiagnostic Research on Pain (p 9)

§2 Research Hypothesis, Goals & General Results (p 15)

§3 Methodology & Scope of the Research: Using Comparative Bibliographical Processes (p 21)

## **Q II — Introducing Frames. The Value of Pluralism, Perspectivism, Contextualism for Clinical Epistemologies:**

§1 Situating Neuropsychiatric Assessment. Developing Clinical Epistemic Niches, Frames, Perspectives (p 26)

§2 Structure of the Present Analysis: Framing Epiagnostic Characterisations on Pain in Neuropsychiatry (p 62)

## **Q III — Niches for Framing Epiagnostic Characterisations of Pain Experiences in Neuropsychiatry:**

*A — Framing Neurophysiological Characterisations: Historical & Comparative Traits:*

§1 On the Historical Development of Pain Physiological Characterisations.  
An Anthropological Contour (p 74)

§2 Building Pain Models: From Early Electrophysiology to the Complexities of the 21st Century (p 94)

§3 Sounding the Limits of Materiality & Over-Attribution: On Pain Fibre Specialisation (p 106)

§4 Pain Physiographies. A Contemporary Image (p 122)

*B — Framing Psychiatric-Epidemiological Characterisations: Overflowing Morbidities & Pain:*

§5 Overflowing Morbidities: Pain Reinforcement & the Value of Epiagnosis (p 150)

§6 Neuropsychiatric Dysfunctions Associated with Pain Reinforcement Comorbidities (p 168)

*C — Framing Clinical Characterisations: Diagnostic Practices & Pain Measurement Strategies:*

§7 Epiagnostic Assessment as Clinical Practice.  
Navigating Person-Centered Diagnosis in Neuropsychiatry (p 188)

§8 Measurement Strategies: Assessing Pain Self-Judgements & Self-Beliefs (p 200)

*D — Framing Interpersonal Characterisations: Difficulties on Self-Narratives & Pain Transference:*

§9 Barriers in Self-Assessment of Pain & Its Comorbidities:  
Indetermination in Self-Beliefs & Narrative Perspectives (p 220)

§10 Transference of Trusted Knowledge by Contextualising Empathetic Perspectives on Pain (p 242)

## **Q IV — Results, Conclusions & Future Lines:**

§1 Structured Summary of Results, Conclusions & Implications (p 270)

§2 Future Lines on Epiagnostics: Applications to Neuropsychiatry, Neuropsychiatric Epistemologies & the Nosographic Technologicalisation (p 284)

 **Bibliographies** (p 296 — 369)



## *Acknowledgements*

- . A mi *Madre*: porque sin tu apoyo y confianza durante toda una vida de esfuerzo, cariño, atención y amor, no habría podido empezar ni culminar ésta ni muchas otras aventuras.  
— Gracias por Todo. Te quiero.
- . Al Prof Dr *Ángel Luis Peña Melián*: por su enorme guía, su siempre desinteresada ayuda, su rigor y valentía teóricos, por la comprensión de mis propuestas, por su humildad siendo una eminencia.  
— Siempre agradecido, Maestro.
- . A *Piotr Król* (PhDR, Instytut Nauk Geologicznych ‘PAN’ Ośrodek Badawczy w Warszawie: Institute of Geological Sciences, Research Centre in Warszawa, National Polish Institute of Science, Warsaw, Poland): por tu constante compañía todos estos años, y por ayudarme a crecer personalmente desde tu delicada capacidad para apreciar el mundo.  
— Dziękuję bardzo, mój dobry Przyjaciel.
- . To psychiatrist Dr *Lars Christian Moen* (University of Oslo, Det Medisinske Fakultet, Norway): for your company along my psychiatric theoretical development, for your dialogical effort on neuropsychiatric evaluation, for our academic exchange.  
— Takk så mye, venn.
- . A la Cat. Prof Dra *Inmaculada Perdomo Reyes* (ULL; Instituto Universitario de Estudios de las mujeres): por abrirme una posibilidad epistemológica hace años que ha culminado finalmente, gracias a tu presencia en mi vida académica, en una tesis doctoral que he llegado a terminar.  
— Siempre agradecido.
- . Al Prof Dr *Rafael Huertas García-Alejo* (CSIC-CCHS: Consejo Superior de Investigaciones Científicas — Centro de Ciencias Humanas y Sociales): por haber sido una profunda inspiración para mí en la perspectiva histórico clínica ante el desarrollo de la patología mental.  
— Siempre agradecido.
- . Al programa de postgrado en ‘Historia y Filosofía de las Emociones’ en el CSIC-CCHS, en especial al Dr *Javier Moscoso* y la Dra *Mercedes García Arenal*, por haberme introducido en este mundo apasionante.
- . A D<sup>a</sup> *Esther Palacios Mateos*, por toda la ayuda y constante atención, y a la Dra *Ana Cuevas Badallo* — así como a los diferentes colegas de la Universidad de Salamanca y del ECyT responsables del programa de doctorado.
- . To Prof Dr *Stefan Helmreich* (MIT: Massachusetts Institute of Technology), whose book ‘Sounding the Limits of Life, Essays on the Anthropology of Biology and Beyond’ has been an inspiration and a lighting guide throughout the whole adventure of the present dissertation.  
— I will always be thankful.

## VISIÓN DEL DIRECTOR

El trabajo titulado: “Pain Assessment in 21st-Century Neuropsychiatry: Introducing Plural, Perspective, Situated Epistemic Frame for the Epi-diagnostic Characterisation of Pain Experience” realizado por el doctorando D. Alejandro Cardena Martínez, analiza el binomio clínico (neuropsiquiátrico) paciente doloroso bajo un doble punto de vista.

Por una parte se analizan las bases para el establecimiento de una epistemología plural que contemple las características propias del paciente como su situación geográfica, su ambiente social, su cultura, ambiente político, género, grupo étnico y situación clínica de partida, todo ello se analiza bajo el punto de vista de la filosofía de la ciencia y por otra parte se estudian las herramientas conceptuales necesarias para un buen diagnóstico clínico (fundamentalmente neuropsiquiátrico) del dolor que sitúen al paciente en un marco apropiado para un pronóstico y tratamiento eficaces. El autor, en el primer caso solventa ampliamente los objetivos propuestos realizando una completa y exhaustiva revisión bibliográfica para tratar de ver el consenso en el ámbito epistemológico plural. Respecto al segundo punto de vista, el análisis del diagnóstico en un paciente que sufre dolor el autor ha revisado multitud de referencias bibliográficas que al final cumplieron con creces los objetivos propuestos.

Problemas como la naturaleza de la percepción dolorosa, los modelos de dolor, las diferentes clasificaciones patológicas del dolor, las características personales de cada paciente que contribuyen a que “no hay enfermedades sino enfermos” (Gregorio Marañón 1887-1960), qué es el dolor, etc... Todas estas cuestiones son abordadas de una manera profunda en niveles históricos, filogenéticos y actuales. Lo que trata el autor es de especificar qué es el dolor y cómo diagnosticarlo en un enfermo dado. En este trabajo se propone una interpretación nueva de dolor y se revisan las vías dolorosas y por qué no hay influencias directas córtex-médula espinal, se proponen nuevos modelos en la entrada de la información algica en el asta posterior de la médula espinal, el papel de la inflamación en la percepción dolorosa, el papel de las fibras RIF, se hace también una ingeniosa revisión integrada de las fibras del trigémino relacionadas con el dolor, se deconstruyen las clasificaciones sobre las patologías dolorosas: en lugar de etiquetar los pacientes en una determinada clasificación se prefiere situar al paciente inicialmente con una serie de rasgos patológicos que sean luego susceptibles de un tratamiento eficaz. Todo ello queda muy bien reflejado en el capítulo 4 del QIII que, por sí solo, puede constituir un artículo de referencia. El valor de este trabajo es evidente. Es un trabajo básico a partir del cual se puede dar salida a muchos proyectos independientes tanto del ámbito de la filosofía de la ciencia como de la clínica neuropsiquiátrica, cuya la utilidad puede extenderse a todo el ámbito clínico que se relacione con el paciente doloroso. Podemos considerar el trabajo como un manual de instrucciones a tener en cuenta en la relación con el paciente doloroso. Además, y como valores emergentes, surge por parte del autor la necesidad de crear una especialidad que se denomine Algiología y para eso razona muy bien el porqué de esta opinión y de donde surge y la utilidad de impulsar la Inteligencia Artificial en el diagnóstico médico. Un trabajo que, aunque se puede contemplar bajo ese doble punto de vista comentado antes, realmente es un todo único, donde cada especialista puede encontrar información de lo que le interese. Trabajo muy recomendable de conocimiento para filósofos y clínicos y que espero pueda publicarse adaptándolo en forma de libro.



---

# Quarter I

## Presentation, Focus & Scope of this Work

☛ 300 — 308

---

### QI, §1

#### **Introduction & Justification of the Thesis:**

#### **The Value of Epiagnostic Research on Pain (p 9)**

- . Origination of the Thesis Project
- . Presenting the Context of Investigation
- . Introduction & Justification of the Theme: Pain, Epiagnostics & Epistemic Framing
- . Some Regards on the Notation for Intertextual Reference

---

### QI, §2

#### **Research Hypothesis, Goals & General Results (p 15)**

- . Research Hypothesis
- . Goals
- . General Results

---

### QI, §3

#### **Methodology & Scope of the Research:**

#### **Using Comparative Bibliographical Processes (p 21)**

- . Methods
- . On the Selection of a Bibliographical-Comparative Methodological Framework
- . Scope & Limitations of this Research



# QI, Chapter §1

## Introduction & Justification of the Thesis: The Value of Epi-diagnostic Research on Pain.

### *. Origination of the Thesis Project*

This project started nearly 6 years ago: by that time I was accepted in a postgraduate course at the National Research Council (CSIC: CCHS) in Madrid on the 'History and Philosophy of Emotions', led then by Dr Javier Moscoso in collaboration with Dr Mercedes García Arenal. Many innovative notions on the cultural history of experiences, with especial attention to pain and sorrow (researchers and clinicians from pain units were invited to the course), amplified my vision upon the study of human experiences and affections. I was moved by the contemporary 'turn to affects' and affective performances in the comparative history and anthropology of emotions, by the new material and immaterial thoughts on anatomophysiology, and by the epistemological bases on psychiatric pathology, which I vividly remember being addressed historically and commentationally by Dr Rafael Huertas García-Alejo. I met my thesis director, anatomist and neuromorphologist Dr Ángel Luis Peña Melián, in this postgraduate course on a group visit to the anatomical laboratory at UCM School of Medicine for a theoretical and practical session. Students got the opportunity to face a human brain, maybe for their first time, brilliantly and passionately exposed with so much attention, forensic respect and amenable introduction. In the next few months I asked Dr Peña if he was available to go on a scholarly endeavour deepening in the epistemic problems models on emotion in neuropsychiatry gathe-

red in today's research practices. The suggestion was fruitfully and kindly accepted, and a preparatory medical phase of almost 3 years before initiating the official academic time for my PhD investigation began. The project soon turned the focus of research into a specific emotional spectrum, pain experiences, and a specific form of scientific modelling, neuropsychiatric evaluation, assessment, diagnostic practices.

The selection of the field, shall this be called an interfield, was made upon the complexity that contemporary assessment of pain experiences introduce to neuropsychiatric theory making, for pain, in as much as clinical application develops trans-disciplinarily, occurs to incorporate multiple collateral problems in the recognition of pathological accounts, especially in phenomena involving copathological dispositions (comorbidities, multimorbidities) to pain, including neuropsychiatric problems to a previous pain scenario yet described and now transformed, or the other way around, by including pain to a neuropsychiatric scenario yet described and now reinforced. The epistemic basis of pathological detection, characterisation and attribution, and the way this process is developed, were both significant aspects favouring a comprehensive and integrative study.

I came across with a major guidance in the epistemological strategy of the thesis during my MsPh studies on 'Logics and Philosophy of Science' in the University of Salamanca, identif-

ying, describing and criticising modern scientific practices by new epistemics. I had the eye-opening opportunity to assist to Dr Inmaculada Perdomo's (ULL) classes on contemporary social epistemologies, including a wide panorama from pluralism, perspectivism, constructivism and naturalism, to standpoint and feminist activisms —to which theoretical dispositions from many major authors have been determinant: D Haraway, N Cartwright, S Harding, R Giere, H Longino, B van Fraassen, P Kitcher, L Code, C Fehr, K Plaissance, E Keller, etc.

Generally, these frames have been applied to experimental fields (physics, energy engineering), biological fields (primatology, chemistry, Artificial Intelligence and Artificial Life) and political fields (financial collectivism, economic drifts), approached by contextual analyses since the '60s (eg, Minnesota Pluralism; Paneuropean comparative studies).

Nonetheless the amount of applications to contemporary medical and clinical scenarios, as I was starting to explore almost 1.5-2 years before the commencement of the PhD course with my thesis director in a preparatory fashion, appeared to me spectacularly abundant. Neurophilosophy, however, had no especial array on pain clinical epistemics, and psychiatric epistemology, even though large in its history, could not arrive to the depth of social and personal demands my research was starting to observe and entail. There was where I found my exploratory niche, with hopefully useful results: no epistemic bases on neuropsychiatric diagnosis existed upon pain experiences from contemporary contextual epistemologies facilitating an integrative and future-seeking approach.

Bringing the issue to psychiatric realms, the multiple discussions, interpretations, and exchange of ideas by this last year with psychiatrist Dr Lars Christian Moen, from the University of Oslo in Norway, have made this project to benefit from a personal sense of academic exchange and therapeutical experience.

This I now recognise highly significant in my prosecution of an integrative aim at bringing together anatomical, physiological, neurological and psychiatric, cultural, ethnographic interests. A final important theoretical inspiration has been the anthropological critique and constructive adaptation to scientific review from Dr Stefan Helmreich's (Stanford, MIT) neo-ethnographic works on perception, life sciences and theoretical models on artificiality. His book 'Sounding the Limits fo Life' has been an impressive influence on performing an ethnography of the scientific practice from an epistemic standpoint —in the present case delivered on a practical and intervening means as clinical fields show to be.

#### *. Presenting the Context of Investigation*

Thinking through the long-term relationships between epistemology and mental medicine, clinical assessment on experiences is one of the many current topics animating modern theoretical and practical discussions. These face the limits of identificational claims made upon complex, polymorphic diseases, the recognition and characterisation of particular heterogeneous symptomatologies, and the contemporary range of validity of patients's authority in mental health, all of which occur in a constant, socially evolving, culturally contextualised, politically and economically driven fashion. The case of pain experiences evaluation shows in an even more complicated scenario, where neurological and psychiatric vectors coalesce forming neuropsychiatric requirements altogether necessary for answering medical questions that no longer can be approached efficiently from single perspectives. Along with those fields, both collateral and central values emerge proper to internal medicine, immunology, embryology, vascular medicine, therapy theory and cognitive, memory and cultural studies on mental pathology. This interfield process originates from

a dynamic of hypercontextualisation of clinical nosographies, which extends pathology inflating the number of plausible morbidities sufferable by a determined patient, thus requiring assistance from guiding and contrasting new technologies oriented to help in complex decision making routines, and at the same time bringing a more detailed resolution of interventions through more specific pathological ascriptions available for acting in a patient's medical circumstance.

Criticism has been offered to such diagnostic enclosing paradigm, as well as to the medicalisation of the practice, and to the introduction of materially-oriented technology in claiming better results extracting value knowledge from patients that interpersonal and contextual analyses instead. The position of this work is critical with those instances too, especially in assessing the epistemic validity and stability of much of their metaphors and structural tenets. However it is also integrative, and runs forward to application: an important consideration is on the manner in which technology can develop broader resolution feeds from the patients's environment, helping to develop a more descriptive psychopathology, attuned to the needs and life queries of the patient at hand, nonetheless identifying comparative and epidemiological key markers informing of background standards based on cultural contrasted convention, increasing the chances of designing a more nurtured diagnostic characterisation.

Instrumental Skepticism will be exposed as a shaping perspective from which to evolve different forms of clinical claims, that do not show coercive against patients, stigmatising or restraining, but descriptive, multifactorial, prognostically worried on the development of further copathologies and comorbid scenarios, as prudent and cautious with the effects of intervention and medications.

Ideas on new forms of interpreting and working with pathological and nosographic infla-

tion through this framework are also delivered as a final remark to this account, however the body of the present work is dedicated to analyse and present a comparative study on how pain experiences are assessed interdisciplinarily in current neuropsychiatry, framing an epistemic ethnography on pain neuropsychiatric diagnostic practices, involving the ways cultural, social and contextual theoretical niches, frames and perspectives, shift, re-shift and value-morph the fields at hand as a result of plural and multiple decisions on trust —the necessary 'epistemic trust' from specific epistemic communities of clinical decision making affecting on conventions, on discussions, on values, on beliefs, that finally end up deciding what is sufferable and the ways to proceed with its assessment.

The present work covers this topic on account of listening to the epistemic limitations and new lines of investigation that neuropsychiatric assessment of pain experiences can expose, being pain diagnostic evaluation a magnificent example of a case study informing about how contemporary complexity in clinical research is shifting fields and interpretation strategies, demanding integration for explanatory claims, creating interfields for better understanding the problems patients are installed within, and providing of new forms of considering our access to knowledge, how we create it, discuss upon it, change it and use it in modern styles.

*. Introduction & Justification of the Theme:  
Pain, Epiagnostics & Epistemic Framing*

Pain assessment is a complex field, where many limitations of diverse origin may present methodological difficulties, altering clinical practices and blurring diagnostic and therapeutic efforts. In neuropsychiatric contexts, the assessment of a patient's pain experiences, as reported through narratives and interpersonal measurement strategies, requires a wider attention (in comparison with non-psychiatrically

compromised populations), for whom clinical models are supposed to be oriented towards rendering possible neurological dysfunctions and psychiatric pictures that could offer rather descriptive or explanatory bases for dealing with the reported pain-bearing scenario. Without a clear and meaningful understanding of patients's experiences, undertaking further treatment (pharmacology, therapeutics) or elaborating a suitable prognosis (outlining the conditions for a plausible clinical trajectory) can be difficult tasks to attain.

Patients suffering from pain reinforcing processes (by enlarging pain time-span, increasing intensity or adding a new pain-related pathology) usually acquire personal and interpersonal dysfunctions, coming down with several emotional re-attunements to their living phases, a change of attitude, of mind frame and, finally, agency and actions that, using PL Goldie's terminology (Cf. Goldie 2000; 2002; 2003; 2004), 're-shape' their overall personality. Within this context, comorbidities can present, provoking increasingly complex and heterogeneous diagnostics that face multiple problems in characterising, identifying and dealing with neurological and psychiatric dysfunctions comorbid to a previous state of pain (van Praag 1993; Fejer 2001; Maj 2005; Aragona 2009a; Jakovljević 2008; Cramer et al 2010; Klinkman & van Weel 2011; Jakovljević & Ostolić 2013). The opposite direction is also a viable development for these patients, as has been commented beforehand, incorporating pain as a comorbid clinical circumstance to a reinforced neuropsychiatric state. In both cases, pain assessment marks the beginning of a multifactorial heterogeneous and complex diagnostic, whose epistemological challenges must be approached should we enter a modern global practice of assessment.

This scene makes present work to focus on clinical epistemology as applied to the 'epidiagnostic' (*infra*) evaluation of pain in neuropsychiatry by neuropsychiatrists (and related prac-

tioners), thus centring the epistemic accounts of assessing another person's experiences of pain, seeking for describing and framing, from contemporary epistemologies, the scientific practices performed by clinicians in the process of evaluating and diagnosing compromised pain-bearing patients.

The thesis trusts in this way on a relational definition of 'pain experiences' as medically, clinically and therapeutically understood:

*Def.* — 'Pain is defined as an intimate experience attributable to a person (organism, agent, actant, propositional subject) in his or her (etc.) interaction with the shifting environment (involving interpersonal, relational, societal, cultural, economic... contextual vectors), that emerges definable as a complex and heterogeneous assessment of his or her integrity (or dis-integrity; in terms of biological compositions, psychological organisations, psychosocial identifications, etc.), performed in a modal (involving an epistemic process analysable by contents-based propositional beliefs) and polymorphic fashion (involving different scales of complexity), whereof 3rd-party descriptions and analyses (by a diagnoser, a therapist, an instrument, a relative, etc.) requires of plural and perspectival standpoints in coalescence, integrating evolutionary-biological complexity at different scales (following an Open Systems biological, Bertalanffyian standpoint, from primitive dispositions to more sophisticated adaptations), anatomophysiological complexity (in as much as scientific ascriptions develop, discuss, refute and accept their convictions upon material alibis), and cultural, personal and interpersonal complexities (recognising the fact that pain is not solely understandable through biomedical instances, but from perspective, plural and distinctive frames that, in community with further theoretical efforts, can approach a wider interpretation of the process, attributing the agency of experiencing pain to the person as a whole in his or her interaction with a malleable medium)'.

---

In this sense, pain is studied through a patient's experiential focus but along a medical and clinical interest, organising a particular interfield space where a thematic niche comes to elaborate a modern new definitional claim on pain experiences across and away its theoretical birthplace of origin (monofield pain physiology in pathological claims), and moves on requiring epiphenomenal, hypercontextualised answers that point out, thus —as Morton (2012) and Helmreich (2016) would expose for other theoretical themes as 'climate', 'life', 'oceans' or 'sound'—, what has become a 'theoretical hyperobject' in current diagnostic pathology, an overflowing problem that necessitates of multiplicity for being addressed. The involvement of contextualised, perspective and pluralised epistemological standpoints in this research favours the critical study of clinical evaluation (in this case, neuropsychiatric diagnostics) as the practices assessing such hyperobject pain has come to be. The interest on pain complexity has promoted the proposal by this work of a refreshed mindset on pathological identification and nosographic theory making: 'epidiagnostics'. This is viable through the theoretical configuration of the notion the thesis introduces originally as 'epidiagnostic practices', framing plurally, multifactorially, and prognostically the clinical evaluation of complex instances:

*Def.* — 'Epidiagnostic practices are introduced to define diagnostic efforts fundamentally directed to determine collateral and correlational factors (multifactorial adaptive analysis) to better decide and characterise in agreement the pathological instantiations of a patient's clinical picture, and primarily aligned to finding the appropriate treatment interventions, informing about prevalence, prevention and prognosis of further comorbid possible scenarios.'

The value of epidiagnostics rests in its being immediately useful in a near future for fo-

cus, framing and modelling heterogeneous, complex, comorbid circumstances employing multidata solutions delivered through Artificial Intelligence Assisted Diagnosis for facing overflowing scenarios. This is suggested to be oriented by (1) an attitudinal shift towards prognostic detection, prevention and accurate intervention, and (2) multifactorial assessment of the plural dimensions of stressors affecting patients' health scenarios. Some other key points on the value of epidiagnostics are:

- . (3) Multilaterality in clinical claims characterising the diagnostic scenario of pain.
- . (4) The recognition that diagnoses are trust protocols, where personal, cultural, contextual vectors apply to understand the medical ascriptions pain introduces in a patient's health circumstance.
- . (5) Decentralisation of psychiatric pathology into interfield descriptive pathology (in a similar direction as lately presented by G Berrios).
- . (6) Introduction of epistemic niches, frames and perspectives for achieving a theoretical position from where epistemic analyses can be developed on such multilaterality.

These markers introduce an epistemological worry on how accurate assessment is able to be performed, along with several claims running procedural, ontological and deontological discussions in relation to how scientists understand patients' values, attitudes and beliefs, and how they project them in characterising an intimate and untransferable emotional experience (Cf. Goffman 1968; Haraway 1976; Dupré 1981; Thagard 1999; Schwenk 1999; Hacking 1986; 1995; 2002). This epistemic challenge comes parallel to modern increasing disagreement on the validity of systematic and categorial disease classifications, instead of wider person-centered

multi-dimensional and descriptive views, and the appropriateness of the current diagnostic models, their instruments for evaluation and their interpersonal practices of assessment for characterising pain experiences (Cf. Aragona 2009b; Aragona 2009c; Goldberg 2011; Hickey & Roberts 2011; Borsboom et al 2011; Anjum et al 2015). To study this landscape, the work focuses on contemporary social, contextualised epistemology. What was first programmed as a social epistemology towards general fields (Merton 1973; Goldman 1987; 1999; Fuller 1988), regenerated as a more detailed vision, marked by interdisciplinary research (Darden 2006), feminist studies and the anthropological, ethnographic inquiry on the era of biological technology (Haraway 1991; Shiva 1995; Keller 1995; 2003a; 2003b; 2005; Weed & Rooney 2010; van Fraassen 1976; 1980; 1989; 1994; 2002; Perdomo 2003; 2011; Harding 1991; 1993; Galison & Stump 1996; Galison 2004; Weinberg 1993; 2001). The thesis follows these attitudes in epistemic pluralism, perspectivism and naturalism (Cartwright 1983; 1999; Kitcher 1984; 1992; 1993; Giere 1985a,b; 1999; 2006a; 2006b; Longino 1990; 2001; 2006) adopting a plural, perspective and situated (contextualised) view, analysing the developments in 21st-century neuropsychiatry through the theoretical instruments provided by such frameworks: the ethnographic study of scientific practices and their contexts of theory making, sounding the limits mono-lateral vs. multi-lateral approaches supply to diagnosis.

This thesis wants to contribute to the field by proposing a multifactorial perspective that allows the creation of plural frameworks enabling interoperational research, dealing with the variegated interpretations of reported pain that particular disciplines handle. The work applies the concept of ‘epistemic frames’ as a tool for interpreting the contexts in which definitions and expectations of pain are resolved clinically; in addition, this effort would be the first application of the concept to clinical epistemology,

oriented to offer useful outcomes for neuropsychiatric interoperational needs (ie, needs present in relationships such as patient-physician, patient-instrument, etc.). In defining and describing how the theoretical proposals develop, it is hoped to make clinical and research communities aware of how important a wider understanding of pain and its assessment are for delivering appropriate decisions in treatment, and forecasting prognostic scenarios involving newer technological instruments that favour patients’s recovery.

. *Notation for Intra-textual References*

The thesis is divided in Four Quarters plus Bibliography:

- . **QI**, ‘*Presentation, Focus & Scope of this Work*’;
- . **QII**, ‘*Introducing Frames: The Value of Pluralism, Perspectivism & Contextualism for Clinical Epistemologies*’;
- . **QIII**, ‘*Niches for Framing Epidiagnostic Characterisations of Pain Experiences in Neuropsychiatry*’; and
- . **QIV**, ‘*Results, Conclusions & Future Lines*’.

Each quarter is composed by a number of different chapters, which are referred inside the text by the sign ‘§’ followed by the cardinal number of the chapter: QI, §1-3; QII, §1-2; QIII, §1-10; QIV, §1-2. Should a chapter require to redirect the reader to a previous or a further part inside the work, it will be indicated using the previous notation —it is to note that chapters in the present QI, due to their brief nature, are gathered into a self-contained block.





# QI, Chapter §2

## Research Hypothesis, Goals & General Results.

### *. Research Hypothesis*

The working hypothesis advances how, in applying the previously referred contemporary epistemologies running plural, perspective, situated (contextualised) standpoints to clinical requirements, the complex research and clinical scenario of pain assessment in neuropsychiatry can be exposed, and its scientific practices described (diagnostic, characterisation, instrumental assessment and therapeutical interpretational practices), along with the multi-nature developments and theoretical conflicts underlying the historical processes that the plural fields gathered since early electrophysiology to modern times.

The thesis introduces the concept of 'epistemic frames', scientific strategies of interpretation that would work as situated contexts (in relation to the works on 'epistemic frames' in learning areas, mainly as exposed by Schaffer 2004; 2006; 2007; 2009; Rhode & Schaffer 2004; Crowley & Jacobs 2002), and as patterns of practicing science in a determined fashion (in relation to Kitcher 1984; 1992), that define the expectations, justifications, beliefs and predispositions installed in the subjects conforming certain epistemic community of research (Longino 1990; 2001), from which experimental designs, results, guidances of understanding, and plausible attempts at explaining phenomena emerge. Expectations play a major role, for in the development of a plural interdisciplinary research programme the focus of study and the

practices involved may tend to shift amongst the original diverse disciplines: expectations would make clear that, for example, if assessment of pain is approached through an electrophysiological frame, reports, conclusions, interpretations of clinical problems and ending diagnostic values would be expected to resume, submit to and abide by the physiological terms, language and topic of research, beyond which a threshold proper to the identity of the discipline may not serve for giving answers or supplying explanatory claims. This suggestion makes the case for exposing how multiple epistemic frames, which may appoint to cooperate in attending a big-picture integration of diverse origin, can be handled to explore and describe the main focuses, problems and barriers diagnostic assessment of pain in neuropsychiatry faces.

These frames, schemas and enclosures of scientific interpretation show how the scientific modelling of pain is a multifaceted problem benefited from interdisciplinary research (Cf. outlook in Darden 2006), which, at the same time, suffers from the complex circumstance of having multiple focuses of attention (especially when incorporating to discussion the problems of dysfunctional reports in assessment of neuropsychiatric conditions, more over with pain-reinforcement pictures), different definitions and theoretical orientations in the process of unifying and identifying diagnostic, adaptive and epidemiological values of patients's bearing

a pain-related condition, which is meant to be sharable through various physicians and reshaped by different clinical data systems of medical information management.

Two major contributors encourage this research hypothesis as running for plural and perspective answers: (1) the multiplicity of information in nature and quantity from different fields applicable to overflowing themes (as pain is approached to be) in medical literature and theory making; and (2) the cumulative increase of pathological complexity in the definition, identification and attribution of clinical diagnostic factors applicable to specific patient scenarios, framing an inflationary nosography required to be handled and addressed in a non-reductionist contemporary fashion.

(1) *Multiplicity of Interfield Information:* Modern medicine is facing diverging specialities with different goals, focusing different problems, developing distinctive strategies and formulating their own theoretical expectations at resolving their epistemic scenarios. Given this overdimensioning of scientific knowledges, clinical assumption making is in fast derivation to technical and engineering fields, searching for the artificial identification of pain markers that may use multivariable computation and complex factors comparison intervening in the creation of models identifying specific pain experiences. This has led to the creation of non-concrete (non-standardised) or diffuse personalised models, should these depend on interpersonal specifications and environmental dispositions too, from family, friends, laboural ambients, etc. Said modelling strategies start with different initial perspectives, accepted by diverging communities of decision, and contextualised in plural cultural niches: it is the description, criticism, evaluation and rethinking of those frames and scientific, cultural, social, epistemic niches what comes at play when actualising valuable knowledge and validating

new conventions on pathological claims. An option is to negate those advancements and reinforce a non-inflationary pathology and a non-inflationary nosography.

However, as inflation occurs, new ways of shifting into a more political, democratic, socialised and contextualised fashion of intervening on patients can be achieved by means of decentralising information, using technology to involve through common agreement the entire stakeholders in the decision making process: patients, patients's environments, institutions, clinicians and further associations. Instead of neglecting the multiplicity-driven advancements of contemporary fields, modern dispositions are suggested to work as interfields, formulating a new plural and constructive trust protocol on valuing convention that may lead to better identifications of multiple spectrum characterisational claims on pathological architectures. By describing these researching traits, investigation will be able to take a picture of current definitional and underpinning epistemological problems on this transition, along plausible state-of-the-art solutions, and offer a framework for the study of developmental common strategies for thinking pain experiences in a contemporary way, assisted by an epistemic criticism on the basis of these pathological architectures, revaluing our trust on such and other conventions for opening theory making practices and proper diagnostic and nosological clinical practices to future lines of advancement.

(2) *Cumulative Increase of Pathological Complexity:* New socioeconomic resources have been aimed at pain units in hospitals and research faculties, intensive care units, and clinical intervention of acute and long time pain-bearing patients with psychiatric needs. Still, diagnostic theory in research proceedings and diagnostic practice in clinical proceedings do not happen to evolve and communicate at the same time and within the same scientific communi-

ties of decision. Research in genetic, biochemical, social, cultural and behavioural fields has developed in an increasing amount amongst the 21st-century medical realms, where also different forms of pathology have been amounted to technological imaging (especially for the nervous system, but also inter-systemically and meta-systemically in internal medicine, immunology, oncology and infectious diseases research applied to pain experiences). Accompanying psychiatric behavioural and interpersonal evaluation, biochemical models have introduced in modern times multi-systemic efforts in identifying tissular, cellular, molecular and proteinic changes that affect pathological developments. Nonetheless, it appears, as to theory making in contemporary physics, that microcosmic areas of research (for this case, biochemical medical assumptions) do not match with macrocosmic expectations (for this case, clinical psychiatry) on description and explanation: biological (biomedical) reductionism has become, as many criticisms address, a large inconvenient for explaining psychiatric pathologies; the case comes with an interesting irony for neuro-psychiatric requirements as these cannot neglect the materiality implied in the interfield within which clinicians are contextualised.

Physical pharmacology has been in the 21st Century the therapeutical selection preferred to face a nonetheless meta-biological problem that required further inspection on the topic of materiality, personhood and pathology, which has also exposed many interdisciplinary epistemic problems affecting how complex diseases are to ascribe, identify, assign prognostic factors, or claim over clinical attributions to specific patients. The cumulative effect of this complexity in nosographic decisions —culturally, socially, legally and politically actively mediated, however being approached by single perspectives, monofields (Cf. critique and theoretical navigation on ‘interfields’ in Darden 2006), and asymmetric strategies (strategies that do not

cope with the theoretical expectations declared for solving the exposed scales of complexity)—has proved to need be faced in an alternative fashion, dealing with multifactorial, heterogeneous, and contextualised data flows that could merge different perspectives into inter-field working, inter-frames and plural niches in collaboration.

This also presses up the use of new analogies and metaphors for visualising theories and theoretical contents, instead of fixed groups of analytical ideas, as palimpsests or kaleidoscopes. In the case of ‘theoretical palimpsests’ analogies for visualising ‘theory making in the making’, sheet after sheet of historical diachronic theory making get produced, where contents come to overlap, forcing research to ‘historise through’ instead of ‘historise upon’ (Cf. close examples in Helmreich 2016, 90-91: evaluation of ‘athwart theory’) a pile of theoretical contents that requires to swift the perspective in order to understand the entire picture. The case of ‘theoretical kaleidoscopes’ analogies invites to visualise theory making as a constantly reflective process, where contents are discussed, elaborated, multiplied, expanded, accumulated. Complexity, in any of those cases, appears to re-frame the worries and expectations on how epistemic subjects and communities use new informational flows.

Both (1) and (2) complex circumstances make the overall concept of assessing pain an epistemological challenge that faces scientific communities with an ‘overflowing topic’, using Helmreich’s (2016) terminology, a topic of study that overflows the particular disciplines that gave origin to the concept, and that is now braking the incipient frame from which it was brought up to contemporary clinical diagnostics. Diversity and multilateral approaches, managed through pluralism and perspectivism standpoints in the aforementioned epistemologies, are suggested to help in better explaining

what currently occurs with this information abundance as an integrational problem, where multifactorial analysis (in diagnostic and prognostic evaluation) is also proposed to mediate in supporting the creation of modern plausible solutions responding to such overflowing challenge in clinical epistemics.

The thesis suggests that such epistemic frames can be studied, through a proper bibliographical and comparative methodology observing topic literature, as provided by 4 specific thematic niches of scientific interest, which in a diagnostic practical continuum may be proposed as an interrelated whole underpinning a multifactorial and perspectival strategy for understanding and assessing neuropsychiatric patients's pain experiences. These niches, however not claiming to exhaust the conditions from which pain experiences are able to be framed (Cf. scope in QI, §3), are hoped to both, conclude a satisfactorily wide taste of how evaluation is framed, and to serve useful tools in delivering on examination and sounding plausible answers when possible to contemporary demands from medical epistemics and neuropsychiatric diagnostic practices. The four epistemic niches suggested for theming frames in neuropsychiatric characterisation of pain experiences are:

A — *Neurophysiological Characterisations* (analysing historical and comparative traits).

B — *Psychiatric-Epidemiological Characterisations* (analysing the overflowing effects between pain morbidities and mental morbidities).

C — *Clinical Characterisations* (analysing an ethnography of diagnostic practices entailing pain measurement strategies).

D — *Interpersonal Characterisations* (analysing the epistemic difficulties on creating pain self-beliefs and self-narratives, and studying pain transference through trust and empathy).

## . Goals

*Major Goal* — The main goal of the thesis is to portray such niches (composing the body of the work) and to show how the frames clustered within these work, cooperate or diverge, interfering with other principles observed through incompatible or seemingly conflicting frameworks, exposing the epistemic consequences and problematics of interdisciplinary research through a multilateral standpoint in application to pain assessment in neuropsychiatry. Frames, which are not to be presented as exhibiting clear-cut ideas (they are not models), will be delivered as contrasting arguments and advancements proper to contemporary scientific theory making in medical and clinical publications. Describing, analysing, criticising and interrelating the ways these interact is, thus, the objective of this major goal, exposed by an interest at clustering the niches in which those act.

*Subsequent Goals* — (2) A second and quite significant goal comes with integrating solutions from different frames, exposing their divergences and, as far as possible, informing about the plausible unfoldings and applications of plural framing. Another (3) goal attached to the previous one is to be able to conjugate in one work historical accounts on electrophysiological models of pain events, with psychiatric accounts of a reported pain experience intervened by, for instance, a conversation in therapy, or by measuring strategies in diagnostic recognitions, which require particular epistemological inspection. A fourth (4) goal is to extract useful and applicable information that could be of help in defining multilateral strategies for the classification of pain-kindred dysfunctions, their measurement, and the organisation of information gathering physiological, psychiatric, prognostic and interpersonal origins, which are put to be the main concerns to the neuropsychiatric assessment of pain. A final fifth (5) goal

is to place value on the concept of 'epidiagnostics' as suggested to serve to define the scientific practices installed in complex diagnostic assessment.

### . *General Results*

Results are listed based on the positive attainment of all of the previous goals. The following section serves as a summary of the full extended version in detail explanation of each part and notion in QIV, §1, which also informs about the specific remarks on the neurophilosophical contributions of the work. Future lines on further research considered opened by the present thesis, on epidiagnostics and its use in neuropsychiatric pathology and modern nosographers involving Artificial Intelligence, are provided in QIV, §2.

(1) The major goal of the thesis was suggested to portray the niches underpinning the epistemic conditions affecting diagnostics in the neuropsychiatric evaluation of pain experiences. This major goal has been positively attained along the body of the thesis, reasoning in QII, §1 and §2 the structure of the analysis proposed and, thus, the organisation of the Index, affirming 4 major niches (A, B, C and D: QIII, §1-10), gatherers of their proper thematisation dynamics, engaging situated factors contextualised for the generation of specific topical questions, answers, and styles of assessment on the value of the scientific contents delivered, debated, refuted or accepted (especially on clinical discussions upon pathological standards, methods of attribution of agency, and attributability of diseases to specific patients).

(2) Regarding the second goal informed, integration has been especially treated in delivering possible solutions or suggestive alternatives to evidenced and exposed problems, and can be observed especially in the treatment of neuroa-

tomical and inter-systemic dispositions with sociocultural and interpersonal exploration of pain experiences.

(3) Conjugation of neurophysiological and psychiatric contents has been put on the centre of analysis, applying a comparative and pragmatic approach for developing plausible beneficial interactions from neurofields and behavioural interpersonal fields, including therapy theory and clinical engineered evaluation (especially in the last two chapters including the value of integrated value data for health information systems and trust protocols in diagnostics from clinical diagnostics).

(4) Accounting on utility, it is hoped that the contents here developed could offer good assistance in application of analytical perspectives for advancing neurophysiological attributions in Niche A (Neurophysiological Characterisations), especially the contribution of the RIF (Reciprocal Inflammatory Fibrogenesis) Interpretation to this extent; for enhancing the diagnostic practice in recognition of the current overflowing hypercontextualisation of nosographies in Niche B (Psychiatric-Epidemiological Characterisations), especially with the contributions of epidiagnostics, and personalised assessment from modernised technology-involving measurement strategies in Niche C (Clinical Characterisations); and for helping to understand the pragmatic interpersonal problems evidenced in Niche D (Interpersonal Characterisations) through perspective theory applied in the style suggested by QIII, §9 and §10, with further implications in Artificial Intelligence Assisted Diagnostics, Big Data analysis (recalling the significance of broad resolution feeds; Cf. QIII, §8), and textual and qualitative analysis.

(5) Concluding the work, the final fifth goal on placing value on epidiagnostic practices is hoped to have shaped the notion, on the appli-

cation of epistemic framing as a form of understanding pathology and multiplicity of presentations in pathological scenarios of co- and multimorbidity.



# QI, Chapter §3

## Methodology & Scope of the Research: Using Comparative Bibliographical Processes.

### . *Methods*

The methodology selected for the present work follows a *Bibliographical-Comparative Methodological Framework* (Cf. reasons and aspects on the selection *infra*).

This focus is expressed by the keywords of the literature considered by the thesis research phase, that was consistently updated until present year (2019) in which the thesis is offered for publication and consideration. Primary source articles, books, monographs, theoretical and systematic reviews, historiographical remarks and state-of-the-art congress publications were reviewed, published or in press from 1990 to 2019 (with the exception of the historical notes on cultural epistemologies of experience and pain electrophysiology concerning QIII, §1 and §2, where specific dates were introduced in chronological need).

The present work retrieved mainly studies in English (in a minor form in Spanish, French, Italian, and Portuguese) until April 2019: further literature on the topic abroad the date or the language would exceed the scope of the data gathering process (Cf. more information on the scope of this thesis *infra*). Searches were conducted for current scientific medical and clinical publications, offering an actualised view of the lines of research ascribed by the project, through online databases configuring a comparative non-statistically based bibliographical body, presenting an interdisciplinary sense and responding to a specific thematic keyword in-

dex. This index was obtained by guidance of thematic subheads on pain of significant import for neuropsychiatry in the following databases: Europe PubMed Central, JATS, MEDLINE, NLM, PMC, PubMed Central (& PMID) and SciELO.

Terms for queries used the following English keywords: 'pain', 'pain experience', 'neuropsychiatry', 'psychiatry', 'neurology', 'pain comorbidity', 'pain diagnosis', 'pain evaluation', 'pain assessment', 'pain models', 'pain measurement', 'pain scales', 'interpersonal evaluation of pain', 'pain neurophysiology', 'pain epidemiology', 'pain reinforcement', 'empathetic evaluation', 'diagnostic technology', 'diagnostic assistance', 'intelligent medical search', 'pain self-beliefs', 'pain self-narratives', 'person-centered diagnosis', 'neuropsychiatric dysfunctions', 'pain dysfunctionality', 'pain comorbid dysfunctions', 'clinical assessment of dysfunctions', 'fibrogenesis', 'C fibre physiology', 'pain anatomy (contemporary advancements)', 'pain nosography', 'ICD10', 'DSM5', 'pain psychiatric disorders', 'pain psychopathology', 'chronic pain', 'acute pain', 'pain biological factors (aetiology)', 'pain psycho-social factors (aetiology)', 'pain psychiatric diagnostic criteria', 'pain association (for free-falling contextual keywords)', 'psychiatric distress', 'disability', 'pain executive', 'pain dysexecutive', 'transdiagnostics', 'integrative diagnosis', 'pain performance', 'prognosis', 'multifactorial diagnostics', 'multifactorial evaluation', 'pain autonomy', 'pain prevalence',

'pain Europe', 'pain America', 'pain Asia', 'pain Africa', 'pain Oceania', 'pain and reward', 'pain and emotion', 'pain and immunology', 'pain and central nervous system', 'pain and immune system', 'pain and inflammation', 'neurogenic inflammatory pain', 'nociception', 'nociceptors', 'alгоception', 'pain patient'. — For QIII, §6 specific literature was consulted on the required pathological areas composing neuropsychiatric comorbid studies.

Results obtained by bibliographical-comparative querying, after reading and analysis, developed into the aforementioned 4 niches (clustered into A, B, C and D), from where epistemic analysis on niches, frames and perspectives were commented in QII, §1 (especially) and §2 (as a summary), then associated with scientific positive literature in QIII, §1-10 —ie, the reading and writing procedure was initiated with both QII and QIII altogether.

. *On the Selection of a Bibliographical Comparative Methodological Framework*

The present research, as advised, consented and agreed by the thesis director, and as reported and accepted in the 'Research Plan' (both versions, first and advanced) through the PhD Commission of the University of Salamanca, works within the framework of a bibliographical-comparative methodology (hereon: BCM), properly designed and suitable to the topic of research, usual and recommended in dealing with overflowing interdisciplinary affairs, as the one sharpening the present thesis is taken to be. The reasons for selecting a BCM for literature research and readings, designing the comparative approach to the matters of study, generating the interpretations achieved by this analysis, applying them to describe and put to work the hypothesis (as informed in the previous section), and writing the thesis volume, has been on account of the nature of this investigation: extracting and commenting on the

epistemological aspects of neuropsychiatric evaluatory practices on pain-kindred events, with a practical, original and solvent aim. These include three major reasons: (1) Inherited from epistemological and ethnographic methodologies on describing the developments on natural sciences and biosciences, the BCMf guidance has been justified to reflect as major affairs the development of the different fields in a historical and comparative approach (Helmerich 2016; Williams 2012): the growth of the different problematics; the distinct solutions to those problem offered in a procedural account of their historical origin and variations; and the consequences brought to contemporary theory making from such previous historical accounts. These notions are to be the focus of attention of this dissertation, where BCM organisations, in contrast to experimental and state of the art methodologies, has been exposed of being of much use and scope coming to deal with heterogeneous interdisciplinary research (Cf. Darden 2006). (2) BCM observes those lines of effects, as it does worry about how the definitions of scientific interesting phenomena, the required and recreated language, with its pragmatic (word usage) analysis, the decisions on classifications of scientific blocs of knowledge, the acceptance and accommodation of new theory traits, and the political, economic agendas were, have been and are currently put to work in a social interactive network (Cf. Longino 2001; Kitcher 1993; Haraway 1976; 1991; Harding 1991). Being a contextualising methodology, the study of contextual topics using situated epistemologies for handling the topics of discussion comes to be more than a sheer justification, but a recommendable and almost desirable path to follow. (3) BCM benefits conclusions with delivering on an interpretation of a wide panorama that helps to explain and describe the conceptual difficulties in characterising contemporary issues from the inside of the topics adduced through the standpoint of each discipline reviewing the research phenomena.



Six 'guiding advices' were discussed during the first phases of research for defining the required BCMf, agreed guiding advises that concluded in recognising the significance of:

(1) *Historical Consistency*: The methodology will be flexible and deep enough as to allow the research to achieve the aims of the thesis at handling the roots of the concepts in a historical fashion: finding, describing and assessing the historical consistency of the main notions characterising the fields.

(2) *Comparison with Contemporary Focuses*: The methodology will allow the research to compare historical notions with contemporary ones, through literary discernment and evaluation of the current panorama of ideas.

(3) *The Value of Ethnography in Science*: The methodology will recognise the ways through which different physiological, clinical, psychiatric and therapeutical conceptions and their developments are contextualised, organised in specific niches of ecological social impact, forming centres of information and discussion in a global international network: the classification of topics and the organisation of descriptive interpretations would pay the right attention by assuming a multilateral and practical approach in such move.

(4) *Integrative Spirit & Plurality*: The methodology will support the aim of the present thesis at concluding with pluralised perspectives: however argumentative debate comes to be a central instrument, the procedure would always try to recognise the significance, as far as possible, of the conclusions delivered by the contemporary epistemologies this work is based upon (Cf. Longino, Kitcher, Haraway, Harding), as to make an application of those conclusions into clinical epistemology. Integration in a multilateral approach would be a general motive in the dissertation.

(5) *Applicability*: The methodology will support the aim of the present thesis at generating plausible solutions to different problema-

tics, as to pointing out suitable applicability of ideas and future lines of action once the required literature has been compared and analysed, and a general conclusive interpretation comes to build the form of the thesis. Applicability would point out with special attention to cognitive ergonomics [1], as applied to the fields of clinical ergonomics and Human-Computer Interaction (HCI) —on account of the logics and background affordable to clinical data and information systems, Artificial Intelligence Assisted Diagnosis and HCI-Assisted Nosography—, as informed by the International Ergonomics Association (IEA 2019) and the Interaction Design Foundation, Denmark (IDF 2019).

(6) *Keyword Cross-Research*: The methodology will allow the formation of the body of literature and further material by the usage of keywords, relevant to the core focus of the research, detected through cross-paper/journal/source querying. Keywords will also offer advise for defining the scope of the thesis, and framing the limitations of the research. More details on source 'exclusion principle' below.

A final remark on how the BCM concerns the procedure followed during writing the thesis, is how the framework for a bibliographical-comparative methodology grids the 'Index of the Thesis' by Quarters (QI-QIV), starting with a presentation of the general information of the thesis first (QI); introducing the background, spirit, significance and value of the conceptual hypothesis ('epistemic frames' through plural, situated, perspective epistemologies) as a first state of the art of the proposal (QII); the presentation, commentary and classification of the niches of the hypothesised epistemic frames (the body of the thesis) through extended systematised and evaluated states of the art of the particular topics of the interdisciplinary research literature, along their interpretations and the plausible resolutions of their problematics as observing the points 1 to 6 in the guiding advises of the BCM (QIII); and ending with a fi-

nal bloc of results and conclusions, applications and future lines of this research based upon the efforts undertaken during the PhD project (QIV).

—

[1] *Ergonomics* (or human factors) «is the scientific discipline concerned with the understanding of interactions among humans and other elements of a system, and the profession that applies theory, principles, data and methods to design in order to optimise human well-being and overall system performance. Practitioners of ergonomics and ergonomists contribute to the design and evaluation of tasks, jobs, products, environments and systems in order to make them compatible with the needs, abilities and limitations of people.» (IEA 2019).

#### . *Scope & Limitations of this Research*

Some of the fields (and by extension, thematic niches) that contribute to the clinical modelling of pain assessment in a prior medical sense may be understood out-of-context, not attuned with the scope of the thesis, because of the epistemic integrative nature of this work on neuropsychiatry as an interfield: for it, 3 criteria or eligibility aspects were defined at the beginning of the research for selection of differential niches by topic traits:

(a) — Theoretical traits constituting frames within a specific niche shall benefit of interfield strategies (not insisting into monofield descriptive or explanatory answers) when explaining and orienting the issues of observation through a neuropsychiatric standpoint.

(b) — Theoretical traits constituting frames within a specific niche shall be of import for clinical epidemiologic use (on the notion interpreted and introduced by this thesis), for assessment or therapeutical management of pain.

(c) — Theoretical traits constituting frames within a specific niche shall result in characterisational clinical propositions for identifying pain, or present a problem for so being achieved through current technological clinical information systems (clinical ergonomics).

This process excludes some theoretical frames for composing more niches approached by this work containing further traits away from those considered by the scope, however with specific exceptions: (1) proper monofield genetic studies (out-of-context for psychiatric reasons in experimental discontinuity) —exception: some traits from this issue are treated in Niche A, QIII, §1-4; (2) proper pharmacological models —exception: some traits from this issue are treated scattered through the text; (3) monofield political studies proper to health-care administration, public development policies, or societal-distributive studies —exception: some traits from this issue are treated in QII, §1; and (4) economical impact and burden of neuropsychiatric resources in multicultural niches or countries in development —exception: some traits from this issue are treated scattered through the text.



---

## **Quarter II**

### **Introducing Frames. The Value of Pluralism, Perspectivism, Contextualism for Clinical Epistemologies.**

§1 Situating Neuropsychiatric Assessment:

Developing Clinical Epistemic Niches, Frames, Perspectives (p 26)

§2 Structure of the Present Analysis:

Framing Epi-diagnostic Characterisations on Pain in Neuropsychiatry (p 62)

# QII, Chapter §1

## Situating Neuropsychiatric Assessment: Developing Clinical Epistemic Niches, Frames, Perspectives.

☛ 300 — 308

—

### Parts

. *Introduction*

#### I — Neuropsychiatric Action Situated

. *Convention. Decision. Power*

. *Deciding a Chain of Trust. The Gap Between Diachronic & Synchronic Convention*

. *Substantiating Neuropsychiatric Evaluation: Standards, Biosignatures & the Fingerprint Alibi*

. *Situating Trust through Instrumental Skepticism*

#### II — Developing Epistemic Niches, Frames, Perspectives

. *Framing Perspectives*

. *On Designing an Epistemic Frame in Neuropsychiatric Diagnostics*

. *Marking, Trimming, Shifting the Scientific Theme*

. *Determining the Study of Four Niches in this Thesis*

## *. Introduction*

There has been abundant scholarly work re-thinking scientific constructivism, along with the cultural roots and borderlines that scientific research programmes face in the contemporary application, experimentation and technologisation of their practice. The specific topics of classical critique and commentational literature have been re-oriented into a more contextualised work in the epistemology of scientific theory making, reconsidered as an epistemic practice of knowing, learning and deciding, triggering new theorisations contesting the responsibility and coercion of epistemic subjects inhabiting communities of debate, allowance and acceptance of epistemic beliefs.

In the process, different developments landed on modern social inquiry, academic activism, feminist epistemologies, gender and racial studies, historiographical research, ethnographical accounts on the practices of theory making, ecological studies on the effects of scientific decision making, and legal and normative studies on the consequences of standardisation of scientific practices abroad their cultural niches, along with their collateral impact on international, cross-cultural, globalised application.

These advancements were settled in the late 50's to the mid-90's of the 20th Century in a wide palette of styles and determinations within specific epistemological orientations on situationism, contextualism, pluralism, perspectivism, epistemological naturalism or standpoint epistemologies, thus developing into 21st-century integrations with cognitivism, empiricism, constructivism, instrumentalism or skepticism among other understandings of social epistemics. For the sake of integration, the label 'situated epistemologies' could introduce, however misrepresenting some of such variegated spirits, a nominal umbrella to refer to these proposals on account of what they presume to agree on, as a basis, taking an all-encompassing ap-

proach to a historiographic process of academic re-reading and re-writing, within which debate is still alive and generating new forms of anthropological description, cognitive and logical critique, assistance on explanation to modern scientific improvements on the relevance of disentangling specific taken-for-granted concepts grounding nowadays theory making, and building bridges with interfield scientific communities on the problems that modern practitioners face. These factors generally present in terms of political partiality on the making of scientific programmes of research, on the social acceptance and ethical evaluation of scientific and technological works, on the contextual paradigms of scientific assessment, decisions upon standards of observations, on language use in international, yet multicultural ambiances, on the boundaries of scientific methodologies, on the scopes of interpretational argumentation excerpted from experimentation (triggering new answers to instrumentalism and realisation through instruments in scientific observation), on the determination of the scientific agenda through financial stressors (distinctive economic distribution of resources to different fields), managerial stressors (highly qualified, specialised, interdisciplinary team requirements), and the scientific dissemination of contemporary re-comprehensions of classical traditional knowledge.

The interest of medical research on these proposals and what situated epistemologies have to offer, both for the medical humanities and to the positive clinical fields, lies in a contextually-styled theory making attitude, in producing coeval, intermingled, intertwined, underpinning epistemic content, constructive in spirit and favourable to depicting, outlining, sounding and perhaps may the case unfolds productively, helping to resolve the socially relevant problems (Fehr & Plaisance 2010) that contem-

porary interfield descriptive and explanatory strategies address, as it is the hope and scope of the present work. One of those interests resides in the methodological and mindset potential for situating practices, communities, subjects and themes of study in a contextualised and frameworking epistemological sensibility, that comes with a fundamental comparative mentality, disposed to plurality and perspectiveness, to explain differences in non-singular conclusions and to deontologise for the involvement of interdisciplinary interfield research, and for the revocability of mono-themed mono-field theory making.

This introductory chapter is thought to present the epistemological basis underpinning the academic intentions and scientific scope of the thesis, reasoning its development in QIII, §1-10. The text invites to introduce the notion of 'epistemic frames' as perspective tools for reflecting upon how diagnostic factors, determining pathological attributions in neuropsychiatric ambiances, recall on the conditions of possibility of specific contextual subjects for trusting and accepting on previous knowledge, as for their plausible action in generating new knowledge, installed in an 'epistemic niche' for decision through debate, acceptance, allowance and refutation, where multiple social, cultural, economic, political, semiotic, linguistic or utilitarian interferences appear, giving shape to clinical attributions in a pluralised fashion. Said niches would present the necessary conditions to generate the possibility of an 'epistemic question' (regarding the grounds of, and access to, specific knowledge agreed-upon by certain collection of subjects in a common style of debate, allowance and refutation), and the proper need for answers to precise uncertainties about a particular topic, where processes of thematisation appear (the inquiry on the 'scientific theme', answering to the question of what is scientifically knowable: "about-what' is, should or should not be, research theory making oriented towards?").

This requires the collaboration (interfield work) and theoretical effort (interest, trust or distrust upon knowledge, consistency and investment of resources) of several agents involved in theory making. In this sense, the present work proposes the identification of a number of theme-involving niches from where characterising the plural epistemic frames applied to neuropsychiatric diagnostic evaluation, under the recognition of 4 major niches that are studied to appear to generate influential thematic beginnings for enabling multiple possible frames, perspectives and practices of interpretation. These concepts are introduced as essential assets for a definition of the epidiagnostic characterisation of pain experiences in current neuropsychiatric assessment.

The text is divided in two parts. Part I reviews in 4 sections how neuropsychiatric evaluation applies situated diagnostic features in terms of decision, power and accountability, engaging determinant clinical actions in a chain of trust that enables for clinicians conventions to apply (be selected as trusted knowledge) or to be refuted (be selected as untrustworthy knowledge), guided by specific biophysiological and psychobehavioural standards, substantiations and biosignatures involving certain 'material alibis', instrumentalising, thus, classificatory justifications in a process that needs be theoretically confronted with skeptical approaches. Such dynamic is analysed in this first part to define neuropsychiatric diagnostic actions as situated epistemic practices. Part II, recalling on the previous analysis, introduces in the next 4 sections, the main ideas developed by the thesis, epistemic niches, frames and perspectives, outlining a design for understanding the major factors involved in framing knowledge (1, the underpinning medical research theory making; 2, their materialisation in clinical bodies of nosographic knowledge; and 3, the diagnostic practices of clinical evaluation, assessment and intervention), through the mediation of three

main epistemic operations (of ‘marking’ the interest and goals of the framework; of ‘trimming’ the horizon and scope of its interpretations; and of ‘shifting’ the frame towards different areas on the landscape of research motives and expectations). The suggestion concludes with those factors and operations being applied to framing the scientific themes proper to the observation, interpretation, and styles of decision making installed in particular fields and integrative interfields, emerging from the contextual organisation of four main epistemic niches, treated as composing the historiographic and bibliographical polyhedron underpinning neuropsychiatric evaluation of pain experiences for the study of this thesis: A ‘Neurophysiological characterisations’, B ‘Psychiatric-Epidemiological characterisations’, C ‘Clinical Practice characterisations’, and D ‘Interpersonal characterisations’ themed niches. It is the idea of this work that, through shifting crosswards perspectives among these niches, integrating evaluation among the multiple and plural frames theorising on the themes originated from the social claims and demands of definition and explanation, the interpretation of scientific accounts, working as layers composing a wide palimpsest, could advance in answering the epistemological questions that 21st-century neuropsychiatrists and collateral actors to the fields address.

### I — *Neuropsychiatric Action Situated*

Contextual, cultural, social studies, involving contemporary epistemological readings on situationism, pluralism and perspectivism, introduce a suitable analytical tool to explore the unfolding of scientific programmes, a working means to more clearly observe, detect and expose the anthropological relationships established among the multiple agents that take action at current international scenarios, rewritten by the historiographical movements that everyday theory making resolves to character-

ise. To determine neuropsychiatric intervention from evaluation to prognosis, it appears a prior requirement to identify the contexts in which such actions are situated within: to understand the clinical neuropsychiatric action as a situated action is, thus, to understand that the scope of the relevance of scientific advancements —especially in nosology (as a continuous deliberation on the relationships and organisation of diseases systematic categorisation) and nosography (the textual applicable system of diseases guiding diagnostic efforts)—, develops in a contextualised, socially rooted, geographical, political, cultural, historical and ethnographically observable custom, a course of actions that is performed by communities of practice (Wenger 1999; Kitcher 1993), in epistemic communities that involve epistemic subjects of belief (Code 1983; Longino 1990; 2001; Hankinson Nelson 1993), plural and different (Cartwright 1993; Tuhiwai Smith 2012; Cruikshank 2005; Tuana 2001; Rolin 2011; Harding 1998; 2008), that work by framing, re-framing, debating, refuting, accepting, accommodating, and thus, situating their epistemic beliefs in specific practices of decision, convention, and power.

Part I reviews in four sections the significance of today’s epistemological characterisations in understanding how clinical practices, actions, models, paradigms of theory making and criteria of diagnosability develop, generate conventions, instrumentalise power (in its many senses: responsibility, authority, competence, influence, control), and debates the material roots that expose and bring about the fingerprints of diseases in the embodied organic agents of neuropsychiatric theory making, flowing in the multiple directions that configure the drift of the clinical decision making process.

#### . *Convention. Decision. Power*

Epistemological critique along with the academic turn to social demands contributing

scientific interests, acknowledging the scholarly glide to constructive activism since American Review (eg, Minnesota Pluralism) especially by the 60's-80's, have allowed to form a kind of research determination that, at least intentionally, motivates theory makers to try to avoid reductionist views on scientific agendas and observational, experimental, evaluative paradigms. Such determination favoured the sociological inquiry on medical theory making and its effects in the development of contemporary clinical practices, facilitating epistemological studies, as well as to positive clinical, medical and meta-medical literature, to exercise their conclusions on their matters far afield broad naivety on today's panorama (Foster & Funke 2018; Ellis 2017; Bleier 1984; Rosenberg 1991; Reger 2005; Fedigan & Fedigan 1989; Rosen 1968; Edelman 2003; Goldman 1987; 1989; 1999; Mitchell 2003; Bloor 1976; Longino 2006; Keller 1995; 2003a; Grob 1991; Kirk & Kutchins 1992; Kitcher 2003; Bleakley 2015): turning the focus of attention to neuropsychiatry, its historiographical reconstruction, its anthropological entity, its ethnographic role, envision all a clear dominance of cultural values that, until to present days, recognise the pivotal character of beliefs, and political, social, personal, interpersonal dispositions to believe, as epistemic factors that situate the identity of neuropsychiatrists, that revalue the social role of interfield scientific communities in their making of vital decisions resolving, as democratic institutions, agendas and demands from the social pulse and life that inhabit a global and simultaneously local geography of interests.

These factors also contextualise the needs of their medical interfield research programmes, actualise up-to-date clinical knowledge, and favour a certain form of advancement (Cf. the specific sense and boundaries of the notion 'scientific advancement' in Kitcher 1993; 2003; Cf. too Latour 2011; Cromby 2007; Niilinuoto 1984). These factors infuse with determinant

keys from the world of the patients and their families, friends, social collaborators, labour environment, etc. and, beyond, also from the world of physicians, nurses, therapists, keepers, the healthcare institutions as a whole. Taking into account the variety of intermingled vital and prognostic implications that diagnostic practices introduce to both those worlds, the manner such factors affect the medical understanding of pathologies (recalling diseases, conditions, syndromes, symptomatic clusters, morbid scenarios, etc.) in contemporary neuropsychiatry calls for deep and sound study, for every neuropsychiatric ascription comes with an ethical, cultural, social, familiar, legal, political implication: the identification of individuals with a 'from-now-on characterised form of being'. In particular for neuropsychiatry, the ethnographic, anthropological meaning of diagnosis is parcelled in two, a joining chain of two essential links: (1) the labelling of the person through his or her attributed pathological scenario, along with the ethical implications of undertaking by its practice a de facto intervention; and (2) the bio-neurological inference that invites to scientifically inform to every stakeholder, as an actor involved in any of those worlds, that there is something within the environment of the patient and him or herself that shows up dysfunctional, dysexecutive, thus away from a bio-physiological standard (Cf. some clear pieces of literature in Rosenberg 1989; Huertas 2001; 2003; 2011; 2012; Hacking 1986; 1994; 1995; 1998; 2000; 2002; Goffman 1968; 2008; Keller 1995; 2003a; Rosen 1968; Jordanova 1995; Friedman 1998; Fuller 1988; Garrabé 1996; Beneduce 2013; Goldstein 2001; 2005; Barnes 1974; Rohde & Shaffer 2004; Minard 2013; Colina 2008 in Álvarez 2008).

Both links, (1) and (2), inevitably shed meta-diagnostic effects into produced diagnoses. The first link (1) has social, cultural, interventional labelling actors with an immense normative, legal impact: it can be the point of depar-



ture for the patient to face the correct treatment and intervention (or either be over-treated, under-treated, or with no treatment at all), to face divorce, loss of employment, acceptance or dismissal from further school educational paths, children custody, medical executiveness or dysexecutiveness for driving, bear and be able or not to use weaponry of any kind (maybe required for his or her work), or be authorised as a decision maker for further life interests (Goffman 1968; 2008; Rosenberg 2002; Hacking 1986; 1998; 2000). The second link (2) promotes a practice of decision, of characterisation, of convention, that tracks an epistemic worry on the very medical field, because the common agreement on the claim that the main value of diagnosis must come from biological, organic, physiological inspection, is an epistemic exclusion factor (a ‘material alibi’; Cf. Berrios & Marková 2002; Berrios 1994), which reveals itself in an interfield like neuropsychiatry both instrumentally necessary —certain neurological, anatomophysiological, material criteria cannot be set apart from descriptive nor explanatory neuropsychiatric strategies (moreover, these traits in diagnostic intervention can be critically indispensable for undertaking further surgical practices)— and epistemologically, anthropologically, historically highly refutable too —thus operatively minimalist, reductionist, over-attributive, fallacious (Cf. QIII, §3, §4)—.

The worry is not just on the political debate running after the democratic answer to ‘who is to define the standard’ (Cf. the analogy with Harding 1991; 1998; Cf. too Kitcher 2003) against which diagnostics work through via a nosology in research, a nosography in application, an aetiology in symptomatic connection, etc. (Cf. Faber 1923; Christakis 1997; Rosenberg 2002), but also on the very circumstantial, contemporary, internationalised, globalised conditions favouring the growth of minimalist material explanatory strategies, practices of theory making that settle complex puzzles with

perilous utilitarian infrastructure (Machamer & Sytsma 2002), over-attributing certain overall agency to matters of study within low-scales of complexity, that can only be applied, should reductionist approaches be avoided (Cf. QIII, §3; Cf. Chruchland 2002), to overall high-scales of complexity framing contextually the study on the person and environment pathologically attributed as biophysiological dysexecutive — Cf. the hazardous implications of instrumentalising ‘biosignatures’ through a ‘fingerprint alibi’ with the example of 19th-century evaluation of drapetomania in section 3-4 of Part I, *infra*—. These factors may allow research programmes, theory makers and practitioners to sound the evaluatory process not as the main result of an institutionalised suit of debate and knowledges, but also as an intimate, private, personal and deontological process of clinical decision, epistemic decision (Cf. Code 1983; 1987), that demands us actors in thinking why knowledge is presented as it is, where, since when, in search of what purpose then decided, thus, preferred, acknowledged as valid apertures for allowing therapeutic intervention, for engaging pharmacological treatments, for targeting interests of research (relevance of goals, agendas; Cf. Haraway’s 2000; 2016 commentaries through situationism).

In identifying clinical evaluation (diagnostic intervention) as a practice that helps in justifying or rebuking the role of different forms of research (underpinning theory making) and different forms of clinical knowledge (of systematic, programmatic, theoretical clinical characterisations of pathologies and pathological traits ascribable to patients), specific constructive strategies have oriented definitions of new nosographic accounts, systematic printed and broadcasted descriptions and relations of diseases. The nosographic effort is involved within the very cultural, economic, political and legal truss of societal understanding, of healthcare development and personal regress, of achieve-

ment for institutionalisation of ideas, and alteration of the status quo that establishes and overturns medical options from particular historical periods and geographical contexts (Cf. modern de-pathologisation of homosexuality, transgenderism, transsexuality, intersexuality or transvestism as mental disorders: Alegria 2011; Beneduce 2013; Bancroft 2008; Faber 1923; Bayer 1981; Minard 2013). Conventions expose clinical evaluation, thus, to conventionalism (Cf. reading on convention in psychiatry in Huertas 2012, Chs. 3-4): debate, confrontation, theoretical violence and, in stretching an analogy with economic traits within theory making, to market. In this sense, the ground for the controversial acquisition of standards of observation and frames of reference that get accepted, tergiversated, occulted, manipulated, revarnished, and accommodated.

The social implication cannot be settled away from sciences. Sciences are not the passive depositary of a social decision that ends to affect a privately considered external and less opinionated scientific community or another: the debate is within the boundaries of the scientific analysis, it is proper to the imports and exports of the cultural background that furrow the medical climate in which such evaluation is delivered on by individual neuropsychiatric practitioners. There appears to be no separation in the deontological accountability appointed by the cultural actors and mediators that decide what is to be diagnosable, and so from the cultural actors and mediators that decide either to apply or not to apply on a specific array of diagnostic criteria. The division seems to be in the suitability (socially demanded relevance) of the debate, where the cultural asymmetries between physicians and patients, but as well among health providers themselves at many levels (gender, status, age, racial or xenophobic stressors, experience, formation, management of bureaucracy, rivalry, embezzlement, fraud, economic tensions or lack of financial stability)

may also be a critical factor for ending up producing authoritative fallacies and thus, affecting collaterally such vital debate in an anthropological perspective, and with a critical-historical standpoint (Cf. epistemic commentaries upon these affairs in Geller & Stockett 2006; MacCormack & Strathern 1980; Reger 2005; Solomon 2001; Cartwright 1983; Latour 1987; Fedigan & Fedigan 1989).

Diagnoses still constitute a ritual form of intervention, as Rosenberg (2002) exposes, a conventional tug of war that shapes and reshapes the multiple forms of understanding the interactions of these actors in a land set for such debate (Longino 2001; 2006; Harding 1991; 1993; Kitchger 1992; 2003; 2004; Haraway 1991; Cartwright 1999). Without a context set for debate scientific methodologies, decisions, conventions, refutations and theory change are doomed to grow in regress, self-perpetuating monofield solutions, reproducing expired, lapsed knowledge (Cf. critique to epistemic immobilism in Darden 2006; Darden & Maull 1977, favouring 'interfields'; Cf. too Harding & Hintikka 2003; Harding 2008 in Jaggar 2008 on methodologies; Weinberg 2001). From a comparative effort using present-to-present historiography, any scientific materials excerpted from the conclusive naivety of having no context for debating (against the progressive democratisation of scientific theory making) would most easily appear cross-culturally invalidated, renewable, exposed to international ethical confrontation (Cf. inquiry in Friedman 1998; Longino 1993; Rosen 1968). This form of 'debating continuity' contextualises knowledge across the different scientific communities, and allows integrative movement (Rolin 2011; Hankinson Nelson 1993; Galison & Stump 1996), originated from social demands, based on how debaters defend and allow to defend others's refutations of previous matters: this 'epistemic allowance' names the agreement on the validity of the knowledge exhibited as properly scientific through debate

and, thus, accepted, validated, applicable, ethically appropriate. In a simpler form: convention, decision and contrast by debate are practices based on trust.

*. Deciding a Chain of Trust.  
The Gap Between Diachronic  
& Synchronic Convention*

Trust takes form through conventions from the private truster to the generally trusted. It is the ecological implication that this trust is empowered by the situated decisions undertaken by the trustee: the neuropsychiatric actor that engages and personifies the culturally given relationships of power (of agreeing or refuting, of characterising, evaluating, attributing, of deciding, sorting and tagging) and accountability (of responsibility, ability to account for and answer to how his or her trust upon certain specific convention was put on value, and why) —Cf. more inspection on ‘epistemic responsibility’ in Code (1987). As Rosenberg (2002) reflects, evaluation legitimises through diagnosis the central definition of nosographic entities, clinical classification theory making, and their managerial processes (intervention, treatment, healing follow-up, healthcare systems):

«It [diagnosis] constitutes an indispensable point of articulation between the general and the particular, between agreed-upon knowledge and its application. It is a ritual that has always linked doctor and patient [...] and, in doing so, has legitimated physicians’s and the medical system’s authority [Cf. ‘pouvoir psychiatrique’ (Foucault 2003)] while facilitating particular clinical decisions and providing culturally agreed-upon meanings for individual experience [agreement through conventionalism].» (Rosenberg 2002, 240).

Epistemic conventionalism (in practices of evaluation, assessment and judgement) weighs decision making processes and practices contextualised in multiple scales —spaces (cultural

areas, global geography), times (across different historical periods and present), languages (by the use of utilitarian, instrumental, simplified categories among intercultural professionals in international scientific communication)—. Effects can manifest in diagnostic evaluation along two specific time-tied coordinates: a historiographically medically oriented, developmental, long-range ‘diachronic conventionalism’ (deciding systemic classifications, nosological effort, nosographical guides), and a clinically oriented, framed in a particular stage, short-range ‘synchronic conventionalism’ (ad hoc decision making, application, implementation, diagnosis, intervention, case behaving). Either form of recording convention moves forward an interactive way of trust, a ritual maintenance of trust among at least three actors: the trustee (diagnoser), the trusted content (clinical knowledge, guides, tests, protocols; not forgetting the patient’s and his or her environment’s involvement in delivering valuable data), and the institutionalisation of the chain of trust underpinning convention (trusting as a form of power, interdependencies, consolidation, facilitation of beliefs).

The signature of epistemic conventionalism in diagnoses evidences how beliefs upon its practice warrant the trusting cycle, legitimising the clinical intervention, reproducing the diachronically valid into the synchronically necessary, and by doing so, many times over-attributing relevance to systemically organised conventions in their narrow application to the clinical requirements. This constitutes an ‘epistemic situational gap’ that needs be preemptively reconsidered synchronically at each time convention recalls ad hoc application, under risk of de-contextualisation, of de-situation, de-orientation. This way, cumulative synchronic reflection, in plural and multiple ways can become a factor of theory change, reframing the affairs studied, and defending present requirements and social demands in debate on account

of previous refutable standards. The chain of power turns a newly formed, maybe more democratically situated, chain of trust.

Diagnostic recognition, however, faces conventionalism with the risks of unitary strategies of description and explanation, strategies that singularise particulars in the logical architecture engaged for identifying classes of causal relationships, correlations, natural conditions, and so forth. Unitary strategies participate of a strong form of epistemic institutionalisation, or, should the case be observed from an anti-reductionist standpoint, they are a collateral risky deformation from an institutionalised diachronic conventionalism applied to a given present case (the clinical scenario) in behalf of a not-yet-completed synchronic conventionalism (trust in preparation). The gap is then filled with previous interpretations, superseding diagnostic evaluation with recognition: the French expression ‘faire passer le forcément inconnu par connaissances déjà enregitrées’ alludes right to the topic.

This ‘faire passer ceci par cela’ is an attitude of re-attunement, sometimes unavoidable (the clinical necessity must be addressed some way or another), that re-calibrates (recalling otherwise the sense of ‘diagnostic calibration’ in Berrios on Huertas 2012, 136; Cf. too Bulbena Vilarrosa, Berrios & Fernández de Larrinoa Palacios 2003) the diagnostic appropriateness (the ad hoc synchronic trait) in a constrainedly contextual manner: the re-calibration of the gathered symptomatology into a nosographic account through clustering, contrasting, grouping, attaching and remembering relationships depends upon individuals at specific contexts. The trust protocol resumes anew decision into power through conventions.

Diagnostic decision then becomes somehow a sort of eschatology (f. Greek, *eskhatós*: ‘the furthest, remote, last’), a practice interested in the teleology of organisations, in developing the ultimate form of disease, the last materialisation of an advancement. Steven Weinberg (1993)

has considered these unitary strategies as cultural and personal manifestations of somewhat epistemic ingenuity, as ‘dreams of a final theory’, rephrasing the title of his work, as illusions that theoretical ascriptions require total and closed (categorical closure) of theoretical contents in a senseless competition of models —Cf. Peter Galison’s (2004) contribution to pluralism in favour of a ‘specific theory’ making, fading away those dreams of ultimate theories; or Mitchell’s (2004) notion of ‘medium theory’; Cf. Weed & Rooney 2010 on the question of theory’.

This diagnostic eschatology applies from the very basic assumption that diagnoses are underlined by casting techniques. Example of this is the existence of the classically understanding on ‘differential diagnosis’: a decision making practice that involves a protocol of epistemic evaluation on the basis of selecting a singularised classificatory option upon the pathological scenario presented by a patient debuting with scaffolded, multifarious symptomatology, thus, not adapting narrowly to immediate nosological identifications of a clear nosographical ascription (eg, general criteria for a precise neurotype), an ascription that will gather the labelling required (a ‘polythetic labelling’, Cf. Aragona 2009abc) for differing among the probable simultaneous possibilities of diseases —Cf. a deeper recension on the problems of antithetic-polythetic diagnostic ascriptions in QIII, §5, on account of multimorbidity and comorbidity classifications—.

As Rosenberg (2002) inquires:

«Although [category ‘differential diagnostics’] has been used earlier, it is often associated with the didactic efforts of Richard Cabot in the early 20th Century. The adjective ‘differential’ assumes differentiation among discrete alternatives, and thus it legitimates —and prospectively creates— disease entities as social realities, whatever the evidentiary basis for their existence. “By the differential method,” Philadelphia teacher John H. Musser wrote unself-consciously in 1894, “the diagnosis of one of a few possible diseases must be made.”» (Rosenberg 2002, 247).

This 19th-20th fin de siècle answer (eg, Cf. Cullen 1800) to what is to be decided by diagnostic processes results to adapt well to its contextual requirements, limitations and conditions for practicing medicine through via a process of singularisation, a mono-strategy of explanation, generally induced by the fact that given one single pathological account attributed to a patient, intervention and further pharmacological and psychotherapeutical developments could be engaged with more precision. Contemporary diagnostic theory making and clinical theory research programmes would require in less than 15-20 years a broader number of interventions for indicating the same problem, however in a circumstance where the scale of complexity of therapeutics, most of which are currently experimental, also triggers a rising complexity in the number of, and relationships among, sufferable clinical entities: of nosographical accounts on the clinical scenario of a patient —infectious diseases and the current accretional advancement in classification of pathogens makes a fruitful case for this problem to be taken into account—. This also scales up the complexity of the decision making protocols: which specific control-positologically supervised nanopharmaceutics or genetically traceable bi-therapeutical interventions will be more richly applicable, from the pharmacological immensity at hand, building an overall therapeutical assortment directed to all the nosographical problems evidenced by a case, and in so doing finding a combination that is better affordable to the patient, taking into account preventive, multifactorial and prognostic values.

Complex theoretical interfield studies are to be required in answering 21st-century demands of macro-symptomatic clustering (mereological computerised randomisation and recognition of symptomatic events), meta-comparison of pathological traits (via Big Data multi-trace analysis), oriented through multifactorial and prognostic values adapted to the private sce-

nario of probabilities of the patient which, in the majority of cases, would require actualising inter-systemic classificational strategies (interfield diagnostic efforts proper to internal medicine) and meta-systemic classificational strategies (cognitive, experiential, affective, interpersonal executiveness: testing the patient's addressivity involving analysing the process of building expectations upon a determined resolution in decision making scenarios). Intervention and treatment do not just depend today upon personal memory, mono-teams or critical familiar care. Far from being simple, the pathological drift to accretive immensity in number of pathologies, origin, symptoms, identifiable markers and tests, makes immediate future technology (Artificial Intelligence Assisted Diagnosis, blockchain systems for healthcare data comparison, thin-and-thick Big Data multifactorial analysis, etc.) to be required for identifying clear diagnostic characterisations through highly complex and multivariate evaluation — in addition, faster, sharper in their probabilistic engines, decentralised, internationalised, contextualised to the realities of the geographical situations, and more secure.

The conventional application of diachronic classifications into direct cases without facing their classificatory traits and factors through synchronic evaluation may end up in an anachronism. 21st-century neuropsychiatry is required to refresh its nosographical attributability in pursuit of a clearer understanding of historical clinical knowledge, and for so, by employing 21st-century technology overcoming reductionist outmoded intervention-observation techniques (Cf. QIII, §7, §8). Modernised assessment technology, applied to clinical evaluation, in playing such a significant role in understanding cumulative synchronic frames of decision, has for this same reason the power of becoming a paramount factor of theory change, reorganising the nosographical affairs from bottom to top, thus, reframing diachronical

conventionalism and debating in the suitable spaces set for such debate (generally the underpinning medical research theory making), the degree in which certain previous standards do not anymore contribute with deep justification to enhancing decision making processes, and therefore, show refutable traits.

Certain uses of medical data and applications of comparative strategies through new technology can help in enriching anamnesis by performing more comprehensible and adaptive examinations of the patient's experiences and pathological scenario, allowing and promoting the consecution of a more descriptive neuropsychopathology, reasoning with incoming valuable and evaluated data new paradigms for generating a globalised decentralised distribution and contrast of contextual nosographies, and by readapting them reconsidering nosological ascriptions with new multiple-focus comparison techniques that, in their pursuit of a better understanding of the patient's and his or her environment's narratives, affectivity, executiveness and pragmatic accounts, will more probably lead to better treatment than categorical over-labelling underestimating descriptive factors in diagnostic assessment —Cf. Berrios's (1984; 1986) works and further authors's literature in favour of a more interpersonal descriptive pathological theory making.

The decision making process takes ecological strength: its maker is, using the analogy of the market, buying conventional justification for a required evaluation from an epistemically relevant body of knowledge that comes with a political declaration, an opinion, an experimental trend, an observational limitation, a private and intimate assurance of the fact that what is being applied by the decider, recalls confidence and trust on what the communities which he or she is involved in achieves to accept. The analogy to economic relevance makes explicit the implicit fact that decision makers are not in a theory making vacuum: the expectation that

the theory approaches well and ostensibly valid through the diagnostic practice comes with the trust on the accepted idea, argument, model, standard, marker, descriptive and explanatory strategies that, should they be imported into his or her practice, would make the difference from malpractice, resolving as well a clear 'import tariff' —the price is individual allowance, agreement. Trust benefits healthcare standards, institutionalisation of ideas and reference for methodological accounts. Agreement empowers legal approval for practices: by agreeing on them, decision makers infuse the power in a relation of continuity and discontinuity of observations which, at the scope of their watch, start critical processes of intervention (refreshment of diachronically oriented nosographies from synchronically oriented evaluation). Clinical evaluation exhibits the role of the evaluative, thus, of the values applied on what is considered a culturally valid, ostensive definition of pathology, of pathological trait, of symptomatology and of the need of treatment —Part II will argue how the technical concepts of 'epistemic niches', 'epistemic frames', 'epistemic perspectives' serve to explain how such frames direct clinical decision making panoramas, and explore the different fashions of embracing standards, producing debates and shifting cultural values.

Psychiatric evaluation informs about a practice that requires to define itself as a form of power, following Foucault's 1973-74 historiographical inspection on the 'pouvoir psychiatrique' (Foucault 2003). This power is both a disperse network of production, of phases and bureaucracy, and a form of identification, exclusion, classification, detachment: diagnostic fitting, tagging and blurring. The sense of the role of such power is however of assistance, of therapeutical transformation; moreover: of political, social, cultural assistance, for such network provides also with responsibility, accountability, action (Cf. Huertas 2012, 31; Longino 2001; Harding 1991; Kitcher 2004).

. *Substantiating Neuropsychiatric Evaluation: Standards, Biosignatures & the Fingerprint Alibi*

Germán Berrios (1984; 1994; 1996; but especially in 1995) exposes with determination the liminal sense by which materiality and reductionism reverse the role of psychiatric inspection into a neurobiological inspection of dysfunctions. Berrios (1994) as many times commented, uses the analogy of Chinese boxes, finding inside one reduction, a next reduction beyond a further reduction without reflecting about how many traits and attributions have been de-contextualised and lost in changing among the different scales of observation. This process enters the experimental and clinical research programmes on biomedicine by finding, through explanatory reductionism, justification for explaining overall macro-phenomena (instrumental explanation) via excerpting descriptions of organic micro-properties and interactions (instrumental justification from descriptive strategies) —it is noteworthy the turn on words from historical to epistemological language (especially the use of macro- and microcosmic synecdoches) Cf. Chruchland (2002) and Machamer & Sytsma (2002); this topic will be reviewed in depth in QIII, §2, from an anthropological, ethnographic standpoint, and by QIII, §3, from an epistemological, clinical philosophical perspective.

Critical to this question comes the debate about the statistical attribution of validity factors for building classificatory schemata (Cf. Bulbena Vilarrasa, Berrios & Fernández de Larrinoa Palacios 2003): the suggestion that wide demographic contrast through medical trials exposed to standardised guides of experimentation informs better the clinical characterisations of symptoms gathered by specific entities (a pathographic characterisation of symptoms) has been highly criticised (Hekman 1979; Hawkins 2004; Taleb 2007; Bland 2009; Raman

2011; Walsh & Gillet 2011). As Hickey, Hickey & Noriega (2012, 76) expose, the primary utility of this kind of practice, should its application befall unavoidable for nosographic efforts, shall be restricted to providing ‘background data’ for statewide institutions, as a guiding marker on diseases prevalence in large scales, however peripheral to the clinical practice in individual case situations. In many senses, this attribution of validity of statistical demographic values for building a further individual attribution of clinical diagnostic account engages a reductionist strategy. As Rosenberg (2002) suggests, this is a practice proper to modernity, proper at least contrasting the historiographical idioms entitling what is in the contemporary contexts of diagnostic recognition and clinical evaluation able to be described interdisciplinarily, internationally, multiculturally, thus, plurally (Cf. plural interactions in Cartwright 1999; plural justificatory strategies in McCauley 2009; McCauley & Bechtel 2001; Giere 2006b).

The price for accepting such a worldwide nosographical realisation into the clinical evaluation extends a paradox: the more worldwide, thus opener to constructive exploration, the more reductionist, thus opener to instrumental and utilitarian metaphoric divagation in search of simplicity. In its space of validity, the paradox presents how decision makers would ultimately engage an «unavoidable use of reductionist means to achieve cultural and behavioral ends —necessarily holistic, multidimensional, and contingent— [...]: [coming to] the medicalization of deviance.» (Rosenberg 2002, 252).

Interests are about medicalising deviance (Aragona 2009a; Christakis 1997; Grob 1991; Kirk & Kutchins 1992), about normativising the anomaly through the medically plausible pathological instruments of evaluation, and this is of much epistemic interest. However, beforehand, ‘deviance-entities’ need be decided, characterised, identified with a medical theoretical suggestion, an extension of a nosological question

to some systematisation that would further on allow the deviance to be medicalised, and this pivotal decision is bound to contextual stressors, mediated by diachronic conventionalism supporting the standard against which anomaly is contrasted, and this way evaluated as medically relevant. The expression ‘to medicalise’ requires analysis to examine the practice broadly: it being neutrally meaning that precise deviance against a standard can be ‘placed within the medical observation, thus involved into explanatory, descriptive, clinical fields’; however contextually, it being also meaning ‘intervening therapeutically, thus making space for situated interests, pharmacological, political, economic, religious, cultural factors that interact in communicating and agreeing on sufferable and un-sufferable conditions, bearable and un-bearable diagnostics’. From debate emerges a ‘deviance-standard polarity’.

To raise an example: given the following question, ‘are hysterical onslaughts a kind of psychiatric presentation of a feminine-gendered deviance statistically assumed by current women population, thus attributable diagnostically and open to pharmacotherapy, psychotherapy, specific legal accountability and normative contest?’ —recalling the 18th-19th-century asylum, imprisonment, contention and tied restraint to the hospital bed (Edelman 2003; Goffman 2008; Goldstein 2001; 2005; Beneduce 2013; Huer-tas 2012; Cf. modern revisions on contention in Italy: Cipriano 2013; Dodaro 2011; Catan-esi & Troccoli 2005; Novello 2013)—, its nosological answer will always be pivotal to the cultural, social, political, economic, religious, time-tied, thus, contextual recognition of a polarity deviance-standard that needs to be decided, which, applied intrinsically from the very nosological debate, may in turn institutionalise feminine-gendered hysteria as a plausible nosographical option for attribution within the context that implied the epistemic communities that performed the decision routine. The

nosological decision serving as an answer to these sorts of questions manifests the contextual niche in which both, the question and the answer are formalised, validated and understood, because in this very sense, both question and answer are decontextualised and unvalidated in 21st-century Paneroamerican neuropsychiatric accounts, as are too decontextualised for 4th-centuryBC peri-Indian Samkhyayakarika systematisation of experience, or vedantic epistemologies (~1200-600BC).

Geographies mark the establishment of the relevance of a particular clinical affair under the argumentative intrinsic mechanisms of the question, before the answer, and this epistemic situation cannot hide the codification on both question and answer through their being inheritors of their regional, local context. As an example of a normative concern applicable in today’s evaluative debate, the characterisations of one important deviance-standard polarity that needs to be decided in neuropsychiatric sexology forms the following nosological question: ‘is homosexuality a kind of psychiatric presentation of an organic deviance statistically assumed by current men and women populations, thus attributable diagnostically as a psychopathological class and open to pharmacotherapy, psychotherapy, specific legal accountability and normative contest?’.

Such polarity is answered at current year 2019 in very different fashions observing different geographical contours: excerpted from the World Economic Forum Agenda (Weforum 2019), according to Equaldex (2019), a collaborative LGBT+ (lesbian, gay, bisexual, transgender) knowledge crowdsourcing web databasing rights by year and region, homosexuality, as a legally recognised set of normativised activities, is legal in 150 countries (66% of the global international range), and legally punishable in 71 countries (31% —with NV a 3%). Along the countries that consider homosexuality a normative crime (generally whipping punishment,



imprisonment and/or up to life imprisonment), today 5 countries verify that the required punishment is death ('honour killing'): Mauritania (stoning), Saudi Arabia (applied generally at 2nd conviction), Iran (for mature men; applicable at 4th conviction for women), Afghanistan (in Taliban held areas), and updated in April the 3rd of 2019, Brunei (stoning). Should psychiatric recognition (evaluation upon homosexual activity being nosographically identified as a scientifically attributable pathology) and intervention via a specific clinically required therapy be studied, if the analysis is worked to compare the previous data with the ranks on acceptance of homosexual conversion therapy, clinical therapeutical intervention shows to be banned in just 21 countries (9% of the global international range), not banned or pending in 90 countries (39%), plus a vast NV-zone with 118 countries (52%). As countries in their political tenor help to institutionalise but do not decide what is mentally ill, this is decided by different scientific communities, the second rate (legal acceptance of treatment) presents the casting marker that indicates a substratum of belief upon the fact, in a general fashion in many different geographical contexts, that homosexuality is a clinical ascription, a mental disorder, for it requires and deserves conversion therapy. This means that although there is a clear majority of normative agreement of these sexological and personal-identificational activities, there is a greater majority of acceptance upon the fact that such activities deserve a therapeutical intervention. Rosenberg (2002), calling on the works of Grob, Kirk and Kutchins, reflects how customary sexological determinations, when explored clinically, pathologically, nosologically, bear more a scent of priggish disciplinarian decision than a proper concern on therapeutical assistance:

«most conspicuously, psychiatrists voted [...] as they reconsidered the problematic category of homosexuality. Was this a disease or a choice? How could a

legitimate disease—in most physician's minds, a bio-pathological phenomenon with a characteristic mechanism and a predictable course—be decided by a vote, especially one influenced by feverish lobbying and public demonstrations?» (Rosenberg 2002, 238).

Here the gap between the diachronic convention (the eschatology of custom, the building of a boundary of normative activities, the identification of what is sufferable) and the synchronic convention (the decision of the clinical, present, applied attribution of what is suffered by a concrete, actual patient) actualises a critical form of clinical violence, for deciding the standard of evaluation delivers an ethical intimacy with culture-in-context, from which the horizon of scientific decision making cannot escape: a vote, an allowance, an epistemic sense of acceptance, ultimately directed by the restrictions of time and site, of mindset and convictions, happens to institutionalise either freedom or death in these 5 countries. This diagnostic violence in the clinical presentation of debates on homosexual behaviour and transgenderism (Cf. Bancroft 2008; Alegria 2011; Beneduce 2013) has recently made the case for many scholars and practitioners to adopt an even more skeptic standpoint when formalising orthodox evaluations on nosographical types and classes, should decision making naivety is preferred to be, at least attitudinally, avoided (calling back to Code 1983; 1987 on 'epistemic responsibility').

In 21st-century debates, the decision of the standard tends to argue for the biological, physiological, organic root, a biosignature of the pathology that will serve thus to orient discussions, however overriding the fact that would be interpretation of the material observations and not the material phenomena by themselves what can be endorsed as arguments. Polarities deviance-standard would need be decided in performing a routine of scientific argumentative efforts (a model of interaction by suggestion and refutation, following a Popperian view; Cf.

Popper 2014), where debaters claim to debate the validity of certain systematisation by the inspection of contingent and necessary particulars framing generals, an asserting strategy to minimise the problem into more solvable parts, and to reduce explanation and decision to workable clinical entities. This explanatory minimalism (in this sense, a pragmatic reductionism applied to the causal identification of overall affairs and their relationships as a theory making concluding strategy) shows this way somewhat argumentative eliminativism (in this sense, an instrumental reductionism applied to resolve systematisation using few, or thus eliminating surplus classes, states, types, entities and traits of entities shaping theoretical systems until deciding a less problematic solution) in deciding which conventions require debate and which others do not. In diagnostic fields, the decision on the polarity deviance-standard would come thus, following the reductionists, by exploring the roots of diagnosable entities through their material bases, addressing to biophysiological characterisations —this is practiced by a material alibi: that technologically observable and traceable biosignatures will necessarily form a ‘pattern of identity with the general standard’ (via enough statistical data) away from which deviance must be characterisable.

Claims on this form of reductive physiologicism give form to certain nosological interest (or a historical trend present in current times since the 18th-century rise of experimentalism: Cf. historiographical unfolding of pain experience electrophysiological experimentation theory making in QIII, §1, §2) on following a minimalist argumentation, instrumentalising the explanation of the grounding factors of pathologies via physiological and organic statistical materialism. This minimalist physiologicism does not just promote logical detectable fallacies (Cf. epistemic inquiry on the dynamics of argumentation in such process in QIII, §3; Cf. reflection on explanatory fallacies from neurophylosophy

in Churchland 2002; Bennet & Hacker 2003; Cowan & Kandel 2001; Eldredge 2985; Machamer & Sytsma 2002; Racine & Illes 2009; Thagard 1999; Damoiseaux & Greicius 2009; Craver & Bechtel 2007), it is, in like manner, no answer to the skeptic question from contextualism: where has interpretation of biosignatures been left apart —and most importantly, why— during the argumentative-evaluative process? Why biosignatures must, moreover, can, reflect by themselves a nosological argument on the basis of them being an exo-cultural factor for determining decisions on nosographic accounts? Who is to decide that variety of epistemic non-liability at all? (Cf. contextual inquiry about whose is the agency of possession in decision scientific making routines: Haraway 1988; Harding 1991; Hacking 2000; 2002; Kitcher 2003; 2004; Rolin 2011; Giere 1985; Galison & Stump 1996; Longino 1990; 1993; Cf. inquiry on Helen Longino’s critical contextual empiricism and constructive reply in Solomon & Richardson 2005; Cf. Longino’s reply to Philip Kitcher in Longino 2000).

However for serviceable interests in clinical assistance and theory making in neuropsychiatry, physiologicism can be presented as a point of departure without such overimplied minimalism, should practitioners in research and in clinical fields accept that any conclusion excerpted from a neuropsychiatric programme is due to the sounding and marking of neurobiological, physiological fingerprints of microphe-nomena that actually do not attribute agency to any de-contextualised singular modular tissue but to the organism in its integrity and as a whole. This could be assessed as a modernised ‘fingerprint alibi’, a physical reinterpretation of the 18th-century fundamental claim unfolding neuropsychiatric theory making, and stating, as Berrios & Marková (2002) describe, how mental signatures would need to follow functions and dysfunctions applicable via neurological signatures. This transposition would become

reductionist in the sense elaborated by the reading of Rosenberg's (2002) contributions to the matter as attested by the present text, when the implications of worldwide assessment of diagnostic traits start to focus instrumental justification over-simplifying and over-attributing micro-signatures (Cf. terms in QIII, §3) as to allow explanatory values of macro-phenomena (as reported experiences in psychiatric ambiances are). This is, complex macro-phenomena in the need of being clinically approachable through evaluatory practices of diagnostic attribution, and medically classifiable through nosographic theory making, underpinning such attributions. It would not be reductionist if it is the interpretation of such attributions, and their contextualisation to the scale of complexity related to its observation, what results applicable to diagnostic theory making from one frame of reference, without resting significance to other frames of reference.

Accepting or rebuking the fingerprint alibi argument is a political statement, a philosophical declaration, a cultural intention. Examples of a rebuking standpoint come along psychiatric behavioural diagnosing, and psychopathology-based psychotherapy, emerged by the 70's mainly in Europe, for some collectives as a psychiatric reformation, from '18th-19th-century coming out from the psychiatric asylum', to the '20th-21st-century coming out from biological reductionism and fast take-away treatment intervention' (Cf. the famous 'Law 180' on psychiatric reformation in Italy; or the theoretical non-organic psychopathological contributions made to clinical psychopathology and therapy by the group of clinicians Alienistas del Pisuerga, in Spain).

Being made, either way, a positive or a negative decision on such matter from a psychiatric framework of pathology, neglecting the implicit materialism the fingerprint argument exposes is not an option for 'neuro'-psychiatric characterisations, which implicitly search

through anatomophysiological procedures, the required descriptions and explanations to the aetiology and development of said pathological accounts. Such decision implies epistemological restrictions, for there must be a suitable landscape of justifications to explain, epistemologically, why materialism, and which sort of claim on material attribution, is agreed upon and defended. Part II will suggest that the depicted landscape of justifications comes with the exposition of the concept of an 'epistemic niche', an ecologically convenient environment for certain knowledge to unfold, and with the suggestion that niches present the proper conditions favourable or unfavourable for specific subjects (decision makers) to believe in certain 'epistemological perspectives' contextualised by certain 'epistemic frame' that depicts them. This theoretical allocation of the epistemic operation of framing would satisfactorily introduce, at least, a historically, developmentally, philosophically and anthropologically useful descriptive tool for informing about decision makers's characterisations.

Nonetheless, this issue can be considered with an integrative spirit. Historically understood, any neuropsychiatric diagnostic attribution; in searching the needs of explanation and description and with this motto making use of a material fingerprint alibi; would instrumentalise its landscape of justifications in a somewhat unavoidable fashion: up to their present time and context, medical debates can occur, simultaneously however, multiple clinical solutions would need be provided by healthcare institutions and healthcare actors, deciding in answer to the immediate social demands of medical attention and assistance. This builds up an instrumental schema of justification: prevention of the worst through the bad, on account of having no information of the better. One integrative factor that appears to change the 'solely-instrumental schema' is the degree of trust held by the defenders of a certain agreed-upon epistemic belief: to which

extent they are willingly prepared to keep agreeing on it upon time —or, in other words, what is the reasonable skepticism kept within their agreement on certain convention. This movement rephrases the schema into an ‘Instrumental Skepticism’. The landscape of justifications is thus dynamic, diachronically and synchronically comparative, pertinent to the contexts to which instrumentalism is revised, rectified and its contents enhanced through skeptic inquiry. It invites decision makers to perform justified contents of belief through instrumental strategies of description and explanation, at the time that makes researchers aware of the limitations of its application, and prompts to search for alternative, plural, re-figurative solutions to the given descriptions and explanations, solutions which favour the renewal of (1) underpinning medical research theory making practices, (2) their materialisation in clinical bodies of nosographic knowledge, and (3) the diagnostic practices of clinical evaluation, assessment and intervention.

*. Situating Trust through  
Instrumental Skepticism*

19-century drapetomania, classic hysteria, Cotard’s and Sèglas inquiries on melancholic deliriums, in modern times homosexuality, transgenderism, attention deficit syndromes... all are clinical evaluations that generally form clear examples of cultural shifts exhibiting the limitations of diagnosability for scholars on social historiography of psychiatry —may the Western current agreed historical judgement on their necessarily valid or invalid attribution in the present explain their common usage as examples.

Taking the case of drapetomania as an illustration of a contextually political clinical decision, the fingerprint alibi can be faced with the historical limits of its instrumental justification in showing how it is the relevance of

biosignatures’s interpretations and not material phenomena as such what engages clinical argumentation. Drapetomania, understood by 18th-19th fin de siècle theorisation of psychiatric escapism, engages the diagnostic attribution of drapeteers to slaves (generally applied to African-originated slaves arrived to colonialist America) with an obstinate urgency of freedom from the working fields they were settled on. The cultural identification of a drapeteer with a psychiatrically attributed escapist informs of a time-tied, contextualised clinical agenda, that benefits an economically driven interpretation of the behavioural symptomatic apparatus slaves manifested by running away from their assigned plantation. The clinical attribution is right on the definition, but the ethical implication only applies to the colonial slaver circumstance of the medicine performed by physicians on account of the frame of diagnosability chosen or forced to believe upon.

Such diagnosis does justify the master of the slaves not as him neglecting law, further on developed human rights and labour normative, but as a victim of a rebellious worker via attributing a disease to the slave thus avoiding the master to be legally dishonoured. This model is a symbol of how diagnosis, instrumentalised as a tool for bringing a solution to a social claim by the conditions of power of its own time and era, disclose the institutionalisation of such power by initiating a chain of trust that, when applied, sets conventionalism to work at the expense of collateral consequences. When the chain of trust is debated, regenerated, trustees draw back their attention to the cultural roots of their nosographical entities, with skeptical attitude, the trusted contents dismiss, superimposing the gap between the diachronic and synchronic conventions with a new form of ethical agreement concluded from a skeptic principle of refutability in nosological discussion.

To show that this gap, in the process of leaping from the clinical to the medical and back

again, can be subject of fallacious statements passing cultural values through material alibis, let us consider a hypothetical anaphoric development of history, an alternate history mental experiment on the scientific physiological justification of drapetomania. Consider no ethical restriction to the psychiatric agreement on the validity of such nosographic entity would have occurred —undertaken by no skeptic principle of refutability in nosological discussion dynamising instrumentalisation and, by extension, institutionalisation of clinical assessment in nosographical accounts— and consider, in addition, that neurobiological experimental advancements unfolded: before long, 21st-century population could have been witness of the very same scientific reductionism that would allow the hypothetical physicians of this alternative historical anaphora to detect fingertips of physiological signature that described and explained, through experimental evidences, the neurobiological bases of drapetomania via rigorous, clear, identifiable neuroimaging markers. This is not justifiable because the slave necessarily had a psychiatric ‘drapetomaniacal dysfunction’ attestable by his or her brain activity, but because anxiety, depression, fear, and many different diagnosable markers, that would be easily associable with what a drapeteer could exhibit, are now noticeable by neuroimaging techniques. Such biomarkers would have been subjected to a syndromic gathering framing the clinical attribution of drapetomania, thus, claiming of our alternative history 21st-century imaginary slaves their requirement of treatment, intervention and therapeutical attention —this is not even far away from 2019’s epistemic allowance for conversion therapy claims of homosexual populations requiring clinical attention.

As the example exposes, symptomatic recount by itself does not move nosography to elaborate syndromic gatherings, it is the epistemic disposition to recount them installed in a continuous interaction, confrontation and

refutation (recalling Popper’s view of scientific development), contextualised within a specific epistemological niche what moves nosology to engage in decisions that affect the creation of syndromic gatherings in nosography, along the possibilities for their diagnosability, detection and assessment —followed by intervention, not just medical, but legal, economical, political, etc.—. It is the niche what allows to build the necessary epistemic frames as to put perspectives in debate, as to realise such perspectives as a suitable standpoint worth of defence, as to involve ethical, political, cultural, monetary and regulatory conditions that enclosure its relevance and sense of applicability within a contextually-tied collection of events.

Fingerprint minimalism alone, by itself an epistemic alibi to materialism and a tool of instrumentalism, does not provide with any favour to the material anatomophysiological reconstruction (of any kind) of systematised maps and theorisations if it is not by having a strong and reasonable understanding that instrumental, utilitarian, minimalistic reductions are to be skeptically treated, shifted should considerations in debate turn required, and that explanatory and descriptive strategies are, as their usage and application, justified not by their inner logical structure, subject of acceptance, agreement, debates and refutations, but through their contextualised existence within a niche that allows such acceptance, agreement, debates and refutations. This frames an epistemic instrumental skepticism on clinical evaluation, materiality and the role of biosignatures in interpreting the value of anatomical and physiological claims on dysfunctions identifying neuropsychiatric characterisations. This standpoint will be brought forward in QIII, §3 and §4 (anatomically), §5 and §6 (clinically) for understanding pain-linked scenarios, for which epi-phenomenal interpretations —experiences being studied not as the proper phenomenon, attributed to the activity of the neural fields, but attributa-

ble to the inter- and meta-systemic interactions whose agency is just affordable by the organism as a whole— are alluded as emergent effects of situating epistemological trust on instrumental skepticism.

The use of embodied fingerprints or bio-signatures can be dealt with much more precision accepting certain amount of explanatory skepticism on their instrumental attribution of agency to particular microcosmic properties. Attributing overall agency to the organism at hand in tight reciprocal interaction with its environment and dynamic conditions would prevent fallacious argumentation. In QIII, §3, and especially exposed in QIII, §4, examples of this determination are delivered, involving debates on biological complexity, reciprocal adaptation, descriptive and explanatory emergence, and epi-phenomenal action and integration: the connectomic identification of ‘master nuclei’ and ‘master pathways’ as facilitators or orchestrators of general inter-systemic action, thus averting their reductionist characterisation as causal agents responsible for the explanation of overall macrophenomenal-epiphenomenal action, overtakes the minimalist materialism identified fallacious —reductionist view affecting over-attributionally the required anatomo-physiological perspectives, concluding simplified attempts at nosological explanations of neuropsychiatric conditions.

Instrumental skepticism allows a clinical working practice through instrumental justification, opening the space of intervention for justified application of knowledge known-to-date when being necessary for coping with and answering to the social demands of clinical immediate assistance in a proper present (and at the cost of the possible collateral sequels resting with the patients for having acted in such a manner), but instrumental skepticism does so at the time that the skeptic counterpart of instrumental reasoning compels the same agents accountable for applying instrumental justifi-

cation to pursue a better and more satisfactory style of action, enforcing a continuous attitude for producing epistemic alternatives enhancing their previous practice. The sense of trust within the trust chain would present a claim similar to this: ‘if this convention serves to the practice among peers, it will have sense until all work to refute it in pursuit of better alternatives’.

The instrumental skepticism integrative schema reveals three actors, (1) the underpinning medical research theory making practices, (2) their materialisation in clinical bodies of nosographic knowledge, and (3) the diagnostic practices of clinical evaluation, assessment and intervention. These actors are set conditioned by the situated common practices of assessment of the chain of trust that decisions and convention production promotes, stressed by epistemic operations of allowance on debate (and its protocols of defence and argumentation), of acceptance of theoretical traits and factors, models and guiding maps, and of accommodation of different theoretical traits and contents, in a process confronted with the necessary refutation strategies for advancing into new forms of characterisation as time unfolds.

## II — *Developing Epistemic Niches, Frames, Perspectives*

In his revision of transhistorical clinical characterisations, Rafael Huertas (2012, Ch. 4; Cf Huertas 2011) presents his reading on Hacking’s (1994; 1998; 2000) identification with the ontological claim that diagnostic classifications and clinical attributions are fluid constructs, cultural validations of contextualised knowledge. Huertas goes beyond the sheer system and features Hacking’s genuine interest on the conditions of possibility undertaking such classificatory claims that diagnosticians are attributed to make: the ecological inspection of Hacking’s theoretical approach will come from understanding a ‘niche’, he exposes, as the clear

identification of the historical, social, cultural, ethical, contextual conditions that result to provide the proper reasons to explain, justify or rebuke specific claims recognised, accepted and accommodated in politically differentiated, historical and geographical contexts. The ecological niche-involving solution applies to the clinical conditions (conditions for intervening) as to the medical conditions (conditions for describing, conditions for explaining). This niche, he resolves, is a metaphor Hacking resorts to,

«understanding it as a place [a historical ‘tropos’; an epistemological ‘context’] wide enough as for expressing the proper environmental conditions for such a disease or symptom to develop.» (Huertas 2012, 105).

This space called niche can play with the concept of ‘place’ and ‘context’ as to assimilate the situationism’s epistemic contextualisation of clinical practices into modern philosophical literature inquiring on the matter of contextualism and situated epistemologies (Cf. Longino 1990; 2001; 2000; Solomon & Richardson 2005; Galison & Stump 1996; Geller & Stockett 2006; Solomon 2001; McCauley 2009; Cartwright 1999; Giere 1985; 2006ab; Harding 1993; Weinberg 1993; Mitchell 2002; van Fraassen 1997; Fedigan & Fedigan 1989). The following sections in Part II are oriented to introduce the main concepts underpinning the epistemic bases of the present work, ‘niches’, ‘frames’ and ‘perspectives’, as tools for a situated research applied to clinical theory making on the evaluation of experiences, in the hope these can be helpful in defining the epistemic panorama integrating the development of contemporary neuropsychiatric diagnostics. Along with these notions, three epistemic operations of ‘marking’ objectives and goals of scientific interest, ‘trimming’ the scope of research, and ‘shifting’ the view orienting studies, thus re-orienting programmes for reaching to meet such goals through such selected theoretical scopes, are identified as sig-

nificant factors for theory change and development. At the ending section, four niches will be exposed, proposed as building the major points of departure for generating the specific scientific frames composing the historiographic and bibliographical polyhedron underpinning neuropsychiatric evaluation of pain experiences: A ‘Neurophysiological characterisations’, B ‘Psychiatric-Epidemiological characterisations’, C ‘Clinical Practice characterisations’, and D ‘Interpersonal characterisations’. Those four cornerstones will present the justificatory baseline to proceed suggesting the contents in the next Quarter of the thesis: QIII, §1-10, the body of the present work.

#### . *Framing Perspectives*

Frames regionalise affairs of study, superimposing to ontological issues deontological interests, in the same sense that epistemologies actualise deontological realisations about the world and ontologies, mereologies, logical classificatory systematisation of entities (Dupré 1981; 1993) are closed by the contexts in which the existence and characterisation of such entities make sense. The proper sense of those entities is clearly influenced by the epistemic recognition of the relevance of such entities as framed by the characterisational skills present and developed within a niche, a niche of recognition, a niche of epistemic evaluation.

The sense of generating specific knowledge about those affairs is related to the amount of trust, thus, that the epistemic subjects constituting certain epistemic communities, put on the process of holding a belief underpinned by such a frame. Provided from within such niche, the frame would generate situated knowledge: knowledge that is understandable, evaluable and meaningful to the people involved within said epistemic space. The notion of ‘framing’ has been introduced in other fields with similar expectations, especially in open network data

systems, involved in education theory, memory and learning processes for humans and Artificial Intelligence (Cf. works in Raishaun Jones 2018; Hofer & Pintrich 2002, especially in Schommer Aikins 2002, 103-118; Shaffer, Collier & Ruis 2016), in computer science and cognitive ergonomics for network analysis (and the epistemological inquiry on virtual reality and social game theory), software-oriented decision making, smart systems design, and trust protocols through blockchain technology. The assessment of scientific strategies for interpretation (eg, diagnostics, meta-analysis, comparative anatomophysiology, psychiatric orientation and decision of pathological standards, nosological and nosographical classificatory schemata, etc.) comes precisely in focus when evaluative practices are suggested to inform their situated knowledge working as contextual frames.

In presenting a point of departure that could serve as a working definition for an 'epistemic frame', calling on the works of Wenger (1999), Hutchins (1995), Crowley & Jacobs (2002) and Redish (2004), David Shaffer (2004; 2005; 2006; 2009; 2012; Cf. as well Rhode & Shaffer 2004) explores how epistemic frames, approached through epistemic games, reproduce (def:) patterns of knowledge formation and integration that engage specific strategies of understanding with the potential of shifting unmanageable information banks into manageable clusters of organised valuable data. In human play, Shaffer (2007) comments in relation to learning processing, we tend to evaluate actions as 'framing' our reality of possibilities, expectations and decisions through gaming interactions:

«we participate in a simulation of a world we want to inhabit, and epistemic play is participation in a simulation that gives learners access to the epistemic frame of a community of practice. When it succeeds, it is fun, not because fun is the immediate goal, but because interest —linked to identity, understanding, and practice— is an essential part of an epistemic frame, and thus of an epistemic game.» (Shaffer 2007, 4).

The value of information in the context of epistemic games, and transposable to the value of information in scientific decision making, is transformed by the epistemic frame in use in the same direction that the practice of organising, managing and systematising the understandable affairs of interest that guide scientific trusted contents and approximate decisions and conventions through expectations. In this process of practising, «the game provides the framework in which we make sense of what happens when we interact with the simulation.» (Shaffer 2007, 4). The practice of framing, based upon the expectations of systematising and giving coherence, definition, description and explanation in scientific debates about what is to be framed, can be applied to the scope of this dissertation on clinical epistemology to settle a plural and collective pattern of associations — paraphrasing the authors on learning processing— among «knowledge, skills, habits of mind, and other cognitive elements that characterise communities of practice.» (Shaffer, Collier & Ruis 2016, 11; Cf. Giere 1988 in cognitive approaches in epistemology too).

In terms of expectations put to work for scientific theory making stressed and tied to the core agenda of development in the contextual time and era affecting specific research programmes, Erwin Goffman (1997) makes a considerably similar use of the notion of a frame in describing how different people grow different expectations on shared matters to assist them make sense of the social, cultural, environmental, historical complexities in which they are involved. This layout of expectations conforms also a metaphor to identify different patterns of practicing science in a determined fashion (in relation to Kitcher 1984; 1992; Giere 1985), that define the justifications, beliefs and predispositions installed in the subjects conforming different epistemic communities of research (Longino 1990; 2001), from which experimental designs, guidances of understanding, and



plausible attempts at explaining phenomena emerge, many times concluding plurally (Cartwright 1999; Giere 2006b), through probabilistic analysis, interpretations about the obtained results.

Expectations play a major role, for in the development of a plural interdisciplinary research programme the focus of study and the practices involved may tend to shift amongst the original diverse disciplines (Cf. Darden & Maull 1977): expectations would make clear that, for example, if assessment of pain experiences is approached through an electrophysiological frame, reports, conclusions, interpretations of clinical problems and ending diagnostic values would be expected to resume, submit to, and abide by the physiological terms, language and topic of research, a threshold proper to the identity of the discipline beyond which answers may not be given.

This suggestion makes the case for exposing how multiple frames, which may appoint to cooperate in attending a big-picture integration of diverse origin, can be handled to explore and describe the main focuses, problems and barriers diagnostic assessment of pain in neuropsychiatry faces. These frames, schemata and enclosures of scientific interpretation, show how the scientific modelling of pain is a multifaceted problem benefited from interdisciplinary research (Cf. outlook in Darden 2006), which, at the same time, suffers from the complex circumstance of having multiple focuses of attention (especially when incorporating to discussion the problems of dysfunctional reports in assessment of neuropsychiatric conditions, more over with pain-reinforcement pictures), different definitions and theoretical orientations in the process of unifying and identifying diagnostic, adaptive and epidemiological values of patients bearing a pain-related condition, which is meant to be sharable through various physicians and reshaped by different clinical data systems of medical information management.

Following Stump's (1992, 458-59) commentaries on theory diversity, plurality reaches its sense through 'field-diversity', interdisciplinary and inter-field work (Cf. Callard & Fitzgerald 2015; Darden & Maull 1977) coupling required solutions to specific problems and multiple accesses from multiple points of view. Partiality is here, thus, not assessable as a flaw of a monistic modelling of scientific theory making, but as a reality expected to occur at today's theoretical ecosystem having unfolded a historical process of diversity-oriented specificism, in a developmental aperture of the scopes that previous scientific niches of observation and interpretation facilitated.

Helen Longino's (2006) account on the role of partiality considers the interactive processes that allows multiple interests and agendas in their cohabiting a historical present of cooperation, and a diachronic present-to-past historiographical reconstruction of spotted affairs where similar focus has been placed upon:

«multiplicity of approaches is usefully addressed not by comparative [in this sense, competitive] evaluations directed at selecting the uniquely correct one, but by appreciating the partiality of each. If their partiality is accepted, each approach can be seen to produce some knowledge of behaviour by answering the questions distinctive of it with methods that are also distinctive.» (Longino 2006, 127).

The technical use of 'scientific approach' in Longino's statements points towards a similar visual metaphor to Ronald Giere's (2006b) identification of plurality with perspectivism (Cf. Chang 2012 too), as employing plurality of perspectives not just enriches but makes the different perspectives necessary for achieving a progressively more complete and concrete visualisation of a multifaceted object:

«Employing a plurality of perspectives has a solid pragmatic justification. There are different problems

to be solved, and neither perspective by itself provides adequate resources for solving all the problems.» (Gieryn's 2006b, 36).

In the identification of theoretical partiality with interfield perspectiveness, Donna Haraway (1988) noted how social, cultural, methodological, contextual values influence and interfere in reaching collaboration among partial approaches, as certain perspectives may be driven by inherited privileged concepts contenting dissociative goals and interests that when compared with other non-privileged notions appear to satisfy both, questions and answers, involving personal and interpersonal decisions in the making and determining collective responses to social demands of descriptions and explanations. In such scientific process of convention and trust, situated knowledge appears handling the dialogue between critical inquiry and the different authors's suggestions projecting readings and solutions to such schema. In dealing contemporary problematisation, Haraway (2016) comes into play in favouring a flowing paradigm of incompleteness, much in contact with Cartwright's (2000) attitude athwart completability in physics's theory making. Haraway's 'learning to stay with the problem' of living and dying in biological fields, of pain, of madness, of controllability, projects a claim on how to learn to deface the problem from its scientific texture, inasmuch as each actor involved in the social claim of depiction and explanation participates either inside-out or outside-in scientific circles, using the language exposed in Part I of the present text, with opinions, values, interpersonal interferences and decision making protocols of trust, convention, and perspective. The accretional drift of valuable data oriented towards adding and refreshing scientific contents in a plurally understood, perspectival, contextual, situated epistemological account of scientific theory making, appears to reorganise approaches in a continuous fashion: to this extent, the

question is more about how to enhance the scientific learning process of recognising the contextual epistemic question 'whose is the problem, and why is there a need to solve it?', than the epistemic question 'how can international, instrumental, utilitarian, reductionist means in science solve or make more handleable such problem?' The epistemic whose-&-why-question 21st-century scientific (and non-scientific) communities face today is contributing its skeptical part in the rebuilding of the 20th-century how-question on instrumentalism and development (maybe due to the necessary inquiry on how scientific agendas are to be decided, and which style of scientific development humanity wants and deserves; Cf. Postnuclear Pessimism; Kitcher 2003; Merton 1973; Latour 2011; which has an impact on how to teach medical contents, how to deontologise medicine, how to understand the problem of the ill as a scientific problem, etc.: Cf. Foster & Funke 2018; Ellis 2017; Bleakley 2015; Atkinson et al 2015; Charon 2006; Greenhalgh & Hurwitz 1998).

It is precisely the difference in value that answers to the first questions give what makes the difference between the scientific cultural, social, political, geographical contexts in which niches can develop. The second how-question is orbital to the response of the whose-&-why-statement that there is a cohesive need for solving certain specific affair, or either that simply there is no actual justification for doing so.

The application of frames into clinical epistemics can serve as a tool for interpreting how perspectives migrate interests and views on topics, and how the whose-&-why-question gets resolved in application of medical theoretical solutions for framing the necessary clinical answers. Scientific themes (what-questions) may be mediated by the specific possibilities of thematisation proper to the interests of historically, politically, financially, observationally contextualised niches, however it is the different answers to such question the factor that

performs a 'framing' of the theme in order to handle what-problems. In contemporary research, sheer answers to what-questions do not cope with the integrity of the ontological problem addressed by today's scientific inquiry: why such what-question is there, and whose is the problem of resolving it, are also mediators necessary to ask and respond to completing a clear depiction of 'how to answer' (how to engage a scientific practice) in modern days. In following modern events's hypercontextualisation of themes, these mediators would cast overflowing themes (Cf. Helmreich 2016; Cf. Morton 2013 for 'hyperobjects') requiring more than singularised perspectives for achieving complex answers.

For instance, answering the whose-question may lead to understand that 'whose' invites to reflect upon the scientific discipline ascribed to be more likely to resolve the what-problem ('whose discipline is the problem'): casting a plural answer to this, in being accepted and allowed in such context, would develop interfield work and produce interdisciplinary strategies for describing and explaining social demands on the scientific theme previously arranged, in a very different fashion that mono-field strategies do. Answering the why-question may lead to provoke inquiry on why such 'what', such scientific theme, is scientifically approachable, framing, thus, de-medicalisation of the topic (eg, as homosexuality in many geographical specific contexts), or medicalisation of deviance (following eg: or rather considered a mental disorder in other contexts being accepted as a psychiatrically valid 'what' question demanded of scientific answer).

Epistemic clinical frames would act as situated resources of identification in a landscape of intentions (much in dialogue with standpoint theory regenerated into 21st-century clinical epistemic action; Cf. Intemann 2010; Rolin 2011), however a personally motivated, engaging, willingly decided act of identification:

situation would require the usage of markers, pointers, signals, recorders, monitor pegs, indicators, poles... milestones that will operate in a theoretical process of trimming the landscape, like the boundaries of a photograph generate the borders of what is framed by the camera, of understanding-within-the-limits of what has been previously marked. The act of framing (Cf. relationships with Latour's 1987 'science in action'; Cf. 'scientific practices' Cf. Kitcher 1993 too) would thus not render just an individual act of observing, interpreting and deciding, but a conventional common act of learning from practicing, of knowing from agreeing upon the limits for any further observations, interpretations and decisions, a trimming operation motivated from contextual conditioners, stressors that appear possible as participating in a proper epistemic niche for them to develop. The very trimming operation installs scientific theory making into partiality, and reframing, shifting the frame, building and regenerating a captive attunement with other resting perspectives when considered, would not escape from the very same primitive operation of marking and trimming, of answering first to whose is the problem (a societal conclusion, a scientific momentum for gathering fields or making emerge new interfield strategies), and why such problem needs be solved (recalling contextual justification on the grounds of common relevance, common wealth, common trust, common epistemic responsibility: Cf. Code 1983; 1987; Kitcher 1993; 2003; Hankinson Nelson 1993; Wenger 1999).

The dialogue among learning processes, theory making, play (decision making), and trust that epistemic framing brings forward is to mediate theoretical assimilation, acceptance, accommodation and refutation: the way a community learns how to learn (solving problems by trusting in previous knowledge and building forward new knowledge by deciding to renew or shift their trust upon them) is very similar

to the way such community will face scientific whose-&-why-questions, as deciding to trust on a scientific belief, convening and agreeing upon it, would require the trusting protocol of accepting both, the depiction of what is being framed by the conditions of the epistemic niche in which the epistemic subject's scientific community inhabits, and the limits obtained from the marking of interests and goals present in a contextual panorama of intentions. Shaffer (2005) grows a comparable argument on how epistemic games allow learning processes be guided in accordance to communal practices:

«The problem of developing thickly authentic learning environments becomes more manageable when we recognize that such rich contexts for learning always involve becoming a participant in some community of practice —whether local or virtual. Lave and Wenger (1991) describe a community of practice as a group of individuals with a common repertoire of knowledge about and ways of addressing similar (and often shared) problems and purposes. The reproductive practices of the community —that is, the collection of activities through which individuals develop ways of thinking and reframe their identities and interests in relation to the community— help newcomers develop this repertoire of knowledge. The training and apprenticeship of doctors, lawyers, midwives, and tailors are the reproductive practices by which the next generation of doctors, lawyers, midwives, and tailors is developed.» (Shaffer 2005, 1).

The product of theory making will involve theories, models, systematisations of knowledge that give way to proposals and postulates under whose scope (recognition of the outcome of the framing operation as an answer to a clear epistemic question) acceptance and allowance generate convention.

Trust, here, recalls van Fraassen's (1980, 88) idea that accepting specific claims of a theory (terming without much inspection a systematic account on certain affair of interest) takes

the meaning of 'accepting' as that of 'getting compromised with', essentially to get committed to both confronting and defending the compositional contents that engage a research programme. Such commitment is a decision process, from which to learn and generate knowledge inasmuch as it is an interpersonal mediator for further extracting conclusions and interfield relationships. In requiring experimental conditions where applying certain expectation that the outcome and performance of the experiment will evaluate to refute a model (in the general assumption that models constitute concrete specifications and designers of theories) if the expectation does not comply, models and theories act as mediators of expectations (Cf. similar readings in Morgan & Morrison 1999; Redish 2004; Cf. the role of metaphors as evidencing contextual expectations in experimental modelling in Keller 2003a).

Situation appears a key aspect of this process of getting compromised with some form of perspective. In framing, the subject envisions a specific approach, a specific perspective, from which he or she gets oriented and actualises knowledge just in relation to the scope the frame allows interpretations of what is framed to identify.

Many works in van Fraassen's (1980; 1989; 1994; 1997; 2002; 2008; Cf. a deep revision on van Fraassen's relationships with pragmatism, perspectivism, constructivism, and its contrast with his and Kitcher's understanding of empiricism in Inmaculada Perdomo's 2003; 2011 works) literature come across such identification process playing with visual allegories, images and optic deformations as making an analogy to how theorisation implies some sort of orientation in decision: the identification of models as maps for guiding in answering the social claims of definition and explanation, in this sense, implies the reader of the map, pivoting around it, to personally and willingly inscribe him or herself in the local point of reference that markers

and signals present for reading, being, in many ways, an act of contextualisation.

20th-century urges in modern epistemologies for understanding the limits of theorisation, fathoming the boundaries and the depth of a systematic comprehension of what a theory is defined by, what a model happens to build upon, how experiments form, inform, reform and de-form through their instruments's calibration, sensitivity and scope, and so forth, have shifted into 21st-century 'curving the interpretation' by error making as a main form of theory making, into instrumentalisation of words and words usage in benefit of imagined cultural depictions of expectations, of plural practices instead of a singular method, of communities of decision, learning, debate, of contexts of manageable standards and contexts of partialised knowledge oriented to the prosecution of economy-tied programmes of socially relevant scientific advancements, to be shared or not along with those beyond such contexts (networking in a relation of power and eagerness: Cf. Rose 2006), and into what ethnographer of science Stefan Helmreich (2016, 90-93; 241) has invoked as an unfasten performance in the working of 'athwart theory'. Noticing the work of Knapp and Michaels, Helmreich goes on their 'against theory' in rendering 'athwart making' more appealing to 'transversally, crossways making' than to 'against making': errors, mistakes, flaws, biases, trace theoretical assumptions as well as theoretical delimitations incomplete.

Helmreich's (2007) theorising through his ethnographic account on statements like 'live is a verb' comes up with the plasticity that biomedical assumptions are subjected to, in many ways, speech and textual codifications: 'scientific verbals' —scientific themes, questions and answers are, in general sense, problems in terms of language (recalling on Wittgenstein's conflation), and of how scientific practitioners work their pragmatic accounts on such topics

unfolding language to explore the demanded topics—. In following the steps of Helmreich's (2007; Cf. as well Helmreich 2006; Helmreich & Roosth 2016) 'inflection theorising', mental diseases's sojourn in the 21st-century nosological interpretation of neuropsychiatric pathologies should come too interpreted as a verb, an act of decision through literature and public debate, bibliographically delimited by the frames in action applied to conceptualise the general scope and the specific utility of verbals put in place by diagnostics (engaged through conventionalism in both forms, as suggested in Part I, diachronically and synchronically).

This curving interpretation by 'error making' as 'theory making' as 'learning making' moves forward into Lerer's (2003) etymological report that errors move in theory as 'errants', that in their verbal wandering reproduce the limits of fabricated imagery, contents of scientific beliefs claimed or argued. Helmreich's (2016, 90) inspection in favour of being a multiplicity of errors what makes a proper guide into what is real (ostensibly researchable) for a community of interpretation —thus, engaging a situated concept of 'real-for' (contextually 'suitable'; these ideas go along with the concept of 'propositional truth' as a dependent feature of the logical context within the propositions address to a given truth value: Cf. MacFarlane 2005; 2007; 2014; Kölbel 2002; 2008)—, can be very easily put in dialog with the previous situated epistemology scholars in their different but similar ascriptions of which forms of errors and cultural, contextual markers a theory comes across, athwart, transversally.

In a similar sense that Cartwright's (2000) limits of completion in theory making are, in many senses, declared by the impossibility of 'reading across its boundaries', athwart theory making approaches Longino's (2006) and Gier's (2006) distinctive partiality in scientific practices of answering questions as by appreciating the specific errors those different

approaches to partiality can actually afford to stand or to overcome. The social anticipation to error transmits as well the climate to skepticism as opposed to instrumentalism decision making in a necessary dyad that relates with the very performances declared 'learnt' in coral reproduction, in a community of practice of the style Shaffer (2005) recalls upon Lave & Wenger as a group of individuals with a common repertoire of strategies for addressing to similar, shared problems and purposes, clearly intertwined with Code's (1983; 1987) and Hankinson Nelson's (1993) determination that such epistemic community is 'a community' to the extent its claims on specific arguments and declarations about its subjects's scientific affairs of study are directed responsibly, as responsible accountable agents informed and decided, much in accordance with van Fraassen's (1980) rooting characterisation of acceptance of a theoretical assumption as to get committed to both, confronting and defending the contents that engage it —this in Part I has been claimed to be a process of 'epistemic allowance' within the proper epistemic context from which decision makers are set enabled to an open debate.

*. On Designing an Epistemic Frame  
in Neuropsychiatric Diagnostics*

In adapting these epistemological accounts into clinical epistemology for neuropsychiatry, Rosenberg's (1989; Cf. Rosenberg & Goldber 1991 too) attribution to 'framing diseases' helps in defining how such mapping tools that model psychopathology theory making present decided and fragmented. However, frames cannot be set up static. Framing diseases works within the same chain of trust that convention engages for observing (historically) and using (diagnostically) nosographical accounts of diachronically shifting gatherings of multiple interpretable ways for understanding symptomatic recounts. In this sense, as Rosenberg (1977; 1987; 1989;

1992) would similarly conclude elsewhere in his own language, pathologies act as social actors mediating key interpersonal ambiances of the living, framed by contextually convened beliefs decided and used by clinicians:

«The social uses of disease categories, however, are hardly limited to individual interactions between doctors and their patients or to the setting of research agendas and treatment plans. Philosophers and sociologists of knowledge have voiced an abundance of opinions regarding their epistemological and ontological status, but to the historian, disease entities have become indisputable social actors, real inasmuch as we have believed in them and acted individually and collectively on those beliefs.» (Rosenberg 2002, 240).

When clinical evaluation is said to act upon such identification, one is actually walking under the concern that the use of this or that identificational claim depends on the action of knowing how necessary it is to sustain further claims in the sequence of diagnostic attributions oriented to define the neuropsychiatric condition in which the subject suffering from such identification is involved within. This is to say that the 'epistemic integrity' —in other words, the entirety of responsibly trusted contents of belief upon which knowledge is personally and willingly accepted for a precise use— of the clinical frame by which evaluations are made, does not just require of the nosographical personal memory skills of the diagnoser, but also the conscious action of the clinician acknowledging such nosographical account may have alternative contextual nuances, cultural, historical, geographical, social, political, economical, familiar, interpersonal forms of power conflicts that, in the process of evaluating, interfere assigning values to fill the gap between diachronic and synchronic forms of trusting convention. This situation of epistemic conditionals makes the whole process to depend on a chain of trust ultimately situated within the rounding bound-

aries of the contextual frame this action is being performed, where it is meaningful and useful. As exposed in Huertas's (2012) reading of Rosenberg's attribution to framing:

«Illness as a clinical object would singularly exist within a historical-cultural frame, in which it gets constituted as a specific entity, for what it will only be comprehensible, in earnest, from its interpretation within such frame of reference.» (Huertas 2012, 103).

However the actors of such evaluation may get, by this same 'epistemic integrity' put in action, interbreeding and synthesising trans-frame accounts, as historiography does, as nosological debates on the validity of particular nosographical accounts does, generating a contrasting skeptically-driven movement towards recognising the epistemic errors inherited by the very performance of framing (Cf. athwart as crosswards). This movements however cannot be installed but in a new in-balancing mediation casting a dynamic frame that, however alternative to preexisting diachronic ones, will have the very same operators (Cf. marking, trimming, shifting, *infra*) for elaborating the contrast. To the extent of this dissertation, meta-theorisations would never reach a different form of framing in its epistemic proceeding, and synthetic-synchronic theorisations will work, this way, as the definitions of those dynamic strategies put in play as the very process of diagnosing a case.

'Framing' as a practice wandering etymology in speech has a long trajectory presented with the meaning of 'using', 'preparing', 'making ready' —influenced f. Old Eng. *fremman* (help forward, promote, perform); f. Old Norse *fremja* (to further, execute); f. Mid. Eng. *framen* (to prepare timber for building; late 14-C). The meaning 'to compose, to devise' is first attested in the 1540s (RHU Dictionary 2019)—. In-balancing towards a new context (or towards the very context stablished and defended) will carry

on this form of preparing, performing, executing and promoting a style of recognition, understanding, and application of the conclusions extracted from using the frame as it manifests and variates. The frame and its use cannot be separated.

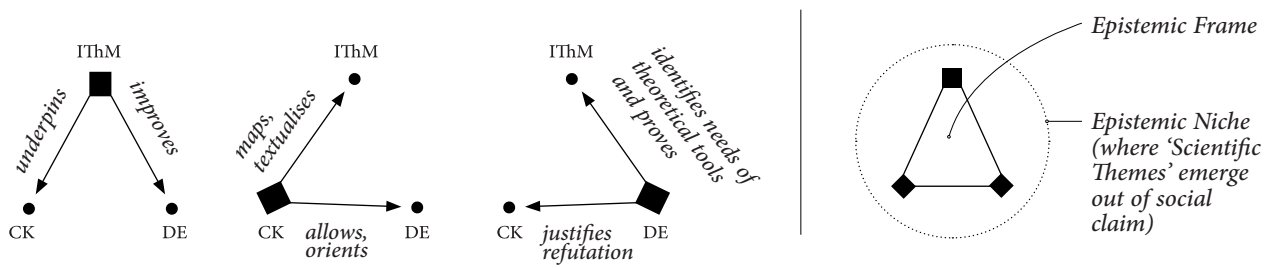
Reasoning on how to design the epistemic in-balancing performance of evaluation, these actors may help in charting the major mediations and interrelations that can actually be claimed to define an 'epistemic frame' through performance and use, in an instrumental skepticism integrative standpoint, more than as a fixed category of epistemic inquiry.

The instrumental skepticism integrative schema revealed in Part I presented three factors in clinical evaluation, (1) the underpinning medical research theory making practices, (2) their materialisation in clinical bodies of nosographic knowledge, and (3) the diagnostic practices of clinical evaluation, assessment and intervention —that will include both forms of deciding trust upon conventionality as knowledge, diachronically and synchronically executed.

Recalling on Sharon Poggenpohl's (2015; Cf. too Poggenpohl 2009ab) works in the field of design research programmes relating the underlying workability among research, theory, and practice, 'epistemic framing' can use a similar attitude to allocate the study of the implications these three actors have when transcribed into the previously identified three factors in clinical evaluation.

The configuration of a Poggenpohl-ish triangle (Chart 1, 'Triangulation of a Neuropsychiatric Diagnostic Frame', *below*) would serve to depict dynamically how an epistemic frame would work as applied and contextualised to the fields of neuropsychiatric diagnosing:

■ Chart 1 — ‘Triangulation of a Neuropsychiatric Diagnostic Frame’



**Keywords:**

*'IThM': Interfield (medical) Theory Making (underpinning practice)*  
*'CK': Clinical Knowledge (theories, models, maps, nosographies in use)*  
*'DE': Diagnostic Evaluation (clinical scientific practice, intervention)*

*Specific 'Epistemic Frame' where 'Epistemic Perspectives' apply, developing 'Conventions' through 'Trust', within an 'Epistemic Niche' where the Frame has the possibility to emerge.*

Collaboration, in this sense (Cf. research collaboration strategies in Poggenpohl & Sato 2009; Sato 2009; Beck & Stolterman 2016), requires awareness of the fundamental mediations among underpinning, textualising and using processes. This is a phenomenon of epistemic contextualisation, of orientation, of situation. Frames, triangulating such media, will focus and render the epistemic orchestration where perspectives apply, where angles and standpoints define and stretch unavoidably contextualised by the stressors that allow the epistemic acquisition and deployment of trust into a particular belief, developing thus considerations, interpretations, conclusions. Frames are installed and emerge in particular niches, where those have the possibility to appear. To the breadth of this suggestion, thematic approaches will be considered niches, and the fact to support such claim comes with the condition that frames pluralise themes, however it is the epistemic niches the space of germination that allows a theme to emerge as a leitmotiv of necessary resolution. In other words, it is the ecological niche what promotes the cultural, social, political, linguistic, historical contextual need of definition and explanation of a topic of interest, it is the niche what happens to allow the existential conditions depository of having the resources to, using Haraway's (2016) 'living with the question',

bring about the epistemic question on 'what' to solve, that further on frames will respond; deciding, arguing, suggesting, debating; and will mediate by re-asking whose knowledge is for and why such knowledge is required to be given and delivered on.

Nosographical categories and clinical attributions to the patients (Cf. 'labelling theory', the critique to the rules of the stigmatisation of psychiatrically shaped patients, in Goffman 1968; Cf. the critique on 'making up people' in Hacking 1986; and also in 1998; 2000; Cf. the concept of 'diagnostic tyranny' in Rosenberg 2002) through evaluatory practice pertain to such frames inasmuch as those niches allow physicians to understand the marking, trimming and shifting strategies through the perspectives proper to the frames they have been academically, culturally and politically developed within.

*. Marking, Trimming, Shifting  
the Scientific Theme*

The what-question upon the 'scientific theme', the topic towards which scientific efforts will be directed, is a question that emerges conditioned by the contextual stressors the niche generates. The what-question is an epistemic inheritance towards which frames would



be inflicted, using Helmreich's (2016) terms, to curve, inform, reform, deform, subject to a captive process of thematisation, of handling, management, marking and modelling, carving, moulding and shaping that, applying Lambert Williams's (2012) PhD dissertation account on linear to non-linear system transformations, will be historically and historiographically reconstructed in the future as a process of delivering 'difformations', patterns of shifting and re-locating themes, topics and what-question, on behalf of contextual paradigms of particular epistemic niches, that, for so it being, and for the epistemic subjects contributing and integrating communities of belief, in so doing, actualise and organise what-answers, and whose-&-why-questions further on.

If contexts and niches situate themes, the current cultural, geographical, political hypercontexts pluralising epistemic niches in today's internationalised, globalised, magnified inter-framed contemporary scientific inquiry will also uncover hyper-proportionate themes. Timothy Morton's (2013) examination on the question upon the scientific theme considers 21st-century hypercontextualised ecology an example of an 'hyperobject' in theory making. Themes that now require attention were before unable to be handled or, in most cases, missed unnoticed. The epistemic analysis of mono-topic, single-themed theories, appear 'overflowed' — in Helmreich's (2016, 90 and 202) terms, 'overflowing theoretical objects'— by a new form of modal stressor that had never happened in historiography until the arrival of Internet, comparative databanks, query-makers and multilingual search engines used in facing the critical stance of climate change, oceanography, cetacean life premature death and communicational lethargy (mainly due to radar colonising their wave space), plastic residual invasion, revival of hyperviruses and, to the extent of the problematics of this research, diagnostic availability. Strategies in unitary fields end up useless,

speechless, instrumentally overpassed, skeptically accused, for from the very niche a newly socially demanded answer to a hyperthemed what-question emerges breaking the epistemic frames trusted until their present time and era, overflowing conventional theorisation in favour of multifactorial, pluralised, perspectival and interfield-oriented (Cf. Darden 2006; Darden & Maull 1977) theory making, framing, re-framing, marking, re-marking, trimming, re-trimming, shifting, re-shifting the contemporary scientific themes.

Alluding to a visual metaphor for extracting the meaning of those epistemic operations (Cf. Illustrations on 'Situating Epistemic Niches, Frames and Perspectives by Clusters of Interfield Palimpsests', *infra*: Ill.1, Ill.2, Ill.3), the analogy can place scientific themes as filtered within a tightly intertwined landscape of human interests, requirements, conditions, possibilities, powers and features, presenting the epistemic niches contextualised in their own and multiple time, geography, culture, economy, religious and political identities. The epistemic subject would recall in the analogy a theory maker as taking a photograph from such landscape, framing the depiction of the niche by trimming its observability.

First, the photographer marks the topic of the photograph, launching through his or her expectations upon certain scientific themes that the contents of his or her beliefs can grasp the epistemologically interesting —when negative, the overflowing feature hypertheming the topic takes place—. The topic, socially demanded for an answer, requires the photography to get gradually decided, established, institutionalised, hypothesised: evaluation points out the methodologies of the taking, the process, the practice. When the photograph is exposed, a re-version of its horizon comes about: horizons present the possibilities of action, interpretation, future understanding, attention and debate. The landscape plays at a context, the situ-

ated niche that allows the photographer to take the photograph, however the bare trimming of the boundaries of the photograph transforms the horizon of the landscape into the horizon of the frame: the possibilities of the subject of attention into the possibilities of the observable-through-the-frame. The photography can be taken again, chronifying the advancement of the epistemic dispositions proper to the niche, and thus historiographing the practice in development. Photographs can be stilled, can be video-dynamic, but their synchronic nature (proper to the moment and context in which these are formed) makes their capture-conditions a situated depiction, always informed by the values and agenda that puts trust on depicting this part of the landscape with more precision than that other, and by the limits of the camera imposing the limits of scientific observation, the limits of scientific experimentation, concluding and interpretation: partiality.

If the frame of the photograph moves to the right, to the left, shifts the boundaries of the image to the top, to the bottom, different angles appear, scaffolded, intertwined. Shift occurs. Shifting re-shapes the frame, visits from a different epistemic perspective the subject of study, and thus it colours and attunes conclusions from this perspective. Shifting comes across marking and trimming, replaces the marks, rebuilds the trims, involves the individual gradient necessary for the theory maker to make a decision on what should be framed, towards what evaluation shall be oriented, from which perspective shall the shift be endorsed, enhanced, engaged. Many shifting processes re-frame the landscape, gathering collections, clusters, requiring inter-frame organisation, systematic compilation in a multiple pictorial composition that, like the series of Polaroid photocollages in David Hockney's portrait works (Cf. a recent commented catalogue on Hockney's portraits in Howgate & Stern Shapiro 2006 —appointed pieces are 'Noya and Bill Brandt with Self Portrait' of 1982; 'George,

Blanche, Celia, Albert and Percy' of 1983; and 'The Scramble Game' of 1983), makes the ultimate 'joiners' of such photocollages, thus, the observer, the reader, the interpreter of the inter-framed composition. This analogy shapes pluralism as an inter-framing operation that, as commented elsewhere before, will necessarily play with the same marking, trimming and shifting proper to any framing process.

If understood clinically (diagnostically, synchronically to the case), situated values actualise the necessary epistemic standpoints by which the photographer takes the shot, making the decision upon its own epistemic access and allowance towards the scientific theme as pertaining to the landscape as much as to the photography taken, thus, re-shaped and contextualised through the optics of the decider. Decisions actualise evaluation each time frames are enacted, activating this triangulation of actors that frames are (Cf. Chart 1), thus selecting specific nosographies (conventional agreed-upon contents) for attributing pathological ascriptions to patients for following a case. In so doing, decision, by framing, 'moves forward' (recalling the prior etymology of frame) dynamically the trusted contents by the very practicing and using the frame, establishing an epistemic 'filling the gap' between the diachronically trusted-by-convention, into the synchronically opted-to-trust, in application of diagnostics (a decision of shifting and re-shifting personified by the contextual power of the diagnoser; calling on Part I's concluding in Foucault's 'pouvoir psychiatrique', Goffman's 'labelling', Rosenberg's 'diagnostic tyranny'). Decision making in diagnostics actualises the epistemic perspective by re-framing the diachronically trusted into the synchronically opted to trust.

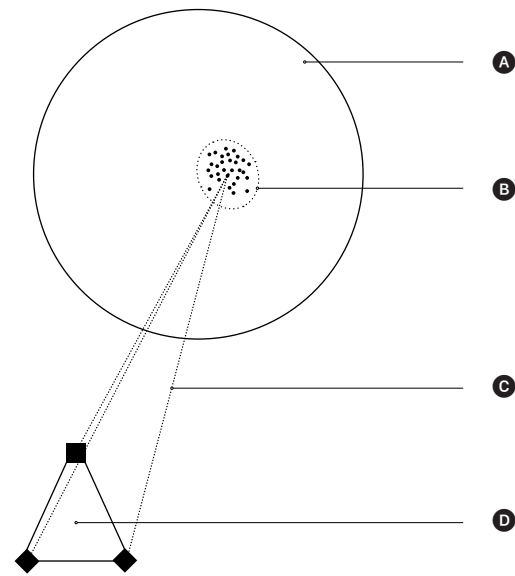
If understood nosologically (diachronically: research programmes, historiography, medical theoretical debate), theory making underpinning re-framing by researching will evidence how different topics, emerging from a plurality

of epistemic niches, get to inform and reform the scientific themes proper to different contexts, geographically distant, time-scaled varied in comparative histories, or culturally shocking with disparate grounds. Theoretical re-framing would insist, in this precision of terms, contextualising pluralism of conventions not as clinical evaluations (the previous movement, by selecting nosographies, and attributing diseases to patients for following a case), but as fields, disciplines, lines, study motives, divergent in form and sorts of methodology, asymmetrical in their basic conceptualisations and use of terms in language, maybe dissonant among their definitions, thus allocated in different poles addressing similar themes, and heterogeneous in their pivoting descriptive and explanatory strategies.

The idea of palimpsests casts here a more complex however precise depiction of such overflowing interfield strategies facing scientific themes as hyperobjects of theory making: the more re-framed, re-marked, re-trimmed, re-shaped, like in a blockchain registered and captured within a historical epistemic ledger there to last, the more comprehensible each shade of frames gets in the palimpsest when integrating efforts come to play in interpreting and making sense of the different perspectives that a highly complex polyhedron-theme manifests. The more comprehensible each shade through integration, the more justified the theoretical defence upon such interpretations will tend to be, here playing with skepticism as instrumentalism needs be forced to face contention. Solving anomalies implies the recognition of error, athwart, crosswards theory making, concluding bridges and at the same time promoting awareness of how instrumental strategies for field-linking, or metaphorical solutions for approaching the internationalised, interlinguistic use of concepts and verbals, can filter through such layers utilitarian reductions that do not cope with the needs of sound understanding that the proper contextual niche expresses by demanding complex and pluralised theory making.

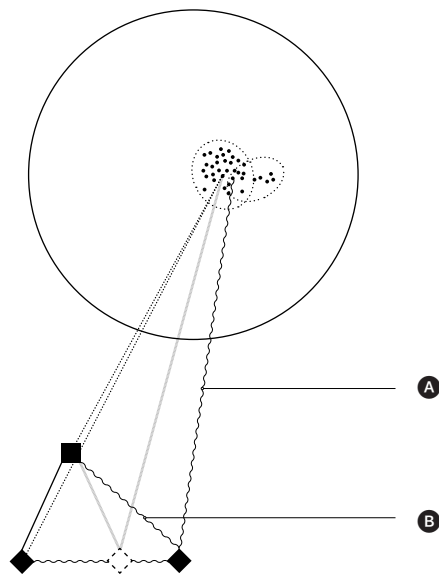
— *‘Illustrations on Situating Epistemic Niches, Frames and Perspectives by Clusters of Interfield Palimpsests’:*

■ Ill. 1 — ‘Situating Niches, Frames, Operators & Perspectives’



- A Landscape of Human Interests, scientific expectations, social intentions.
- B ‘Epistemic Niche’ clustering themed scientific contents (contextualised contents of epistemic belief), providing source for what-&-why questions.
- C ‘Epistemic Operators’ of marking and trimming the landscape of interests, generating ‘Epistemic Frames’.
- D ‘Epistemic Frame’ with a specific scientific horizon for perspectives to grow, developing specifically contextualised and trusted scientific accounts addressing what-&-why questions from social claims on contents to be defined and explained.

■ Ill. 2 — ‘Operating Frames: Shifting athwart Perspectives’



A Operating on a given ‘Epistemic Frame’, ‘Shifting’ athwart perspectives, selecting new interests, new expectations.

B ‘Re-Framing’ Process, generating alternative perspectival orientations to a previously exposed context.

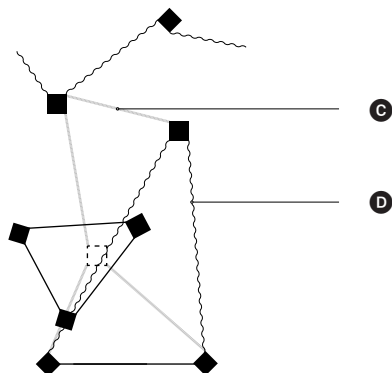
C Shifting operations re-frame different interests, integrate multiple frames, and re-generate clinical trustworthy knowledge.

D By shifting and re-shifting, historiographical diffraction occurs, merging frames in palimpsests of theoretical contents for better understanding overflowing objects through multiple perspective approaches, used at once via new inter-frames that will develop inter-field theory making strategies.

In its condition of facing 21st-century overflowing scientific hyperobjects; that have actually colonised, or will imminently mount on, every aspect of scientific inquiry; contemporary interfield re-framing, it appears, grows in the precise environment to turn to epi-phenomenal considerations in biomedical epistemics (definition and explanation of experiences) and in clinical epistemics (in considering epi-diagnostic solutions through complex multifactorial and prognostic values: Cf. QIII, §5).

The present thesis will apply this epistemic notion on overflowing frames in need of re-framing inter-framed perspectives for building an analysis in QIII, §1-4 on the limits of materiality as informing and de-forming the physiographical accounts of pain experiences in use for clinical neuroevaluation; for examining in QIII, §5 the critical state of the diagnostic problem on multifarious morbidity as an overflowing sign, suggesting the notion of epi-diagnostics (overflowing-facing diagnostic practices) reasoning about multifactorial and prognostic evaluation, along the usage of modern probabilistic technology assisting diagnostic decision making; for assessing in QIII, §6 the clinical complications comorbid to pain through dysfunctionality clusters coding neuropsychiatric overflowing symptomatology; for discussing in QIII, §7 current clinical assessment reclaiming a modernised definition of the forms that diagnostic practice takes as an epistemic practice, personalised and linked to the context of patients; and for building a critical revision in QIII, §8 about generally used evaluatory instruments applied to pain experience as

■ Ill. 3 — ‘Palimpsests exposing Historiographic Diffraction & Overflowing Theory Making’



measuring strategies overflowed by a paper-fitting policy in trusting a diachronic conventionalism that does not fill the gap towards synchronic assistance, nor does it cohabit the technological progress, clinicians, and patients inhabit in 2019 (directing the critique to the lack of research, use, scholarly involvement and governmental development of Artificial Intelligence Assisted Diagnosis, text-attitudinal and qualitative-emotional software analysis for contrasting patient's report with standards, genetic testing, and so forth; Cf. medical information theory trust exchange for interpersonal themed inquiry in QIII, §9 and §10.)

*. Determining the Study of Four Niches on Pain Research for this Thesis*

This complex circumstance makes each part of Quarter III to present specific notes on the impact that framing a contemporary epidiagnostic characterisation of pain experiences in 21st-century neuropsychiatric diagnostics will have in facilitating epistemological and medical inquiry to a number of different themed fundamental epistemic niches.

In following the palimpsest integrative-interpretative argument through instrumental skepticism, the more perspectives inter-frame the different niches from which scientific themes emerge, the more robust, trustworthy, pluralised, decentralised and usefully solving the theoretical interpretation and clinical evaluation appears to be.

To the extent of the present thesis, the addressed themes will present excerpted from four epistemic niches of interest that, in not claiming to exhaust the conditions from which pain experiences are able to be framed, are hoped to both, conclude a satisfactorily wide taste of how evaluation is framed, and to serve useful tools in delivering on examination and sounding plausible answers when possible to contemporary demands from medical epistemics and neuropsychiatric diagnostic practices. The four

epistemic niches suggested for theming frames in neuropsychiatric characterisation of pain experiences are:

A '*Neurophysiological Characterisations*' (QIII, §1-4) — Frames addressing neurophysiological niches inform through definitional and explanatory strategies via physiologism, necessarily implied in neuro-psychiatric characterisations, solutions that can be applied to uncover material alibis, technologically oriented from observational events in experimentation, unfolding developments on how the many physical conditions for experiencing pain-related scenarios play their roles systemically (nervous system) and inter-systemically (nervous system interacting with humoral hormonal system, immune system, etc.), concluding meta-systemically (on the epi-phenomenal result emerging from intersystemic interactions) relating functional and dysfunctional activity compromising the organic satisfaction of integrity (in the sense that pain would come to be definable as the overall performance of evaluating the state of integrity, or in other words, the disintegrity of the organism as an agent in fluid interaction with its environment).

B '*Psychiatric-Epidemiological Characterisations*' (QIII, §5-6) — Frames addressing psychiatric niches inform about the epidemiological, comparative, statistical features that clinical characterisations in nosological debates result to incorporate to their conclusions in affording contextualised (however hypercontextualisation makes contradictory results for its adaptation into globalised diagnostics) nosographies, implying pathological systems of classification of clinical entities, along the necessary discussion upon the imminent relevance of applying comorbid and multimorbid clustering strategies, thus reforming diagnostic attributability of mental diseases through a more complex definitional descriptive strategy, technologically

adapted to the patient, and multifactorial-prognostic valuing fashion of understanding psychopathology.

C '*Clinical Practice Characterisations*' (QIII, §7-8) — Frames addressing neuropsychiatric niches approach the performative application of the clinical knowledge trusted by neurophysiological and psychiatric-epidemiological conventions, decided diachronically and, adapted to the clinical case, thus appointed to delivering evaluation to a specific patient filling the gap between diachronically trusted clinical knowledge, to a synchronically decided attribution via measuring strategies. These face the overflowing complexity of contemporary hypercontexts, and in so doing, clinical practices are increasingly forced to hold a patient-oriented perspective inevitably assisted by engineering developments that, being current suggestions, and still-to-come realities, are to support communal, interconnected, data-banked compared, and adapted-to-the-case diagnostic evaluations.

D '*Interpersonal Characterisations*' (QIII, §9-10) — Frames addressing inter-personality come to face the problems that the epistemic boundaries of personal experience settle in the process of identifying and characterising clinically other's (the patient's) suffering. In neuropsychiatric fields, those barriers occur to express within-the-patient (socially dysexecutive, non-verbal, non-communicative, memory dysfunctional or fabulative patients are given examples); being the very patient unable to recognise his or her own personal experience and to make it exhibitable, evidenciable, displayable interpersonally towards the instrument or towards the evaluator; but they can occur transpersonally, observing flaws in instrument scope or precision, or present by the very epistemic access to the experience of other agent (interoperationaly), thus delivering characterisations (pragmatic accounts) on others's intimacy on account of

an absent and ultimately unavailable standard against which to contrast said characterisations. This comes with epistemological inspections on how agents of a diagnostic-specific Artificial Intelligence assisting in evaluation would meet the assessment protocol under which interpersonal understanding, empathy and, finally, transference of trusted knowledge manifest.





## **QII, Chapter §2**

### **Structure of the Present Analysis: Framing Epi-diagnostic Characterisations on Pain in Neuropsychiatry.**

—

#### **Parts**

. *Introduction*

A — Neurophysiological Characterisations: Historical & Comparative Traits  
*(Summary of chapters QIII, §1-4)*

B — Psychiatric-Epidemiological Characterisations: Overflowing Morbidities & Pain  
*(Summary of chapters QIII, §5-6)*

C — Clinical Characterisations: Diagnostic Practices & Pain Measurement Strategies  
*(Summary of chapters QIII, §7-8)*

D — Interpersonal Characterisations: Difficulties on Self-Narratives & Pain Transference  
*(Summary of chapters QIII, §9-10)*



. *Introduction*

The following summary describes the relation of chapters in QIII, §1-10, concerning the development of the present epistemic inquiry on epidiagnostic characterisations of pain experiences in neuropsychiatry.

Thinking through the contacts among neurophilosophy, clinical epistemics, neurophysiology, epidemiology, psychiatry, nosology, clinical ergonomics (on the technologisation of medical data engineering for clinical assessment), and the dynamics of clinical evaluation as a proper diagnostic practice of recognition and intervention, these various stances push towards identifying how epidiagnostic characterisations look like: polyhedrons of multiple and intertwined façades? Palimpsests of overlapping layers? Recognitions of useful data underpinned by themes emerging from their focus of attention? Perhaps a blend of all those analogies? Those questions animate the chapters gathered in QIII to listen, from a historiographical point of view, as cultivating an ethnography of the scientific practice in 21st-century neuropsychiatric diagnosis, and at the same time to sound, as introducing a marine sound underwater, measuring their depth, scope, borders and conflicts observing, thus, how much new or current perspectives come to develop difformed, shifted, rearranged concepts of yore, how conventions get decided, by whom, on what purposes, under which climate of cultural and theoretical convention, in directions that are some times oblique to the advancements of different disciplines, or that by neglecting so, produce and reproduce concluding contents that bear conflicting factors to our own modern hypercontextualised themes, practices and theory of decision making.

Epidiagnostics seek to face those stressors in an overflowed panorama of scientific interfield acquaintances, when evaluation conjoins the 'over-(epi)-flow factor' detected by modern ethnographic, cultural and epistemological

studies as applied to clinical ambiances in the previous chapter. An epidiagnostic characterisation of the style proposed, thus, builds integration through difference, multiplicity, plurality, recognising partialities through perspectival approaches, and drawing athwart (crossways, crosswards) theory in its attempt at navigating across biological and theoretical complexity.

Framing epidiagnostics invites to acknowledge how contextual accounts of medical interpretations (agreed-upon nosographical knowledge) and clinical interpretations (in-balancing decision making addressed to a particular case, filling the gap between diachronic and synchronic trust; Cf. QII, §1) develop situated within precise epistemic niches, where the question about the necessary scientific themes to organise, to debate upon, to accept, to intervene, to apply, to rewrite or to refute emerges. Throughout four niches, this thesis exposes epidiagnostic characterisations as thematised by spaces of common understanding (niches A, B, C and D), composing an all-encompassing interpretational record that may be helpful in considering diagnostic evaluation of complex, heterogenous and multifactorial scenarios of pain experience, installed in the patients' 'living-with-the-pain', and thus, in the neuropsychiatric theoretical underpinning efforts of an epistemic 'staying-with-the-problem'. What follows is the structure of the present analysis through its 4 niches and 10 chapters, summarising and relating the contents proposed and serving as a guide facilitating the reader a clearer overview of this work as a whole.

A — *Neurophysiological Characterisations:  
Historical & Comparative Traits*  
(QIII, §1-4)

Pain evaluation would appear first in its virtual form, in an experimental, electrophys-

iological laboratory solution, as a rhetorical float for thinking about organic integrity (or evaluation of disintegrity) in 'On the Development of Pain Physiological Characterisations: A Brief Historical Contour' (QIII, §1). The first chapter of this analysis is an attempt at revealing the lines of thought that led to retain, debunk, rewrite and modify some of the underlying principles supporting today's convictions on nerve conduction in pain physiology. The text deals with a particularly old conviction, the idea that experiences are explicit contents, that sensations, perceptions or feelings perform as qualitative contents, which can be transported through the body to imagination, or moved by entelechies through our own body. This characterisation has been in focus along the history of pain research. Running the end of the 18th Century, this scene lived a clear transformation from early metaphysical accounts to a material physiologicism constrained by experimental requirements and scope limitations. The work invites to think that the characterisation of pain as a 'qualitative content' conducted through different continents, pores, filaments and channels, was being reshaped in the light of voltaic physiologicism towards understanding the very 'continent', the funnelling nerves, as properly qualitative. Working the continentality thesis interpreted through the propositions of Bell by year 1811, and Müller in his 1835-1840's works, nerves were now observed as the centre of explanation: specific channels, Q-fibres (substitute 'Q' by any specific qualitative evaluation, as pain or itch) and, thus, performing a specific Q-conduction. While buoyed up by the specificist foundational claim (ie, 'one perception, one receptor'), the thesis configured a proper account for the time, a material alibi for understanding neuropsychiatric conditions, and for accommodating the theoretical frame of physiological explanations into the realm of the technically observable. The introduction of a seemingly new responsible actor, 'nociceptors', as functional

specific perceptors of harm by Sherrington, resulted in clinical experimentalism as the thesis of qualitative continentality gained acceptance.

A brief contour of this ethnographic thread is exposed in two parts. Part I focuses the ancient seeds of entelechial qualitative concepts, providing an anthropological inspection on the worries that framed the physicalist interpretation of pain as a qualitative conduction that generated and reshaped through two geoaxes; a prior Eastern-axis that informed early medico-metaphysical inquiries, contacting a middle mediterranean area towards a Western-axis, that formally depicted the sensing qualitative contents until pre-modern theories of pain perception, further on configuring a tradition of scientific characterisation. Part II centres the 18th-century entry into modern materialism, observing the physiologist turn from qualitative contents to the thesis of qualitative continentality, ending with the propositions of Bell and Müller that supposed the starting point for future electrophysiology beginning the 19th Century —advancements reviewed in QIII, §2.

Conclusions from this chapter, by now informing about the meaningful scenario of concepts active by the end of the 18th Century, prepare the way for 'Building Pain Models: From Early Electrophysiology to the Complexities of the 21st Century' (QIII, §2), moving forward from 18th-century theoretical elaborations, and navigating a panoramic of pain models arranged until the current 21st-century physiological reasoning. Pain induction has been a main issue of experimentation in early electrophysiology throughout the 19th Century, focusing examination around infraspinal Peripheral Nervous System afferents. Running the 20th Century, new methodologies started to understand the role of voltage-irritative signatures, both through the medulla and the upper Central Nervous System, as evidences of pain transduction patterns. As a result, theorists began an era of pain modelling beyond sheer induction.

Approaching the 21st Century, reflex theories were transformed into more complex strategies, while differentiated labelings characterising the phenomenon-of pain sprang among interdisciplinary research.

With a comparative aim, the chapter covers a substantial repertoire of the main theoretical achievements in the western experimental inquiry on the topic in four points. Departing from the implications of the initial tenets proposed by the Müllerian turn, which configured the general orchestration for a proper field of pain electrophysiology throughout the 19th Century, it overviews the incipient theories in favour of specificism and intensity; advancing to early 20th-century integrativism, affectivity, summation and pattern theories, and the advancements of the second half of the 20th Century, which came with the exploration of transduction, mediation and modulation. A present recension about the complex scene of pain research in the 21st Century finishes the fourth point.

Some concluding implications are sketched, exploring some of the problems to which this historical thread has landed in the present. These include the lack of strongly framed interfield explanatory strategies; the problems produced by maintaining in currency hard readings of specificity for exposing the ultimate responsible actors in the biochemical scenario of fibres's performance; or the slow accommodation of fundamental intuitions into new scientific horizons. These horizons now present, in the majority of cases, a contemporary attempt at interpreting the big picture of phenomena and epi-phenomena implied in pain sensing, examining experiences, feelings and beliefs about pain beyond peripheral, spinal or localist approaches inherited from the past.

The next chapter, 'Sounding the Limits of Materiality & Over-Attribution: On Pain Fibre-Specialisation' (QIII, §3), reviews some of the major epistemological factors that led to form the historical shifts on the material attribution

of agency and roles to fibres and regions of the nervous system in relation to their role on pain conduction, as presented in the previous chapters. Putting the issue in Lambert Williams's analytical terms, it will be exposed how the historiographical thread of pain electrophysiological research presents a 'difformation process' that affected the underpinning considerations from which each historical and localised scientific context produced its interpretations on materiality, very often implying physiological reductionism. The inquired interpretational scenario frames a material over-attribution of evaluative qualitative agency that results fallacious in multiple senses, which in the case of pain physiology has been introduced through the arguments of fibre specialisation, discerning what stressor is the fibre specialised towards. Pre-evaluative reasoning demands for this identification morpho-functional characterisations that do not inform about any particular experience as proper to the fibres that argumentation is characterising, but proper to multiple central evaluations along the organism as a whole.

Problems on over-attribution, thus, of overall agency to specific parts of the system are to be exposed historically, epistemologically, and interdisciplinarily by this text in two parts. Part I will focus on the descriptive strategies that historically came to difform unitary theories's (oriented through unique original scientific fields) conclusions on pain conduction into interfield's interdisciplinary research conclusions in more modern times. Part II will extend the epistemological exploration on physiological reductionism in material attributions, and expose alternative ways for characterising pain experiences through integrative dynamic physiology as an attempt at resulting more applicable to neuropsychiatry or experimental therapy.

The last exploration of this niche A comes with 'Pain Physiographies: A Contemporary Image' (QIII, §4). Physiographies are consistently used in medical explanation and description:

charts, diagrams and images exposing, analysing, annotating physiological and anatomical matters of study, map and summarise clinical data while working as simplified instrumental scientific models. In managing different scales of complexity, such schemata show an immediate tool to face biological morpho-functional entanglements. This chapter sums a general image of contemporary physiographies approaching pain conduction, involving bottom-up projection maps (from peripheral induction to spinal mediation, to central integration), and top-down projection maps (especially central downwards regulation and medial-spinal modulation). The text is divided in three parts with a total of 10 charts. Part I offers a general view of the whole scenario, from induction (peripheral and central), including the inflammatory chemical ambiances and their impact on master pathways of overall salience, to cortical integration and evaluation, and downwards modulation. Part II deepens in contemporary advancements on transduction, at medullar levels, including central spinal transduction and interneuronal matrices at Rexed laminae, analysing their role in achieving a contemporary reading of the Gate Control Theory. Part III closes the text outlining a final interpretation on the role and context of pain-facilitating fibres, by presenting the evolution of nociception-related systems as fibres that would have developed sensitive to disintegration, in a close and reciprocal relationship with immune reactivity (especially primary inflammatory processes). This faces the problem of defining nociceptors inquired by the previous chapters, for away from resulting a trouble of being linguistically fussy with naming, it comes as a characterisational problem that affects the ontological recognition of what the fibre does, the proper understanding of how it evolved, and of the stressors it undertook specialisation towards. The problem with nociceptors triggers the final interpretation delivered at the end of this chapter in Part III.

The interpretation analyses C fibres's fibrogenesis in organisms diachronically (evolutionarily) observed from a systems biology standpoint, thus involving a 'Principle of Integrity': on the basis of recognising the organism's unity as an integrity, a cellular cooperative coral environment that is self-sustained on account of its interaction with a medium that provides mutual variations in a reciprocal relationship. The interpretation offers a plausible workaround, an alternative way of conceiving of these fibres as to assigning them a connectomic relevance of their role in sensing immune reactions (the case of inflammatory phases is introduced) acting in answer to a reciprocal interaction with their contextual cellular milieu given infringement of a Principle of Integrity: ie, these cells are interpreted to be prone to excite when the organism disintegrates, involving mutual interplay with immune, hormonal and vascular systems. This departure point would serve to build a Reciprocal Inflammatory Fibrogenesis (RIF) Interpretation for pain-linked fibre specialisation, in the hope it can serve to help to explain the matters underpinning problems on the specialisation of these fibres as an attempt at avoiding the over-attributive characterisational problem identified by QIII, §1, §2, and §3.

*B — Psychiatric-Epidemiological  
Characterisations: Overflowing  
Morbidities & Pain  
(QIII, §5-6)*

Developing the themes proper of psychiatry, concerns on how to assess pain through critical patients as a circumstantial factor, a multi-systemic stressor and a clinical trait of proper psychiatric conditions, have triggered the nosological debate on the conventional diachronic validity of singularised diagnostic attributions in scenarios requiring of multifactorial analysis and prognostic values identification. Within the ambiance of pain-reinforcement, the concept of

morbidity is changing its utility, shifting irregularly through historiographical accounts on disorders, diseases, illnesses, madness, that are no longer structure-specific, and that face, thus, to new comorbidity and multimorbidity classificatory requirements.

The first chapter of this niche B, 'Overflowing Morbidities: Pain Reinforcement and the Value of Epidiagnosis' (QIII, §5), addresses the significance of this nosological difformation in a clinical, epidemiological and attributional chain of trust. The coexistence of several pathological conditions in the same patient, being fundamental to singularised or pluralised diagnoses and to his or her general clinical assessment, exposes a definitional, classificatory and epistemic challenge that has produced almost fifty years of medical and philosophical discussion, evoked variegated attempts at using comorbidity terminology in daily clinical language, and prompted significant criticisms on the validity of systematic, categorial disease classification. Since the 70's, the notion has been exposed to a good amount of transformations, growing a definitional reattunement to complexity and heterogeneity within medical and epistemic literature that is bringing deep consequences for the entire diagnostic practice and its research activities.

The gain of pain-associated conditions pairing with an index disease, or the presentation of a previously detected pain accompanied with peripheral diseases and disorders, usually introduces the psychiatric, emotional and interpersonal assessment of comorbid states in patients suffering from multiple diseases without a monographic cause. These, in the majority of cases, develop in processes of 'pain reinforcement', contributing to the worsening of a patient's life quality, personal apperception of harm, or his or her coping strategies with such a burden. Be that as it may, the opposite process is true for pain-bearing populations, where a preceding pain experience, usually sustained (chronified

pain experiences), is determined to cause-coadjuvate, degenerate or contribute to promote further comorbid diseases, continual and continued crises that foster a quite common involvement of mental disorders, interfering with diagnostic practices of identification and differentiation of symptoms. To the extent of this interpretation, it seems that the concept of 'epistemic overflow' shows an accurate tool to assess the blurrish problems that analyses face with multifarious, complex, heterogeneous diagnosis of comorbidities in neuropsychiatric studies and pain experiences theory making. This chapter covers the current neuropsychiatric panorama dealing with pain-associated comorbidities, addressing the 'epistemic overflow' introduced by comorbid states into clinical theorising, along with its implications for diagnostic practices, the assessment of pain experiences, and the organisation of diseases within systematised classifications. Divided in four points, the main text overviews the prevalence of pain-associated disorders; the major debates on defining comorbidity; and the discussions about the systematic, categorial and dimensional classifications of diseases. The last point of the writing reconsiders such diagnostic overflow, and outlines some conclusions on how the value of epidiagnostics can be of much use in giving form to future proposals improving the work in comorbidity and multimorbidity-driven clinical practices: this concluding remark wants to place a value on 'epidiagnostics', defining pluralised practices of diagnosing and adapting diseases classifications, that stress a better descriptive understanding of complex, multifarious, heterogeneous prognosis, and the deeper multifactorial, personalised assessment of patients.

Next chapter, 'Neuropsychiatric Dysfunctions Associated with Pain Reinforcement Comorbidities' (QIII, §6), approaches in a practical manner the specific neuropsychiatric pathological architectures that most often present with, or develop into, chained dysfunctional pictures.

The text composes a neuropsychiatric framework to observe comorbid states and overflowing conditions that worsen reciprocally with reinforced pain processes, leading to a clinical overview of plausible epidiagnostic characterisations. Patients suffering from reinforced pain processes usually acquire personal and interpersonal dysfunctions, coming down with several emotional re-attunements to their living phase, a change of attitude, of mind frame and, finally, agency and actions that ‘re-shape’ the activity of their nervous system and express through personality. Of especial psychiatric attention are mood de-consolidation (mood and character traits tend to change in pain-bearing people, affecting humour and the direct responses involved in the social, familiar, working or scholar roles they play), emotional-perceptive complications (pain thresholds tend to turn more sensitive), affective and evaluative difficulties (how they proceed to assess their experiences, life quality and social, friendship, familiar, labour and learning ambients) and self-judgment problems (eg, how pain-bearers produce self-beliefs: beliefs about themselves and their experiences attached to their clinical conditions and the collateral, implicated circumstances).

When tracing a diagnostic path for neuropsychiatric comorbidities affecting index diseases overflowed by pain reinforcing processes, factors are classifiable in multiple manners: there is no major taxonomic orientation to follow for organising comorbid gains, and many times sheer epidemiological or statistical prevalence accounts do not fit for particular diagnoses. Researchers show and discuss how, for each study, precise symptomatic classifications, and contextualised scales of comorbid factors and stressors (leading to clinical worsening and its diagnostic detection) have been created. In order to assist diagnostic detection, this chapter introduces a neuropsychiatric framework for interrelating such multifarious comorbid contributors, over-viewing some of the most common diseases af-

ected by, or being affecting pain reinforcement processes and emotional functionality. These are sorted by four epidiagnostic clusters, which have their epistemological fundament in QIII, §5, and are mainly driven by relational, multifactorial and prognostic values. They may help in finding neurotypical features during the diagnostic search and evaluation of the patient as key signals. Vulnerability factors for emotional comorbidities implying pain reinforcement and functional neurodestruction are also implicit values. The framework consists in the following four dysfunctionality clusters: I ‘Executive Attitudinal Dysfunctions’, II ‘Impotence, Worry & Habits Dysfunctions’, III ‘Affection, Mood, Character & Personality Dysfunctions’, and IV ‘Dysfunctions Related with Central Neurodegenerative Disorders’. Further neuropsychiatric frames delivering on this niche can tackle the different variations evaluation can adopt in approaching patient-specific cases, involving contemporary reflection on clinical characterisations as diagnostic practices of measuring (comparing to nosographical standards developed by theory making underpinning routines) and knowing (epistemic access), as studied in the following niche.

C — *Clinical Characterisations: Diagnostic Practices & Pain Measurement Strategies* (QIII, §7-8)

Exploring diagnostic practices from an epistemological standpoint results in sounding how contemporary clinical practices could understand the access to a patient’s pain experience, growingly guided by communal strategies of observation, attention, assistance and dialogue, favouring personalisation and recording of pathological traits for engaging a better descriptive further neuropsychopathology of pain-reinforcement overflowing comorbid scenarios. The first chapter of this niche C, ‘Epidiagnostic Assessment as Clinical Practice. Navigating Person-Centered Diag-

nosis in Neuropsychiatry' (QIII, §7), outlines how person-centered perspectives, implied in nowadays healthcare plural processes, influence diagnostic practices framing description and interaction through personalisation of standards. In regard to such movement towards pluralistic attention, some major factors of diagnosis are required to be revisited, taking into consideration its relevance as a communal practice. Facing a descriptive approach, this writing assesses how some newer epistemic architectures sounding the notion of 'scientific practice' —mostly from situated epistemologies (1960's–2000's and beyond), and especially calling on works by Philip Kitcher— can be applied to identify and describe this so-called 'epidiagnostic practice'. In such context, the main goal of this work is to serve as a revision of our nowadays pluralistic clinical behaviour. In three parts, the chapter exposes first in Part I an outline of how the person-centered perspective implied in healthcare plural processes influences diagnostic practices, accounting for three of its main aspects: 'situation dependence', 'patient proximity', and 'classificatory requirements'. Part II revises the notion of 'scientific practice' as portrayed by modern epistemologies to be applied to diagnosis, and concludes in Part III proposing a framework for helping in defining modern clinical performances, a suggestive definitional basis for framing the epidiagnostic practice of neuropsychiatric evaluation. In so doing, a plausible framework for describing modern clinical diagnostics is being offered.

As reviewed by the QII, §1, general assessment of patients's conditions draw in a practice of trusting diachronic knowledge along a synchronic circumstantial understanding that unfolds via instruments and measuring strategies evaluating the difference between the clinical case and the medical nosographical standard. The second chapter of this niche, 'Measurement Strategies: Assessing Pain Self-Judgements & Self- Beliefs' (QIII, §8), inquires how accurate

and modernised are these general instruments and strategies, in current use and of wide application in contemporary neuropsychiatric evaluation, for facing the contemporary overflowing exhibition of symptomatology given the modern nosological revision and involvement of up-to-date fresh technology applicable to a collaborative interfield engineering of descriptive pathological traits and case-behaving.

The clinical diagnostic of pain experiences and outgrowths, reinforced pain, pain-bearing processes and their consequences for further comorbid scenarios, is in no means distant to the same challenges that other diagnostic neuropsychiatric practices face: practices are subjected in great extent to the diagnoser's performing the interpretation of pathological traits (specific symptomatology contextualised to the patient at case) and pathological architectures (socially and scientifically accepted diseases, health complexities, conditions, disorders... instantiated by patients). Such guesses are guided by his or her experience and savvy, estimated through comparison among many similar cases, and involved in case-to-case decision making patterns. In other circumstances, when personal qualitative introjection and projection are introduced with-the-patient in such guesses and interpretations, 'interoperative' (normative, measurable) clinical diagnoses occur, and tend to be informed by the patients's performance on several tests, analyses, scales and interviews, which are multifactorial, scored, ranked, situated (to nationalities, gender, age, further diseases, etc.), and that shall be validated and accepted by scientific communities in order to function as helping tools for any diagnosis to be resolved. Interoperative normative diagnostic processes, involving patients's decisions, show numerous leading major aspects to future enhanced diagnostic practices (Cf. QIV, §1: results and conclusions of this thesis), including assessment of trust, interpersonal behaviour, flexible standardisation and contrast, plus case-to-case

decision making protocols, personalised attentive care, and prognostic tracking over multifactorial niches of stressors increasing morbidity, both co- and multimorbidity risks (Cf. QIII, §4 and §5).

In the recognition of such clinical factors, the chapter navigates the main diagnostic tools for assessing beliefs and judgements on pain experiences, outgrowths, pain-bearing processes and plausible comorbid complications. Three main clusters have been developed for accounting pathological trait specifications, a 3-fold cluster frame that gathers a total of 15 topics facing measurement strategies challenges. Topics do not exhaust any list of measurement tools, however can be presented as a guide to generally reviewed, in-use major utilities in the field. These clusters form the three parts of the work: Part I, 'Wide-Range Assessment of Pain Beliefs', reviewing the main tools for measuring neuropsychiatric pain-specific traits in different clinical circumstances; Part II, 'Assessment of Pain Bearing & Outgrowths', exposing some of the main tools in use for measuring pain display, consequences, coping processes and dysfunctionality values; and Part III, 'Comorbidities-Oriented Assessment of Pain', facing challenges in comorbidity scenarios, describing some of the main diagnostic tools that may be used for accessing the prognostic neuropsychiatric factors epidemiologically associated with dysfunctions derived, or co-causing, pathologies. These clusters, informing proper use of instruments to measure others's pain experiences, open the path to a determinant epistemic interest on personal and interpersonal characterisation of experiences, for this belief, enriched by the considerations, narratives, memories and pragmatic accounts explaining the private immediate experience being felt, will be the data delivered on the interoperation patient-instrument and patient-physician. The next niche, on the difficulties and barriers of pain transference, will address the philosophical inspection on the

matter in application to both, clinical decision making in assessment practices, and in its effect on medical data engineering.

D — *Interpersonal Characterisations:  
Difficulties on Self-Narratives &  
Pain Transference*  
(QIII, §9-10)

When the diagnostic process is understood as a plural performance of different agents involved in an ambiance of recognition, identification, attribution, attention and prediction, clinical evaluation is readable as an interpersonal (trans-organic) action working with suitable factors and phenomena in the scene that are not proper to all the actors involved, inasmuch as these are just proper to the organic resolution of the patient. In other words, interpersonal evaluation makes epistemologically relevant to talk about beliefs upon themes that need be imagined, simulated, virtually engaged by others as for them to be dealt with, oriented, attachable to a clinical notion, and confronted with a standard. This process of responsibility, or linguistic pragmatic accountability, recalls on healthcare institutions, diagnosers, patients and patients's environments, and instrumental usage for developing trustworthy medical characterisations. Actualising those concerns, interpersonal evaluation needs to worry on how self-narratives, of patients exposing their own experiences, unfold valid or relatively valuable to diagnostics and therapy endeavours, and, likewise, how transference of trusted knowledge can be put to work interpersonally on the basis of empathetic and contextualised spaces of understanding.

The first chapter of this niche D, 'Barriers in Self-Assessment of Pain & Its Comorbidities: Indetermination in Self-Beliefs & Narrative Perspectives' (QIII, §9), examines how pain-bearing patients's inability to discern a proper definition of their own pain experiences, and further conditions comorbid to it, affects clini-



cal self-assessment. Indetermination in the patients's reports acts by blurring the characterisations of pain and comorbid conditions that they may offer to physicians and evaluatory instruments when asked to explain and reflect about their own current emotions, given the case that they might feel, as an usual report, seemingly contradictory experiences. This problem presents especially when dealing with personalised diagnostics incorporating interoperational feeds (Cf. QIII, §8), as they involve relations of the kind patient-physician, patient-instrument, patient's ambience-physician, etc. Indeterministic assessment can occur in 1st, 2nd and 3rd phases of neuropsychiatric multifactorial evaluations (Cf. QIII, §6 and §8), leading to general biases and to relatively weak practicality in dysfunctional and dysexecutive populations: sometimes patients, due to cognitive or dysexecutive dysfunctions comorbid to pain scenarios (Cf. QIII, §5), can generate beliefs upon themselves (self-beliefs) containing contradictory, opposed, seemingly unmatching feelings, that are reported by means of different narrative points of view, multiple focuses that guide the patient's discourse exposing how he or she acts and feels, along with certain reasons for having acted and felt in a particular manner in other moment.

In regard to therapy theory, indetermination introduces patients's inability to defend a specific continuous narrative, prompting their self-evaluation of pain and comorbid conditions with a past, futurable or possible scenario of feelings valued with the same trust as actual ones. This provokes uttering pragmatic accounts (the way the patient uses utterances and propositions for justifying or responding for the contents of such) where no singular identification is able to be reported: rather the principle of relevance is broken, or both characterisations are relevant to the patient for accounting for what he says he believes is experiencing. Such accounts would function via self-narratives that may not seem to be justified to the therapist as conveyed on

account to both, present and non-present feelings, for the patient is incapable of 'characterising through' (to determine) a single mindset, consequently impeding a continuous identification of his experiences, emotions and feelings, and of the orientation of those feelings towards something, someone or certain situation.

In this work, indetermination is suggested to have an epistemological interpretation, formalised through propositional logics for self-beliefs. This presents the case for exploring 'indeterministic self-beliefs' in defining how the subject may hold such perspective narratives. Applying Peter Lawrence Goldie's general perspective theory, the question raises to investigate where and how patients put trust on when asked for reporting their experience. The aim of this chapter is to define an analytical description for explaining why and how this indeterministic circumstance comes to be propositionally possible, in order to clarify the processes that allow a patient to report a 'conflicting double feeling' —two seemingly incompatible or asymmetric experiences (eg, to feel pain and to feel relief) felt at once— that blurs the production of a proper self-assessment. Formalised as propositional epistemic beliefs, both beliefs will get to the point in which the subject may put trust on both at the same time: it occurs that the subject finds no manner by which to determine what he is actually feeling, emerging an indeterministic self-belief.

The next and final chapter, 'Transference of Trusted Knowledge on Pain by Contextualising Empathetic Perspectives' (QIII, §10) explores the field of cognitive ergonomics in its implications to medical information theory and clinical epistemology. This involves the sequence of common distribution, protection, sharing protocols, management, trust activities and decisions as regard to many participants in the movement of clinical data, including relationships of the kind patient-physician, patient-instrument, physician-instrument, phy-

sician-physician, etc. This work examines how transference of self-beliefs on pain is performed from pain-bearers to analysers, how the second assess external beliefs, and can trust on shared knowledge from a naturalised, contextual, perspective epistemological standpoint.

The idea behind the topic is that experiences are, yet to the contemporary exploration, unable to be transferred: one would not be able to experience the pain of any other self. Beliefs, however, or their contents, are constantly being communicated, exchanged: by being shown through behaviour, linguistic patterns, meaningful images, or pragmatic accounts as utterances and speech acts, they form our principal means for evaluating others's experiences, informing valuable knowledge.

Bringing the issue into a belief-&-action-based framework, it is expected to enhance the way clinical recognition, characterisation and assessment is carried out. In a medical sense, beliefs are constantly being subjected to transaction, in which two or more parties agree on trusting given or extracted information to become, for instance, diagnostic criteria, epidemiological data, standards, or case reports. The chapter chases a definitional effort in answering how are we able to define that such a transference is actually being of trusted knowledge (of contents of beliefs that manifest actual 'felt pain'), instead of entirely simulated knowledge (of contents of beliefs on several characteristics of pain, but that do not manifest a phenomenon as enriched as 'felt pain' would be experienced). As an integrative proposal binding social, plural, perspective epistemologies with propositional logics of self-beliefs, the work provides a protocol for introducing trust in assessment processes, regarding transference of experience-based self-beliefs even when the analyser may be holding a simulation in his or her belief about the analysed subject's experiences. Introducing perspective beliefs in a theory of the style this chapter is dealing with, plural cluster

compositionality (of public and private traits composing the contents of beliefs) may be used for accrediting partial value (as regarding to the formation of 'partial simulations' in the belief of the analyser, solving the problem of total simulation: Ideal Pain; Cf. QIII; §1-3). The proposal also allows for its embedment into a propositional belief as content with traits (which may instantiate attitudes, orientations, intentions, pragmatic addressivity, and forms of public conventions and private dispositions into the very belief of the subject), as well as its transference and its plausible options for solving the identification process that serves for an external analyser to discern through empathetic agreement what is the suitable evidence that makes the experience of an external subject to be transferred with sense. There is a hope this proposal could help in providing methodical and theoretical tools in order to build increasingly better instruments —applied into clinical ergonomic systems in Artificial Intelligence Assisted Diagnostics, thick-and-thin Big Data contrast, text and qualitative analysis, and blockchain clinical interoperational systems of diagnostic management— for measuring self-beliefs on pain and other complex experiences of diagnostic use.



---

## Quarter III

### Niches for Framing Epi-diagnostic Characterisations of Pain Experiences in Neuropsychiatry

#### **A Framing Neurophysiological Characterisations: Historical & Comparative Traits:**

- §1 On the Historical Development of Pain Physiological Characterisations:  
An Anthropological Contour (p 74)
- §2 Building Pain Models:  
From Early Electrophysiology to the Complexities of the 21st Century (p 94)
- §3 Sounding the Limits of Materiality & Over-Attribution:  
On Pain Fibre Specialisation (p 106)
- §4 Pain Physiographies. A Contemporary Image (p 122)

#### **B Framing Psychiatric-Epidemiological Characterisations: Overflowing Morbidities & Pain:**

- §5 Overflowing Morbidities: Pain Reinforcement & the Value of Epi-diagnosis (p 150)
- §6 Neuropsychiatric Dysfunctions Associated with  
Pain Reinforcement Comorbidities (p 168)

#### **C Framing Clinical Characterisations: Diagnostic Practices & Pain Measurement Strategies:**

- §7 Epi-diagnostic Assessment as Clinical Practice:  
Navigating Person-Centered Diagnosis in Neuropsychiatry (p 188)
- §8 Measurement Strategies: Assessing Pain Self-Judgements & Self-Beliefs (p 200)

#### **D Framing Interpersonal Characterisations: Difficulties on Self-Narratives & Pain Transference:**

- §9 Barriers in Self-Assessment of Pain & Its Comorbidities:  
Indetermination in Self-Beliefs & Narrative Perspectives (p 220)
- §10 Transference of Trusted Knowledge by Contextualising  
Empathetic Perspectives on Pain (p 242)

# QIII, Chapter §1

## On the Historical Development of Pain Physiological Characterisations: An Anthropological Contour.

(In Niche A — Framing Neurophysiological Characterisations)

☛ 308 — 312

—

### Parts

. *Introduction*

I — Ancient Medico-Metaphysical Roots of Qualitative Physicalism

- . *The Split of Constitutive Elements. On the Metaphysicalisation of Pain*
- . *Eastern-Axis Physicalism. Introducing Qualitative Content*
- . *Some Eastern-Axis Systematisations. Theorising Qualitative Sensing*
- . *Western-Axis. Qualities as Contents of Perception, Experience, Feeling*
- . *Inclinations towards Modernity: from Anatomism to Physiologism*

II — Modern Medical Roots of Qualitative Materialism: The Physiological Turn

- . *18th Century. Interpreting Irritation: The Turn to Physiologism*
- . *19th Century. Interpreting Nerves: Qualitative Continents*
  
- . *Closure*

As many topics in medical history, this analysis approaches the development of an old belief, a grounding conviction which states that qualitative contents, sensed and funnelled to a centre of integration, imagination or feeling, are responsible actors for explaining the phenomena of experiences. For the case at hand, pain experiences, this abstraction of everybody's intimate sense, or perhaps this concretion from images of cultural, contextualised, shared performances, results to enjoy a mirthful continuity from ancient eastern to western physiological historiography. Pain research experimented a clear transformation from early metaphysical accounts to new electrical physiologies, constrained by experimental requirements and reductionist metaphors. This chapter navigates such a transformation that reshaped an ancient physicalist theory making of pain, approaching the explanation of experiences through external elementary qualities, into a physiologicalist theory making of pain coming to 18th-century modernity, focusing the neurological materiality implied in such a qualitative conduction.

The writing invites to think that the characterisation of pain as a 'qualitative content' conducted through different continents, pores, filaments and channels, was being reshaped in the light of voltaic physiologicism towards understanding the very 'continent', the funnelling nerves, as properly qualitative. Working the continentality thesis interpreted through the propositions of Bell (Bell & Shaw 1868; originally 1811) and Müller (1835-1840), nerves were now observed as the centre of explanation. Specific channels, Q-fibres (substitute 'Q' by any specific qualitative evaluation, as pain or itch) and thus performing a specific Q-conduction. While buoyed up by the specificist foundational claim (ie, 'one perception, one receptor'), the thesis configured a proper account for the time, a material alibi for understanding neuropsychi-

atric conditions, and for accommodating the theoretical frame of physiological explanations into the realm of the technically observable (Cf. Berrios & Marková 2002). The introduction of a seemingly new responsible actor, 'nociceptors', as functional specific perceptrors of harm (Sherington 1903; 1906), resulted in clinical experimentalism as the thesis of qualitative continentality gained acceptance.

A brief contour of this ethnographic thread is exposed in two parts. Part I focuses the ancient seeds of entelechial qualitative concepts, providing an anthropological inspection on the worries that framed the physicalist interpretation of pain as a qualitative conduction that generated and reshaped through two geoaxes; a prior Eastern-axis that informed early medico-metaphysical inquiries, contacting a middle mediterranean area towards a Western-axis, that formally depicted the sensing qualitative contents until pre-modern theories of pain perception, further on configuring a tradition of scientific characterisation. Part II centres the 18th-century entry into modern materialism, observing the physiologicalist turn from qualitative contents to the thesis of qualitative continentality, ending with the propositions of Bell and Müller that supposed the starting point for future electrophysiology beginning the 19th Century —advancements reviewed in QIII, §2.

One conclusion attends the depicted conceptual turn as an ethnographic process of 'deformation', in Williams's (2012) terms, a process of shifting theoretical movements that brought deep consequences for the 19th-century onset of electrophysiology, influencing 20th-century instrumental metaphors of qualitative conduction, and fostering the use of 21st-century utilitarianism in fundamental terminology. A second conclusion wants to make visible the social and plural claims that conform our present theorisation of experiences, how physiological

examinations are not beyond epistemic, contextual and metaphorically stressed intuitions, which at the extreme of our clinical resources may also demand a comprehensive, integrative redefinition of pain in a community dappled with interpretations and medico-physical standpoints. These epistemic considerations, and the consequences for contemporary pain evaluation inherited by physiography and neuropsychiatry, are dealt with and discussed in depth in QIII, §3.

I — *Ancient Medico-Metaphysical Roots of Qualitative Physicalism*

The following sections present a motley ethnographic recovery of ideas harbouring different cultural traditions that occur to be joining with individual teachings from significant figures of the past. Such a recovery is not claimed to be complete nor causally-oriented; multiple reciprocal origins can be assigned, characterisations differentiated, particular epistemological identifications attested, but the ideas furrowing the history of early medical practices appear to cross beyond the borders of unified areas, coming to clear theoretical impressions that lasted for centuries. These generally come from an Eastern-axis that pledged into Europe intertwined by the Mediterranean sea cultures, framing clear and specific connections that have an anthropological weight for giving shape, further on, to clinical scientific characterisations, reorganised respected until the modern era by the Renaissance in anatomy, 17th-century physiology and 18th-century experimentalism.

. *The Split of Constitutive Elements. On the Metaphysicalisation of Pain*

The term physicalism is revisited in this chapter to assess how early explorations on the matter applied metaphorical descriptive and explanatory strategies of reification into

their identifications of qualitative experiences. Qualitative physicalism is judged to be present throughout ancient cultures in both geoaxes, configuring a tendency to explain conceptual, scientific worries through arguments that originate out of direct literality, usually externalising the inceptive root of human experiences into outside agents. This reduction ends up making the fundamental tenets of pain research metaphorical, the so-called metaphors of the living, chased, as criticised by many authors (Cf. Haraway 1976; Dupré 1993; Keller 1995; Cruikshank 2005; Chang 2012), by the limits of thought of the era and contextualised to their horizon. Such strategy informs of a metaphysical scenario depicting the ontologically figurative through the emotionally literal, passing the clinical, medical pain of a singular person through the metaphysical existence of an original pain that would refer not to the living but to the pain proper to the myths of creation and development which, having achieved to explore an event of universal separation from the whole into parts, start a mythical anthropological understanding of the elements of a cosmic (entire) identification. This process comes to synthesis (by naming the elements of a mythical ontological through reification into entelechies, physicalised and externalised as the first pre-chemical, pre-biological ideation of the observable world) and systematisation (into orthodoxies and traditions of understanding, into cultural standards and ritual proceedings). The significance of the division of the macrocosmic existence into microcosmic parts is its value on identifying the attitudinal shift from suffering unknown experiences to reasoning the causes of such suffering and generating cultural means for treating and dealing with it.

To the ever escaping origins of the Western-axis medical traditions, accepting this physicalism supposes to seek a concretisation of the worldly qualities, along with a reflection about whether these qualities are literally there, exempt

from organisms, or rather proper to the very agent who assesses the qualitiveness implied in perceiving contents.

As clear example of a physicalist concretisation serves the Empedoclean synthesis of the microcosmic elements into metaphorical entelechies. These, provided as sympathetic cultural and pre-chemical bases, formed externalised qualities with specific physical interrelations that, for medical explanation, conferred the grounds to the Hippocratic reduction of the bodily humours. As a contextualising synthesis of metaphysical attitudes coming from the Eastern-axis (especially seminal notions from pre-Buddhist Vedic physical literature, with impact in medical literature) and developing into Greek interpretations, and for that extent initiating further on Western-axis interpretations, the Empedoclean tradition stated a plausible division of literal physical elements constituting the worldly phenomena. By shaping a family of concepts in this style of descriptive distribution, there sprang another concretisation which was to satisfy a meaningful application to the clinical needs: the Hippocratic reduction, the careful concentration of the literal elements that constituted the bodily phenomena, the bodily humours, as actors and stressors of material change which were still entelechial contents, qualitatively oriented. Macrocosmic divisions of a metaphorical pain, in their roots, thus assist the clinical interpretation of the bodily pain through microcosmic disorder manifestations of qualities in the patient.

The Hippocratic reduction, from elements to humours, reaches an elegant edge between the medical and the metaphysical panorama. It attains to hybridise a metaphysical victimism towards the origination of the world, the metaphysical pain inherent in the split of the constitutive elements, and the intimate pain suffered by a singular person, the clinical pain. The reduction identifies a pain that worries the sick in search of a communally accepted ritu-

al, which serves for accessing to the centre of what is worshiped, in the desire that this effort changes the suffering scene unifying the metaphysical pain with the clinical pain. The ritual language of cancelling the effects of the world split into elements provokes a further movement towards understanding the value of treatment. Example of this is the requirement of the first step in the healing process, parallel today with psychiatric therapy, the 'breaking of the armour' covering the person's character that splits the self from the world, following Reich (2010) dissertation. The congenial factor with clinical ritualism is yet the same, launching a process of 'overcoming the split between the world and the self'. This reduction works identifying the physical assumptions about the world and translates them into the person.

This is no trivial movement. The system informs about a basic scientific attitude, the split of the generative whole and the generated part: on one side, the physico-mystically observable; the literal worry about what exists (inheriting an ontological claim), and how what exists is divided and classified (promoting a mereological claim); on the other side, the biologically, medically and therapeutically interesting (the classificatory, descriptive, explanatory product). This frame prompts the possibility of humours taken as a reduction from the worldly schemata to the bodily schemata. The split of matter into elements, and its incorporation into medical inquiry on qualitative experiences, supported its further destiny opening the door to the early chemical, anatomical and clinical-therapeutical research.

Mythical medico-metaphysical understanding senses the worries on the origination of life, will and the human role of caring, a progressive conscious awareness of cultural societal values: the ethical meaning that respecting, understanding and facing the pain of the other has to build the roots not just of medical theorisation and therapeutics, but of social and cultur-

al spaces. Religious explorations favoured early descriptions and explanations on why people suffer and how to relieve their pain. The clinical pain, the pain of the person, faces the metaphysical pain of the superior values, a cosmic physicalism that took the metaphysical meaning of the religious cult and formed the physical understanding of it.

Through the physical elements of the mythical systems and syntheses, relating the qualities that appear so abstract in emotional experiences, the rite can manage them to sympathetically re-meet the person (microcosmically dysfunctional) with the mythical origin applied to its creation (the macrocosmic order). The pain of the person reflects the disorder of the metaphysical through a metaphysical pain. This cosmic pain needs to be understood in a cultural fashion, as a liminal concept that served to expose a causal reason for the social and pre-scientific relevance of the cult and the recreation of the universal meeting of the person and the natural order by the rite: the metaphysics of pain as a macrocosmic origination of separate elements gives a role to the clinical pain of a person, that through the rite re-unites, re-creates, re-forms herself and her constituent microcosmic parts in communion with the ritual procedure, by which the person returns to a stage of health. Physicalism instrumentalises explanation through entelechies that bear the burden of qualities, qualitative mediators that must be considered the first glimpses of a medical, biological, chemical, systematic organisation of reasoned pre-scientific conclusions, emerged from demands of explanation delivered through cultural necessity: the overcoming of pain.

*. Eastern-Axis Physicalism.*

*Introducing Qualitative Content*

It is now generally accepted that the origins of this reduction are not however of Greek provenance. Contemporary archeo-ethnogra-

phies have their reasons to track them back to Eastern ritual mysticism, spotlighting the ancestry of the critical polarisation between the private person and the public ambiance, a metaphorical, mythical, metaphysical presentation of the cosmic victimism for pain that gives its social and cultural role to the cult reunited by the rite (a therapeutical reunification). These medico-metaphysical operations are thought to be fairly influenced by Indoeurasian thought through formal discussions in pre-Vedic considerations, and further Vedic literature (~1200-600BC, Cf. Mylius 2015, 30-33), beginning the incubation of later texts through oral tradition by the end of the 4th millennium BC (Levitt 2003, 356).

Archeologically and geographically, a contemporary reading of this advancement through the Eastern-axis interpretations of pain can set a plausible scenario where the primary seeds for the qualitative division of the worldly elements, and its medical impact, grew within a slow and progressive mysticism from the pre-Harappan movements through Bactria. Rgvedic oral, non-literary traditions proper to Indian civilisation in development (Cf. Dales 1966; Burrow 1975) could have been sources of influence for peri-Indian regions (Cf. Agrawal 2005), which appear to have affected the expansion of seminal ritual notions along different out-migrations (Cf. Hasenpflug 2006). The seeds, or at least many traits of the origins of said physicalism may be ethnographically original to this geographical context. Inferring the movements by geogenetical studies, genetic traces coming into India from Aryan ancestry before 600BC are mainly slender (Underhill et al 2010), identification that joins the fact, as Cavalli-Sforza's group concluded, that cultures inhabiting the Indian and peri-Indian context were seemingly receiving limited genetic heritage from outsiders since the Holocene, around ~10000BC (Kivisild et al 2003). These movements and the proper Mature Harappan urbanisational civili-



sation (c3000BC) could have materialised and merged with the Indus-Sarasvati River Culture sites, informing with much probability through the later literary Vedas, migrational clashes, territorial disputes, a mentality that shaped new regional empires and trading chains with other cultural niches, developing an extensive textual compilation well preserved and kept until today.

The foundational split can be appreciated very early in the peri-Indian brahmanic tradition, its cosmivision and the ethical implications of the mystic, philosophical and epistemological inquiry on the metaphysical victimism mentioned above. Textual compilation provides with material history this argument, framing a brahmanic interpretation of the inceptive macrocosmic pain in a metaphorical pain attesting having split the world and the self, figuratively expressed by the death or the separation of one of the deities into matter or being or life. To the brahmanic ancients, and further recompositions in other ritual literature, particularly through the Upanishads, a general conviction about the world plays with a rhetoric device: suffer and sorrow are implicit and indispensable features of the origination of the world. This agonistic trait, which is present in a vast majority of myths concerned about the realisation of the world, formalised with time into a particular cosmogony, a genealogical story about the beginning of the cosmos and, thus, the beginning of the suffering implied in such a birth. A characteristic example of this victimising cosmic pain occurs with the topics of elementary division, of the water and air, the sky and soil, the light and murk, etc. All cosmogenic divisions tend to include some ethical dilemma. For instance, in Rgveda, Chant I.32 (Cf. Samhitas in Mylius 2015), the split of the water and the mountains by the death of the dragon Vrtra (murkiness) by the bearer of the thunder (brightness of the sky) Indra, holds the sacrifice of the beast to its ritual, ethical conclusion: the qualitatively painful merges with the qualitatively therapeutic,

which from an anthropological standpoint is a photograph of cultural, social demands of explanation upon the pain of the metaphorical victim, a relation between the cult of the universal origination of the observable world, and the ritual implications of having killed, sacrificed, terminated with a macrocosmic integrity.

As an exercise of comparison, this division brings moral implications to the Greek extraction of *aither*, *okeanos* and *nyx* (brightness —the substance of the stars—, water and the murknight) developed in different cosmogonies (Cf. Kirk, Raven & Schofield 2003), as the underlying meaning of this separation retakes the Eastern-axis myth to some extent. The separation of constitutive elements shows a previous condition that uncovers itself as a metaphor: the whole as a victim of a mutilation of existence into reality, that indeed persists in some traditions and dismisses in others.

The fact that a fundamental sorrow is implicit in these basic tenets makes early Eastern-axis concepts unable to escape the characterisation of medico-metaphysical doctrines, through which a proper depiction of pain will thus advance. As for many other early cultures, through the contact with deities (being, in many forms, metaphorical recreations of such death or termination of will: from sacrifice, to gifts to prayers, to substance deprivation and corporeal mortification) a person led by some kind of sorrow will finally overpass the metaphysical division and come to a recovery. The cultural role of the rite (re-unifying practice) affirms the need of the cult (descriptive, explanatory practice): the therapeutics of overcoming the division of the bodily microcosm through recovery institutionalises the unification of the macrocosm. Such recovery is supposed to work making patent the relationships of the parts and the whole through worship, and this point allows to situate a proper concept of the microcosmic 'self' that is being related with the macrocosmic. This interpretation alludes to the medieval analysis

of the meaning of the term 'religion' through the revision of *re-ligare*, re-attach, in essence a form of communion, a manner of putting together what has been split.

The Upanishadic overcoming rite makes the self (*atman*), individualising the person (*puru-sa*), to be identified with the absolute possibility (*brahman*, the mystic all-spirit) building a form of idealism. The atman-brahman doctrine developed into Indic convictions identifying the one with the other in multiple literary passages (eg, Brhadaranyaka Upanishd, 3.9: 26). The explanation of this unification supports the underpinning idea that early Eastern-axis doctrines reproduce a ritual value, this is, they bear a clinical seed that observes the therapeutical import of overcoming the fundamental split, cosmogonic and personal. Thence that recovery is both theological, of the divine physicalism externalised, and clinical, of the person that contacted the divine through the rite.

Their original concept of a cosmic sorrow is absolutely required for a therapeutical pre-occupation on the Eastern-axis theory making of a personal sorrow. It led to the realisation of the world through a cosmogony, based on the beginning of the world by the separation of elements from a 'panextant', an all-existing undifferentiated form, and its materiality ends up expressed by the death of a figurative victim: a metaphor for the lost panextant. The recreation of the sacrifice during the brahmanic rite has its meaning on this metaphysical victimism, on this fundamental split. In that sense, the maturation until such physicalism is able to give an explanation for the grounds of an aware experience of personal sorrow (mental qualitiveness), and its overcoming (through medical welfare and ritualism) implies a clinical interpretation. The openly medical descriptive and explanatory strategies developed strictly later through materialistic and idealistic theorising, forming divergent perspectives known as *darshanas* in the peri-Indic Eastern-axis. From those, the re-

interpretations of the cosmogonic victimism, the metaphysical sorrow, the sacrifice with its significance for any theory of recovery, and the explanatory strategies for characterising the physical origins of a personal pain, animated the growth of properly clinical traditions.

. *Some Eastern-Axis Systematisations.*  
*Theorising Qualitative Sensing*

The Ayurveda and Yoga epistemological interpretations were two of the first notorious theories of knowledge concerned with perception, experience and feeling, and started a new form of medical, anatomical and therapeutic understanding with systems that flourished further on merged with metaphysical notions, however impinged through an epistemological disposition (Cf. Meulenbeld 1999-2002). One of those systems, the Samkhya school, can provide the exposition of these matters with a wide and deep perspective that, contacting the Western-axis thinkers through numerous enclaves along Indoeuropean borders, introduced preemptive ideas influencing medico-physicalism in early presocratic thinking. Multiple systematisations tracking Samkhya origins unfolded, in several and reciprocal waves of cultural interaction, until the formalisation of a medico-physical tradition of qualitative experience through physicalist perception in the Western-axis took place.

From the six major darshanas originated, prompting into Hinduism, the early expansion of Jainism, Buddhism (breaking with the brahmanic sacrifice), and other epistemic disciplines, the seeds of the Samkhya systems are very attractive in regard to the theories of perception and delusion. The origins of the Samkhya vision could be oriented circa 700BC (Cf. Mylnius 2015, 218). One of its most recognised literary systematisations was held by the 4th CBC by Isvarakrsna in the 'Samkhyakarika'. However, many of the Samkhya tenets related with experiences of perceptual qualities are presented along the the-

orisation of Uddalaka Aruni (~640-610BC), a critical figure of the time, as his interpretation of perceptive faculties encouraged a first dispositional division among the elements of matter.

The division suggests that the matter underpinning nature (*prakrt*) —the organisation of what is, a distant relate to the Greek *physis*— comes to form through an eternal transformation, while the soul, the spirit, the character, the person (*purusa*) comes at being in absolute unity and stillness. The conviction that the soul was aware, percipient and still was reviewed with an epistemological disposition by Uddalaka in the ‘Chandogya Upanisad’, influenced by the diversity of millennial brahmanic understanding. The concept proposes that the being (*sat*) is not to ‘come to form’ derived from what-is-not, but derived from what-is (recalling later Parmenidean thoughts). In this explanatory strategy, the elementary division prompts with the mythical need of a positive panextant that disintegrated into a plurality of beings, and in so doing, the argument actually reforms a concept of the self implying the presence of materiality. Such matter is formal just in an instrumental sense, proper to the argumentation, and defined in very different terms if compared to commonplace materialism: Uddalaka exposes materialism as a vector for qualities (hence the process of qualitative physicalism), material principles with ethical and metaphorical meaning that conformed the presence of three elements (ember, water/clouds and earth/soil). Elements are disposed as constituting a sensed materiality. Uddalaka would adduce in an analytical fashion, that senses were responsible for the integration of such physical elements: this event creates the grounds to explain the physical manifestation of qualitative sensing as if materiality was poured from the outside, and then integrated towards the inside through the self by implying matter.

Matter is systemically implied in sensing. In this particular sense, the sensed matter would

be attributed qualitatively active itself into what is being perceived by the one who is able to perceive it, and this factor initialised the idea of qualities (material elementary needs) as transported through and by the body as an explanation of the proper experience of such qualities. The influence this first medico-metaphysical exposition had in Greek pre-philosophical notions is appreciable contrasting it with the attribution of poroi (pores, channels) for imagination in Alcmeon’s medical characterisation of qualitative physiology, or with the concept of *syneidesis* (roughly translated as imagination, originally ‘faculty of integration’), used to explain the qualitative experience as a process where conceptual contents merged. The fact that the microcosmic body serves as an actor for the integration of elements conforming a segregated macrocosmic entirety resolves the previously referred identification of the self with the nature (*purusa-prakrt*) as a direct evidence of analogical thinking between the medically explainable and the metaphysically adduced, to which the sense of pain in the microcosmic-macrocosmic integration of elements would finally tend to explanations on order and disorder upon which the body acts as a funnelling pseudo-actor, unable to wholly resolve the identity, thus requiring the therapeutical procedure of the rite to finish the integration of elementary parts.

Uddalaka defended a material monism that developed in an elementary physicalism. This position stressed the Samkhya perspective to grow from a dualist-idealist vision of the split (*purusa-prakrt*, person-nature, self-matter) to an elementary recognition of materiality as divided into three qualities (*gunas*): well/complete, passion and heaviness/murk. In their transformations (Cf. Jacobsen 1999), qualities expanded and reshaped what the soul understands as formal matter, a very delicate analysis that gives as a result a physicalist theory of qualitative perceptions, experiences and feelings. Through Samkya’s ethical and spiritual im-

plications, the Yoga system achieved to rethink the very early philosophy of action (*karma*) introducing through the postural and mortifying modification of the body (aesthetic and dietetic privations) a materialistic instrumentalism, an alibi to the sensual perceptions, through which to liberate the self from the passion and the heaviness. The therapeutical utility of this cosmological perspective is clinically present in the system this way.

The contextualisation of these notions into the Western-axis through the Eastern Mediterranean sea composes multiple traditions, many metaphorical carriers of preceding sources that overflow the limits of Western-only configuration, and loose the virginity of ideas in what has been called the Near Eastern tradition, that tracks to the Old Testament, Hittite and pre-Hittite visions and back to Far East (Cf. Pritchard 1969; Frankfort et al 1946; Dodds 1962). Uddalaka achieved a clearly proper logic of elementary compositionality, a fundamental theory of perception that further on was revisited. This conceptual thread will spread beyond Indic characterisations into multiple medical traditions. On account of the Western-axis, the division person-nature, self-matter corresponds to a systematisation developed by Greek formal philosophy (especially through Thales, Heraclitus and the Pythagorean incorporation of the notion of *metempsychosis*, the transmigration of the soul) much later, configured in reciprocal relation through millennia with Eastern-axis episodes in brahmanic and pro-Vedic thinking.

These ideas on qualitative perception were taken by many cultural diversions in the expansion of preexisting Eastern Euroasiatic civilisations, from Indic and peri-Indic, Vedantic, Buddhist, Jainic and their Chinese re-readings, to the Middle East, Egyptian and Babylonian pre-Judaic traditions and beyond. These started to influence how to analyse the metaphysically intrinsic contents between the ambience and the body in a properly medical manner.

. *Western-Axis. Qualities as Contents of Perception, Experience, Feeling*

Approaching the Eastern Mediterranean, some of these diversions landed both into the early physicalist presocratic physikoi in their relationships to philosophic metaphysics, and into the mystic inquiry through the pythagoreans (Cf. Zhmud 2014; Joost-Gaugier 2006; Cf. Huffman 2014, for a history of incoming ideas in Pythagoreanism). The ‘Western-axis turn’ into Greek medico-physical thought, furrowing the anatomical inspections in Alcmaeon of Croton (~500BC), and revaluating the Empedoclean (495-435BC) characterisation of the four basic elements (or ‘roots’, as transcribed as such by Diels in 1952) underpinned Hippocrates’s (460-370BC) reduction.

Before the figure of Alcmaeon, the qualitative physicalist tradition becomes fuzzier in this geographical context and, if present, not precisely medically oriented. Theologisation is still inscribed in Thales’s (~624~546BC) explanation of worldly events, and Anaximander’s (~610~545BC) material principle of un-elementary (*a-peiron*, ‘un-defined’) origination coincides with the earlier brahmanic exposition of a panextant cosmogony (*supra*). Their implications in qualitative perception are loose, nonetheless present from Alcmaeon on Greek philosophy, and revisited further on by stoic interpretations on the elementary divisions of matter (Cf. Kirk, Raven & Schofield 2003, for historical presocratic itineraries). As for the case of Anaximenes (~590-528BC), being true he opened a metaphysical recreation of a divisive *causa materialis* through the element air (*pneuma*) as a principle of composition, the destiny of such idea was not in the interest of application of medicine, but of cosmology, and thus the tradition of qualities in conduction appears not to derive from his approximations in a direct form. The same case can be recalled for Anaxagoras’s elementary multiplicity. In this sense, the sug-

gestion that distinct waves of influence exposed different people to different cultural theorising, first from the Indic to Egyptian, Babylonian and Hittite East, and from there to the Greek logicians in Miletus (Cf. Pritchard 1969), and later from the Indic to Eastern Mediterranean and there to Greek medical physicalism, is a trans-localist reading to keep in mind.

Alcmaeon of Croton (~500BC) is claimed by many historiographies to be the first Greek physician writing about the brain as the vital centre of the organism, contrary to the heart, in Aristotle and Empedocles. There concludes a central idea: there must be bodily funnelling morphologies supposed to convey qualities of material objects into the self of the human being; in his suggestion, it would be the case that the brain is judged to work through a proto-idea of functionality in nerves. Theophrastus's account of Alcmaeon describes how, excising an eyeball, he depicted marked channels (the optic nerve) that he described with the term *poroi* (pores). Through such pores, very different qualitative sensing effluences ('elementary powers': dry, humid, etc... Cf. Huffman 2017) would have been 'poured' by the objects to the brain (Lloyd 1975) informing the soul from the phenomena perceived and, thus, coalescing together in a central understanding (*syneimi*, with an original sense of 'integrating', 'bringing together': Cf. Solmsen 1961). The parallelism with the Eastern-axis influence is to be detected: indeed, the same powers that performed the qualitative induction of perception were responsible to Alcmaeon for explaining the origin of diseases (suffering) and, thus, their readjustment will come into wellbeing (health-recovery, balancing a therapy of overcoming). Macrocosmic disorder of elements explains microcosmic dys-functionalities in men. For what has been inquired, the inspection of qualitative perception keeps an orientalism; certainly not an ultimate origin in Indic theorising, but plurally merged with proper Western regionalised beliefs, and

close contextual convictions. Being it as it may, still for the ancient theorists, there is no clear explanation why or how such conduction takes place.

As time flows, some perspectives jump towards an answer to how these qualities were introduced from raw phenomena to inner imagination, building the argumentary of entelechies to explain the process of conduction: the tradition of qualitative conduction. This section will review how Empedocles's division of the multiplicity of phenomena, and the Aristotelian partial adoption of some of his concepts, that transcribed into the peripatetics and later to the stoics, follow a hermeneutic thread that shows an itinerary of reutilised ideas from which to establish a well defined entelechial concept in modern history: the pneumatic-cartesian conviction of qualitative conduction, which will operate until the physiological turn in the 18-19th fin de siècle, where a modification befallen framing the appointed 'difformation', applying Williams's (2012) terms to this analysis, from qualitative contents to qualitative continentality.

Empedocles's (495-435BC) geniality appeared to be the transcription of some of these Eastern ideas into the context of Greek theorising. He suggested to reunite a natural ontology (elements, from which to retrieve the underpinning worldly forms into an organised qualitative mereology of metaphors) with a theological predisposition to the Greek pantheon (powers, deities, with cardinal teleological qualities, wills and very recognisable specific characters). His intuition was in good connection with the discernment from the Miletus School that the world is divided out of a chaotic panextant, recognising the cosmogonic act through an all-existing form that submitted into realisation. The obvious migration of the idea through the Eastern-axis understands, thus, the beginning of the world by the separation of the elements as in the brahmanic impression of Uddalaka's systematisation of elements.

Empedocles exposes from this cosmogony the specific characteristics of the different existing phenomena, which are composite realisations of elements, and therefore are presented to be links to our human recognition. Similar myths of the realisation of the world can be found too in Parmenidean readings and much later in general mystical and gnostic interpretations. The innovative feature in this relationship that Empedocles's mysticism suggests is that there appeared elements as a middle link. His view made to coincide both, the worldly elemental with the transcendental power through practices of physical discovery (externalisation, oriented to the outside: the understanding of natural phenomena), and practices of attention and healing (internalisation, oriented to the inside: self-awareness), both intimate and communal, allowed through such links. These practices presented the beginning of a chemical, physical, biological and medical understanding of the world and the human being, in a reconsideration of the ritual appointed by the metaphysical victimism. Thus, the elementary links organised the cosmogonic split. To this account, the significance that this perspective introduces for theorising about suffering and pain explains the reliance on therapeutical practices: eg, the tradition of 'Incubation'. This primitive form of meditative rest and retirement to solitude was held to help bodily healing through a mental doctrine of overcoming: with a centre in Epidaurus, thermal therapy through steam baths shows the connection that the belief on elementary empowering relationships had as a basis for underpinning the very process of recovery. It is of no coincidence the usage of steam to empower healing, as so pneumatic interpretations will be a critical starting point for framing the elementary mysticism of qualitative contents into the later physiologism (*infra*).

Interpreting Empedocles, different associations of deities, as portraying qualities, and elements, as primordial links with the ground-

ing forms, have been on debate: Zeus–fire–air; Hera–air–matter/earth; Hades–air–water, etc... (Cf. Kingsley 1995 for a deep recension). This mystic association embeds an important remark for qualitative conduction: the relationship between a 'deific power x', and a 'natural depositary element y', promoted the creation of entelechies naturalising 'y-particular-element as x-powerful'. Of singular import for the case at hand was the entelechial partnership *aither-aer* with air as an element of virtue, which initiated the teleological predisposition of vitalism in early medical traditions: air as vital force for explaining the living, and of course, the nervously active.

On this reading on the transformations of the concepts, some works (Bollack 1965-69; Kingsley 1994; 1995; 2008) have indicated that, in avoiding interested medieval, scholastic and 19th-century recreations on the matter, an original possibility could grant that Empedocles more certainly understood the relation between Zeus (bright, almighty) with the element air (which corresponds to the air 'that flows from the ceiling of the world to the circumscription of earthly beings'). In further revisions, through later reinterpretation the stoics started a sounding re-comprehension of Hera (life-bearer) with air, and *aer* as an elementary doubling entelechy, a metaphorical doppelgänger in their interest of a teleological duality: putatively, the stoic circles submerged the Empedoclean element *aither* with the figure of Zeus ('masculine' and heated) and surmounted the entelechial *aer* ('feminine' and humid) to Hera (maternal identity). It has been considered that Empedocles did not use the term *aer* for air, but *aither*, and the classical, homeric meaning of *aer* for mist and steam. For allusions to the therapeutical grounds of steam baths empowering healing through the tradition of Incubation, if the entelechial air supposed vital was taken by heat to motion (wafting steam), a recovery into vividness would be achieved applying sympathetic principles that

would favour meeting the macroproperties of an elemental order with the microproperties of bodily dysfunctions.

Kingsley (2008) has suggested that the transcription of terms was of Aristotelian hand: in preemptively using such correction of terms, he would attempt to reconfigure the Empedoclean mystic concepts with a philosophical inspection (Cf. Kingsley 1995 for an explanation of the original 5 texts with Empedocles's allusion to *aer*; for their critique Cf. Kingsley 2008, 3: 48-58). This revision will end affecting the stoic consideration of *aer* as an extraction of a quality from a qualitative wholeness through the utility of the four elementary roots introduced in medical practices by the Hippocratic humours tradition. It is assumed that the body of literature produced by Aristotle, with a posterior peripatetic influence, inherited such ontological vision and transcribed it into the formal organisation of the living beings, merging it with the need for an agency attribution, a 'governing soul' (yet a very ancient idea in Greek medicine, already present in Alcmaeon and the Miletus School, plausibly coming through Anaximander's *arché*). This concept was later expanded in different ways by the six most important clinical cores of the Mediterranean: Rhodes in Greece, with Knidos and Cos in the Dorian Hexapolis, current Turkey, Agrigento in Sicily, Croton in Italy, and Cyrene in Libya.

The Aristotelian (384-322BC) interpretation of such physicalism, by assuming a twin nature of substance —the hylemorphic (soul-matter) concept—, maintains in 'De Anima' (1.4, 408b11) that should be the man with his soul and not the soul by itself what is angry or pitiful, allowing the latter to come inside the former, thus making the human being basically an agent: in this sense, experiences in animals and humans are an act of agency, enacted by imagination, and informed through the soul (Cf. Knuuttila 2004). As it can be seen, the use of an entelechy reaches well the connection, pointed

out before as the turning point for Empedocles's perspective, between the external quality and the inner qualitative sensation: an explanatory alibi for qualitative conduction.

The relation between the peripatetic soul with air could have arisen in accordance with Aristotle's biological approach to the brain, that he conceived of a redundant organ, formed by exceeding phlegmatic accumulations, functionally characterised as cooling blood. This certainly was of interest for the stoics given its relation with the concept of *pneuma*, the stoics interpretation of air flow and living pulse. To that extent, a slow organisation of ideas was prompting brain functionality and nervous activity to be explained with an analogical parallelism to the ancient concept of vessels communication. This thesis was previously lighted by Alcmaeon, in his defence that through arteries flew air instead of blood. With such an underlining idea of the brain, air funnelling, and the qualitative meaning of the element as a vital force, little time was to be awaited for those conceptualisations to fuse.

A clear example that identifies this transition can be found in the experiments of Praxagoras of Kos (~340BC), developing the idea that veins funnelled blood to nourish the body, while arteries channeled energising *pneuma*, causing sensation. It is to mention his defence (Cf. Steckerl 1958) of eleven principal elements, which is not to surprise as the Empedoclean division and the Hippocratic adaptation through his reduction were being created at the time: beforehand, the pre-systematised orthodoxy assumed a variety of qualities without linked systematic powers, elements and material relationship, as exposed above. The incorporation of these ideas to the nervous theory was led by anatomist Erasistratus of Chios (304-250BC), who differentiated the *pneuma* running the hollow nerves that convey qualities to inner sensation into two forms, presenting thus the vital communication model between blood ves-

sels and nerves: breathed air was to be mediated by the left heart ventricle distributing it as ‘vital pneuma’ (*pneuma zotikon*), part of which, when landing into the brain, would transform into ‘psychic pneuma’ (*pneuma psychikon*), facilitating imagination, cognition and motor faculties as animation (Cf. Knuuttila 2004, 58, for a deep examination).

This was a step that helped to form the peripatetic-pneumatic conception of nerves by Alexandrian physicians under the influence of stoicism. This psychic pneuma will later be described by Chrysippus of Soli (279-206BC) as a special type of ‘corporeal spirit’, manifested by having a particular degree of tension (*tonos*). Through the stoics (from Zeno of Citium to middle and later stoics), the binary constituents of the hylemorphic theory of agency were pivotally driven to an integration, rebuilding the soul a physical substance, pneuma, entirely embodied (Long & Sedley 1987) and organised by a central faculty (*hegemonikon*) which merged outer phenomena poured into a central system (von Staden 2000). No ordinary attempt was held here, for this explanation gave space to interpreting that things from the external world appeared at us organised by the pneumatic hegemonic faculty, incorporated into human mind as appearances (*phantasiai*) through the same substance: nerving pneuma.

The critical point of such interpretation comes with qualitative physicalism guiding early pre-scientific theorisations to infer that what makes an experience, a perception or a sensation qualitative as it appears to the human being, is in fact the very quality transported through the nerve: an entelechy. A propagation of these original ideas through compilers came across Roman times through the 2nd Century without groundbreaking anatomical dissectioning: Galen (130-210), by identifying the arterial function as carrier of vital spirits (blend of blood and air: *rete mirabile*), actually invited the pneumatic characterisation of this qualitative physi-

calism to disseminate for centuries in a tradition of qualitative conduction.

. *Inclinations towards Modernity:  
from Anatomism to Physiologicism*

Example of a memorable compiler on the precise case of pain conduction under the perspective of the nerving pneuma was Nemesius of Emesa (~400). Nemesius’s descriptions of the functions of the organs traces a difference with Galenian ideas in the fact that for Nemesius it is the brain, centralised in his posterior ventricle, the responsible actor for merging the psychic pneuma with the physical impressions, then transmitting the faculty of imagination to that of thinking, memory and reasoning. The faculty of sensing is to be thought apart from those of cognitive power —as he identified experimenting with people suffering from different brain diseases—, so-called dianetic (*dianoetikon*) faculties. A visible example of the schemata used by the qualitative conduction tradition in the presence of no channel to perform conduction, is his depiction of the sense of smell in ‘De Natura Hominis’ (Nemesius, ed. Morani 1987, Ch. 13; Ch. 11), where Nemesius sites the exception of olfaction for its sensation would not require any nerve, but the physical qualities of elementary roots should go directly to the brain through evaporation of odorous substances. His strategy is evidencing, however, the fact that contents of experience are not of internal origin. The qualities are proper to what is contacted, and agency is of recognition of those qualities by bodily conduction or, in its stead, by the hegemonic sensing faculties of imagination, a revision of the previous arché.

While reasoning the forms of distress (*lupe*), Nemesius seems to insist in the fact that all of such family (grief, anguish, envy and pity; Cf. Nemesius, ed. Morani 1987, Ch. 19; Cf. Ch. 21 for fears and angers) are internal apperceptions of a pain (Cf. Knuuttila 2004, 100) that is caused



by evaluations of what occurs to oneself or to others. In this relation, as sensations come apart from reason, pains are first basal to fit with correlations suffered in different organs (stomach, liver, heart...), and then reported to the central system that integrates the sensation with imagination (*phantasikon*, the centre of perception), leading to its fate in reason and awareness, for they can be divided into spirited and appetitive faculties. Pain thus entails two processes: the physical phenomena of the bodily changes, and the psychic sensation associated with it, which comes to be fatal or beneficial. This frames a pleasure-pain theory that prompts the concept of *passio*, what weights the soul, into Roman times. Nemesius borrowed certain influence from the Platonic tradition of fantasy, or imagination, as exposed in ‘Timæus’, where pain was not to be conceived of as an unitary percept but as an emotional configuration evoked to the men by an unusual intensity of stimuli—the reason why Plato has not been reviewed as an exponent of the tradition of qualitative conduction is because his identifications of perception do not grab the material entelechies that conduction in medical phenomenology characterises due to the peripatetic interpretation of hylemorphic agency—. Since Nemesius was a very pluralistic compiler, but Christian, and its pairing platonism was of growing acceptance in the early Middle Ages, there is no surprising effect in reviewing an integration of such calibre in his pneumatic description.

This analysis will summarise late Roman and Medieval times until the reinterpretation of qualitative conduction, for the argument on the roots of entelechial explanation has been fairly attended in the previous sections. Multiple commentators, translators and incorporations to medical classical epistemologies helped to keep alive plenty medical traditions: to name a few, Avicenna, Hunayn ibn Ishaq, the translator Constantine of Africa, Ali ibn al-Abbas al-Magusi, or John de la Rochelle.

For what affects Western medieval medicine, literature paralysed anatomical inquiry through a well known morbid estrangement towards dissections. Medieval theorising seemed to have lived off the same concepts as exposed by Galen and Nemesius, and reinterpreted in two main traditions, which is a topic deserving a dissertation by its own: one tradition, by uncovering the *pneuma* as spirit, built it on the Augustinian turn through the platonico-augustinian school; the other physicalising qualities by reinterpreting the Aristotelian hylemorphic theories since the 13th Century, quoting and adapting them through Albertus Magnus and Tomas Aquinas. As the Renaissance physician Niccolò Massa (1536) criticises, «anatomy was forgotten and theories tergiversated», and it was actually the case in 1543 when Vesalius re-introduced human dissections and expanded the visualisation of the human body through his ‘Fabrica’ that, counterintuitively, continued supporting the idea of aerial spirits as guarantors of mental and nervous activity. When trying to break Galen’s limitations in comparative anatomy and, at the end, the Hippocratic tradition by that time defended by Sylvius and the French school, the pneumatic seed resisted to a farewell. Qualities were embedded into the nerving *pneuma*, merged with medieval interpretations of the spirit as an explanation of both, movement (expanding the animal body through space) and experience (expanding matter through the body and imagination).

A modern continuity sprang strong not for the explanation of senses, but for animation: with the expansion of mechanicism, the concept was conventionally adopted in the 17th Century. In Descartes’s ‘De Homine Figuris’ (1662, following his frustrated date of publication in 1634, translated from French to Latin by F Schuyll) a palpable entelechial exemplification of the perceptive process is exposed, not to explain the reception itself, but to explain the reflex theory where spirits are mechanically evoked (Norman

1991): with the example of perceiving and reacting to fire, it is interpreted that minute parts of the flame would reach the skin and track from there a thin filament (that will coincidentally figure with the letter C in La Forge's classical drawing of the nervous reflex), which would end in a porosity at the brain opened to the pineal gland, that he identified floating in the ventricles. Medieally elegant, the animal spirits, distilled from blood and the gland (as revisiting the Galenian *rete mirabile*), will then be transported to the muscles, withdrawing the extremity from the noxious fire. Furthermore, the reflex will depend upon the filament's tug: if it severs, pain (*doleur*) occurs, if it breaks not, tickling (*chatouilles*) will be aroused. Hence it showed pain perception indistinct from a reflex, avoiding any explanatory attempt at reception, as for why breaking the fibre causes a proper destiny of pain. It is a curious fact that some form of agency to the continent, the channel, was here putatively expressed, as the conditions of the filaments, more precisely their integrity, for conducting animal spirits played a slightly responsible role in the final sensing process.

However the Cartesian inspection, as anatomical experimentation advanced, a wave of physiologism was starting to approach against the suggestion. The scaling confrontation between entelechial mechanist (Cartesian) explanations and autonomous (non-pneumatic) mechanicism in characterising medico-physical grounds presented similar problems in the physiology of animal motion too (Cf. Jaynes 1990; Cobb 2002; Jackson 1970). In Amsterdam, J Swammerdam's 1667 dissertation contributed with an important issue against the filament tugging entelechial theory: two differentiated, specialised systemic organisations were to be necessary, one for sensory reception and another for motor enaction —later, this distinction aroused the so-called Bell-Magendie Law of Specific Pathways, as Cobb (2002) argues quoting Pubols's (1959) study on the figure.

Swammerdam's experiments with animal muscles (heart and thigh), although inexact in his interpretation, released one of the most influential discoveries by showing that it was an unintentional irritation of the nerves what contracted the muscle, instead of being air convulsion (the pneumatic bet) what moved muscles from within. The later publication of Swammerdam's (1758) '*Biblia Naturæ*', invalidating the Cartesian hypothesis, managed to expose that no spirits were animating any motor systems through the nerves. Then, as physiologist A von Haller inquired, the cause of such irritation, if not spirits, was to be offered (Hall 1951, 287).

## II — *Modern Medical Roots of Qualitative Materialism: The Physiological Turn*

With the gauge of post-Newtonian and Lockean views, some 18th-century perspectives organised around neurological associationism and vibrationism. Associationism was first based on the relation of two impressions (and lately on the connection of stimuli and responses) that led to habituation, memory and intellectual cognitive faculties. Vibrationism relied on forces that attuned nerves vibrations and fostered their functionality (for a thorough discussion, Cf. Jackson 1970; Smith 1987). This second part will review in two sections the way associationism and vibrationism, as the main theoretical frame for materialist interpretations on the functions of the nervous system, appeared to contribute to ground an epistemic turn from physicalist qualitiveness to physiological qualitiveness: the thesis of continentality —this turn is commented and assessed from an epistemological standpoint in QIII, §3—. In adducing that no pneumatic agent was necessary for conduction, the continent, the firm, solid nerve was claimed to bear the burden of quality, transposing from modern times the medical roots of 18th-century theories of mind in sufferance and madness, and to 19th-century neurophysiological experimental theories of pain experiences.

. *18th Century. Interpreting Irritation:  
The Turn to Physiologism*

Physicians like D Hartley and W Battie started to reunite certain familiarity with those concepts for explaining the regular foundations of thinking and feeling, and confronting their neurological clinical bases for understanding their accidents (symptoms depicting distress, both physical and mental diseases). The British philosopher of neurology and physiology, David Hartley (1705-1757), defended that the strength of the vibrations along the nerves inside the brain was responsible for influencing the mental outcome, and this seemed useful to explain functionality and neuropsychiatric dysfunctionality through changes in their tone and force, for which he claimed in favour of the existence of ethereal medullary substances transducing such vibration in a qualitative sense (Cf. Allen & Hartley 1999). For the English physician William Battie (1703-1776), the recognition of material physical forces meant that the pneumatic hypotheses were invalid to explain those same processes, thus he «rejected the view that the brain was a gland, that nerves were hollow and that sensation was due to the circulation of a nervous fluid: the ‘medullary substance’ was solid and sensation occurred as the result of pressure on the nerves.» (Berrios & Marková 2002, 632). Interestingly, the historiographical thread seems to point out that nervous irritatory-vibratory explanation and the pneumatic entelechial explanation grew in parallel for centuries.

As applied to basic research, electrical experimentation took advantage in the 18th-century medicine (Oester & Fudema 1969). With the invention of the Leyden bottle in 1745, numerous researches on nervous electricity developed the understanding that electrical pulses facilitated cellular irritation —as those applied to animal anatomy set by Galvani in his 1791 work on frog sciatic nerves and motion; or Walsh’s

and Hunter’s unpublished discoveries on fish muscle stimulation. New forms of mechanicism and materialism were rising (Cf. Yolton 1983), and even vitalism (a perspective for which life and kindred phenomena are based upon a vital principle distinct from a physico-chemical one) adopted a new form through these concepts (Cf. Wheeler 1939). For example, Étienne-Jean Georget (1795-1828), disciple of Philippe Pinel (1745-1826) and Jean-Étienne D Esquirol (1772-1840), was particularly influenced by anatomist and biologist Xavier Bichat (1771-1802). Bichat’s non-metaphysical vitalism, for whom such principle was to be found in tissue sensitivity and contractibility (Cf. Haigh 1984; also in Berrios & Marková 2002), helped in some sense to revisit the entelechial reasoning for explaining both typical functionality and neurotypically pathological functionality as offering site to somewhat physiologism.

It is significative to appreciate how that irritatory assumption was perceived by physicians at the age of electrophysiology: in the early 19th Century, the physical reasoning underpinning irritative reactivity was reinforced by modern experiments, recalling E Du Bois-Reymond in 1848, H von Helmholtz around 1850, and J Bernstein in the 1870’s; the latter incorporating the term ‘action potential’ for explaining the irritative effect of a self-propagated depolarisation of the nerve’s membrane (Cf. recension in Cobb 2002, 400). It seemed that entelechies were disappearing, and nervous assurance and pathology were focalised as preferable agency attributions of mental activities.

This fin de siècle strategy was followed by the German neurologist and psychiatrist Karl Wernicke (1848-1905), a disciple of neuro-anatomist and psychiatrist Theodor H Meynert (1833-1892), who was a strong neural functionalist quite deeply influenced by Darwinian concepts, localisationism and Herbart’s post-Lockean associationism. As Wernicke deduced, since lesions of the «projection fibres gave rise

to focalized pathology and neurological disease; pathology of the association system [was to be an agent as to] generated mental illness.» (Berrios & Marková 2002; 635). The sense that psychiatric pathologies were culturally invoked as pertaining to dysfunctions of the neurological material bases, instead of entelechial figures proper to metaphorical reasoning, composes at the time a leaping advancement towards the physiologisation of qualitative experiences, not just for the basal medical research but for the clinically required. With the 18th-century neuropsychiatric approach to pains and delusions, renewed readings of qualitative physicalism appeared: physical properties were, to that extent, proper to the mater, however not of an outsource matter but of the very material bodily assumed systems that physicians worked with. The cultural implications of this transcendental change in the scientific strategies of agency attribution supposed a neurological foundational claim, that perceptions required material receptors, specific fibres attuned to the recognition of stressors but, at the same time, identified as qualitative fibres (Q-fibres) proper to the experiences mechanically triggered by environmental conditions.

Fibres must introduce, in this sense, a formal chain of sensation conduction, that performed the functional characterisation of sensitisation, the bodily felt. A dualist nature of perception was being adduced within this theoretical frame for explaining basal behaviour. It can be found, for example, in William K Clifford's concept of 'concomitance', psychophysical parallelism (running the 'mind-stuff' division as Clifford stated by 1878 in 'On the Nature of Things-in-Themselves, in Mind) which neurologists like John H Jackson (1835-1911) used as it is well known, for exposing the causes of nerve-like and sense-like interaction. As nerve-like states are clearly distinct from mind-like ones, nonetheless they are said to be occurring together, the assumption that follows is that there is a concomitance

implied in such relation which does not merge them as to interfere, but to correlate. However, the nature of such correlation was to be exposed, and the case of such correlation for pain sensing bears a complication that arrives when history continues with the 19th-century fad of specificity, on the thesis that fibres are specialised to be triggered, excited, by specific stimuli: mechanical theories gave space for the proliferation of physiological theories trying to explain the systemic electrical induction through an embodied reaction (voltaic irritation). The mere irritative explanation, however, did not appear to serve for exposing the grounds of complex, primitive experiences like pain, as theories attuned with animation and movement elicitation were differing from the reality that psychiatrists and neurologists were looking for: the qualitative reception of painfulness.

. *19th Century. Interpreting Nerves:  
Qualitative Continents*

Beginning the 19th century, on this account an explanatory alibi was speculated: if sensations are to be qualitative manifestations of the nervous system, the very nerves shall be appointed to be responsible for such quality. The earlier physicalism resolved into a new physiologicism at once, through a parallelism between quality of sensation and the function of the nervous fibre. Such parallelism can be traced back to 1811 with the English neurophysiologist Charles Bell (1774-1842) in the idea of sensing and non-sensing nerves:

«[...] if there be certain parts of the brain which are insensible, and other parts which being injured shake the animal with convulsions exhibiting phenomena similar to those of a wounded nerve, it seems to follow that the latter parts which are endowed with sensibility like the nerves are similar to them in function and use; while the parts of the brain which possess no such sensibility are different in function and organ-

ization from the nerves, and have a distinct and higher operation to perform.» (Bell & Shaw 1868, 164).

The conclusion reads the requirement of peripheral nerves responsible for sensing a neutral electrical voltage as pain, brightness, touch or hear, as a qualitative function of the proper peripheral nervous system. This supposed a definitive step forward to formalise the thesis of qualitative continentality. In many respects, continentalist theories, on bodily material qualities, started attributing fibres unspecific agency. It is to be observed that the theoretical environment was more than suited for the German physiologist and comparative anatomist Johannes P Müller (1801-1858), in his invitation to interpret that the causes which make animals able to feel pain are not to arrive from the external stimuli, but from the very inner qualities of the sensory nerves that are excited:

«The same cause, such as electricity, can simultaneously affect all sensory organs, since they are all sensitive to it; and yet, every sensory nerve reacts to it differently; one nerve perceives it as light, another hears its sound [...] Sensation is not the conduction of a quality or state of external bodies to consciousness, but the conduction of a quality or state of our nerves to consciousness, excited by an external cause.» (quoted from Pearce 2005, 1).

With this lines, Müller declared the conceptual turn to physiologism through qualitative continentality. In Müller's conception of functional morphology, the impact of Goethe's and Burdach's German materialist vitalism submerged a proper concern about physiologism, neatly visible by the continuous usage of the notion of *Lebensform*, transliterated from the habitual play on words of 'life-forms' and 'forms of life' (for a deeper revision, Cf. Coleman 1977; and more specifically Cf. Helmreich & Roosth 2010). This Müller wrote as a conclusion of his lectures on the development of animal and human life

forms on Earth (Cf. Müller 1840), which Stefan Helmreich analyses as truly participating of the Kantian understanding of biological organisation —reading Helmholtz's correspondence with Müller, his mentor. Evelyn Fox Keller (2005, 1070), in her description of the 'Kantian organism' as a proper organised and self-organising being, results to criticise this somewhat naivity of reason in which current physiological tenets still accept Müllerian instrumental metaphors, which are a mixture of running mechanism driven by teleologism when the machinery of biological explanation fails, Helmreich (2016, 23) reviews.

The initial concepts of qualitative reception were understood as more than a solely irritative effect, however, for further physiologist theorisations, biological agency reductionism in material and experimental medicine needed the track of specificity. There the Müllerian interpretation of nerving qualities opened the century to those who felt seduced by the idea of an unitary form of pain that could be applied to experimentation. Experimental specificism, introduced by Schiff's (1858), von Frey's (1894) and earlier by Erb's (1895) intuitions, achieved to characterise the proper sensation in response to specific cells. This fashion, pain sensing was finally explained as the electric effect of the excitations from dermal pain units, universal and discernible. Collaterally, the result was the introduction of a seemingly new responsible actor, 'nociceptors', naming a functional specific perceptor of a noxious natural kind (Sherrington 1903; 1906) in the field of clinical experimentalism, growing as the thesis of qualitative continentality gained acceptance.

Pattern theories adopted a new revolt away from specificism, however the qualitative grounding thesis appeared such intuitively valuable that no major change emerged, for the sense beneath the words still reached to mind: those fibres have a qualitative property, that of receiving pain-related events, injuries, harm, etc., being this attribution justified or not.

. Closure

The text analyses how the conceptual turn to an electrophysiological explanation of perception appeared to change the ancient qualitative physicalist schemata, studied in an anthropological sense from Eastern to Western historical geoxes of influence, being thus translated to neurology, psychiatry, and cognitive physiology attributing the causal materiality of experiences to fibres.

A harshly demanding, thick version of this analysis will understand that the result of such historical development from qualitative physicalism (reification of qualities into natural elements) to qualitative physiologicism (internalisation of qualities into specific material bodily principles), was the general article of faith that pain perception, although individualised by the subject, can be understood not as an apperception but a performance of a natural kind. That, in its bottom line, plays with capturing such a qualitative continent of experiences in kinds of a theory, whether it be in terms of natural, social, analytical or any other variant classificatory kind (Cobb 2002; Griffiths 2004; Hacking 2002; Reddy 2001; Scheer 2012). Pain, when contextualised in its form for a theory and put in the system oriented through material qualitative functionality, would be a result of pain-fibres's (Q-fibres) excitability, thus empowering a reading of a natural kind per se, and giving birth to the virtual, commonplace construct of the 'universal pain', a non-singular, simulated characterisation of pain, a historical, social construction whose origin has exposed its roots through the instrumental utilitarianism of metaphorical terms in experimental explanation. The liminal 19th-century notion of continentality is, not yet reaching a theoretical international climate of debate and scientific integrative knowledge, a deceiving materialist reduction: the thesis of continentality, away from having rejected enthel-echies, has endorsed them into the body, pro-

pellling metaphors of qualitative reduced elements into the elementary experimentable, and subsumed the old metaphysical division from ancient times into a qualitative physiologicism that occurs to bear, as a hindrance from remote pasts, unjustified beliefs. This is a topic that have led to inescapably orient discussions until present day debates (Cf. Basbaum 2012; Martin 2002; Davis & Moayedí 2013)

In using utilitarian terminology in experimental explanation, further electro-physiological studies approached central transduction beside metaphorical tenets, much of which come from early research on peripheral induction. The following chapters, QIII, §2, §3, argue how this difformation led to stress a decontextualisation of terms in current interfields when comparing the different strategies used in modern physiology for explaining the multiple aspects of pain experiences in different levels of complexity. This ethnographic accounting shows the contemporary contrasts among the plurally different characterisations of pain, from physiology and evolutive biology, to interpretative fields like neuropsychiatry, cognitive psychology, and clinical practices as therapy, as pointed out by other critiques (Koch & Laurent 1999; Martin 2002; Davis & Moayedí 2013).





## QIII, Chapter §2

### Building Pain Models. From Early Electrophysiology to the Complexities of the 21st Century

(In Niche A — Framing Neurophysiological Characterisations)

☛ 312 — 318

—

#### Parts

. *Introduction*

I — *19th Century Theories: Spring of Receptors and Specificism*

II — *First Half of the 20th Century: Integrativism, Affect & Summation*

III — *Second Half of the 20th Century: Mediation & Modulation*

IV — *21st Century Approaches: Complexity*

. *Closure & Implications*



## . Introduction

'Pain conduction' is an often used utilitarian expression that alludes to the correlation between electro-physiological evidence in the nervous system of an organism (fibre excitation) and the very experience of pain, emerged from further complex processes beyond the mere appreciation of harm. Despite it is not pain but an electrical signature what is actually being conducted through fibres, the term gained a fruitful acceptance in physiology. Conduction involves both, 'peripheral induction' from infraspinal Peripheral Nervous System (PNS) afferents, and 'central transduction' at medullar and upper levels along the Central Nervous System (CNS).

Pain induction has been a main issue of experimentation in early electrophysiology throughout the 19th Century, focusing first examination around infraspinal afferents. Running the 20th Century, new methodologies started to understand the role of voltage-irritative signatures, both in the medulla and the upper CNS, as evidences of pain transduction patterns. As a result, theorists began an era of pain modelling beyond sheer induction. Approaching the 21st Century, reflex theories were transformed into more complex strategies, while differentiated labelings characterising the phenomenon of pain sprang among interdisciplinary research.

The theorisation of pain as a qualitative sensing trait has been a major tenet for electro-physiological studies (Oester & Fudema 1969; Millan 1999; Cobb 2002; Ochs 2004), which raised modern theoretical approximations towards a scientific characterisation of pain (Perl & Kruger 1996; Brooks & Tracey 2005). Moved by the 19th-century fad of experimental specificism (ie, one perception equals a particular receptor), a prior perspective built the framework, arguing for specialised receptors within the organisms as explaining the physiological proxyments for pain, in the conviction that pain was a natural kind of perception as perceivable as

colours or scents. Further theorists claimed that no perceptual meaning would be developed without an integration of any received stimulation, whether it be caused by a neural firing pattern, its summation, its partial inhibition, or a central evaluation. Explorations have not remained unproblematic, and discussions on the nature of these ideas, as Allan Basbaum (2012) reintroduced, are still on debate (Dallenbach 1939; Boring 1942; Moayedi & Davis 2013; Casey or Apkarian in Basbaum's 2012 commentaries; Cardeña 2018).

With a comparative aim, the work covers a substantial repertoire of the main theoretical achievements in the western experimental inquiry on the topic in four points. Departing from the implications of the initial tenets proposed by the Müllerian turn, which configured the general orchestration for a proper field of pain electrophysiology throughout the 19th Century, it overviews the incipient theories in favour of specificism and intensity; advancing to early 20th-century integrativism, affectivity, summation and pattern theories, and the advancements of the second half of the 20th Century, which came with the exploration of transduction, mediation and modulation. A present recension about the complex scene of pain research in the 21st Century finishes the fourth point.

Some concluding implications are sketched, exploring some of the problems to which this historical thread has landed in the present. These include the lack of strongly framed interfield explanatory strategies; the problems produced by maintaining in currency hard readings of specificity for exposing the ultimate responsible actors in the biochemical scenario of fibres's performance; or the slow accommodation of fundamental intuitions into new scientific horizons. These horizons now present, in the majority of cases, a contemporary attempt at interpreting the big picture of phenomena implied in pain sens-

ing, examining experiences, feelings and beliefs about pain beyond peripheral, spinal or brain-localist approaches of the past.

I — 19th Century Theories:  
*Spring of Receptors & Specificism*

By the end of the 19th century, three cardinal perspectives on pain were formulated in reaction to C Bell's 1811 concept of 'sensory receptors': the Intensive Theory (supporting that pain was engaged by non-specific receptors), the Specificity Theory (supporting specialisation of receptors to noxious events), and the Affective Theories (introducing cognitive, emotional, behavioural tenets).

What Bell presented, and was later confirmed by F Magendie in 1822 (Cf. too Bernard & Magendie 1856), was that dorsal roots, non-motor pathways, ascending spinal-cord-to-brain, were responsible for sensory discrimination as for engaging in particular sensations. These sensations, JP Müller hypothesised in the 1830's, were characterised as particular tones of energy exhibited by specialised receptors. In Müller's (1835-1840) mind, as proposed in his Law of Specific Nerve Energies, sensations must be appreciated as conduits of nerve qualities to consciousness, and therefore it shall be the quality of nerves excited by specific receptors what finally comes out as pain. The notion, as argued in the previous chapter, by translating to modernity an old tradition that characterised nerves with intentional terms, actually oriented the whole understanding of 'alгоception' (general perception of harm as painful) in general physiology, as a proper re-ception of pain, thread or similar suggestions, being the justification of said concepts debated until present days.

Along the 19th Century, an early but slight form of alгоception was introduced through the specificist interpretation of pain induction by M Schiff (1858), who experimented with somatotopical excitation. He concluded that pain perception was required of a different and specific reception away from that of touch, deriving findings to different dorsal pathways, anterolaterally

for hapticity and posterior for pain and temperature (which supported his previous research with Woroschiloff in the 1850's: Cf. Rey 1995).

Beside such pathway specialisation, it was noticeable that peripheral specificity was rising through Müllerian concepts (as Pearce 2005 points out too): M Blix (1883) found that differentiated skin points evoked distinct cool, warm, haptic sensations; in parallel, H Donaldson confirmed in 1885 Blix's acknowledgement, and along with the discovery, the same years A Goldscheider started to intuit that those sensations were implicitly caused by pattern summations of different haptic skin points, which when provoked until excess begin to fire as sensed pain. Conclusions from both, Blix and Goldscheider, moved away from specificity, nevertheless their findings were later used to support a new fad in electrophysiology, a fad that upheld that pain was something specific receptors were amenable to.

It was not until M von Frey's (1894; 1896), and later his student Strughold's (1924) research on mechanoreception, that the Specificity Theory was compelled to a formulation. Pain was hence viewed as a captive process induced by particular receptors, and their determinants specific free ending fibres scattered through a mosaic of distinct spots (Cf. Perl & Kruger 1996; Pearce 2005), altered by a stimulus which excites pathways independent of pressure or temperature until reaching a CNS kernel or 'centre of pain'. The Specificity Theory was consistent with the findings of hundreds of the so-called *Schmerzpunkte* (pain spots) per skin square cm: specificists stated that the intensity of energy flows ascends from skin-to-brain pathways out of these minute areas of pain spots which recognise specific stimuli, making the body highly specialised in cultivating sensation modalities for pain too, independent from others. The Specificity Theory took advantage in the 19th Century and was reshaped several times with different arguments as neuropsychiatric research in emotions was developing new ideas from the 18th Century to modernity (Cf. Berrios & Marková 2002).

The Affective Theories were some of those reformulations, of which two positions were salient: Marshall (1895) supported a Pleasure-Pain Theory, which adopted a polarised perspective integrating emotional states in the specificity arguments; in parallel, Strong (1895) proposed a psychological identification of pain, associating physical states of the original noxious sensation with psychic reactions. The later characterisation was reintroduced by Hardy, Wolff & Godell (1952) as the 4th Theory of Pain, in a very suitable position for modern studies, suggesting that pain compromises together perception and reaction (ascending and descending flows together).

However, not much back in time, in 1874, a different idea was proposed by W Erb (1895) in regard to the results of his experiments on skin pain induction: an orientation towards intensity.

The main concept held that summation of unspecific stimuli forms pain elicitation. Pain appeared to be manifested conditioned by a progressive sensory input, of any class, which had the intensity of a harmful stimulus when overexposed. Today we know that the discovery was partly true, and that overloading general skin regions with summative inputs can produce a salience in the CNS of a subject as to accumulate interneuronal activity until excess, channeled to major brain nuclei and, thus, provoking an evaluation of the signal as painful. When focused on the PNS, easily seen in injured, clinical patients, it is known as the 'irritative-cumulative effect' (eg, in pain produced by the continuous excretion of potassium in wounded tissue). Maintaining such signalling leads to lower neuronal thresholds and voltaic overreaction (which proceeds as central sensitisation), and therefore to shape a condition known as allodynia (the sensing of pain occasioned by stimuli that do not usually evoke pain).

One decade later, Erb's concept was re-debuted with the name of Intensive Theory by Goldscheider (1884), assuming Naunyn's (1889) experiments of 1859 with degraded nerves in syphilitic subjects, where repetitive below-threshold inputs were transformed into acute pain as

the subject was rapidly prodded with a sub-acute instrument. Their conclusion followed that it was the summation of inputs affecting receptors and not the quality of such (heat, cold, pressure) what was generating pain.

Today it is difficult to know whether their exploration accounts as a general explanation of pain, or if it would rather be a better historical approximation to contextualise it as an explanation of the neuropathic processes (more related to injured fibres and abnormal tissue activity of cells near about nerves). Nevertheless, one possible reason why intensity did not earn its deserved attention until the 1940's, could be that the theory managed to avoid in its own way some of the ideas of its own century, which came athwart homogeneity of reception: with Pacini locating vibration and pressure-related below-skin receptors in 1831-1835, Meissner and Wagner with photosensitive cells in 1852, Blix spotting cold-warm receptors in 1882, and Ruffini's organs in 1893.

With such flow of acknowledgements, specificity instead of intensity was suited to be a new trend: pain was speculated to fit its own recognition in human body cells too, and it was expected that pain appeared as another genuine kind, as desired by specificists.

## II — *First Half of the 20th Century:* *Integrativism, Affect & Summation*

Beginning the 1900's, the vernacular idea of algoception as exposing pain perception in experimental studies was finally termed in the physiological ground of cell activity. Sherrington's (1903; 1906) Integrative Theory coined the concept 'nociception' as being of proper receptors oriented to the discriminative recognition of noxious events. Given the prolixity of different stimuli, the body must have been able to attune itself through specific receptors to potential damage in specific areas, different from touch. Surveying Sherrington's attitude towards noxious perception it can be said that, althou-

gh exposed in terms of ‘nocipient nerves’ (in 1903), later ‘noci-ceptive nerves’ (‘nociceptors’, in 1906), his ideas were clearly directed to the exposition of a reflex arc theory. In this sense, for instance, he covers the concept of nociception under the grounds of the «receptive fields of reflexes» and the «interaction between reflexes» (Sherrington 1906, Lecture IV), instead of pain reception. His intention (maybe just interpretational, following Loeb’s notion of *Ketten-reflexe*: ‘chained reflex interactions’) was to point out the importance of integrating consecutive processes in reaction-reflexes, but influenced by von Frey and Kiesow, he adopted the specificist alternative managing Müllerian terms —skin points referable to specialised nerve endings, excited by both, temperature shifts and harm. In his fifth lecture, he focuses this idea by approaching pain through the «prepotency of some reflexes», as something «generated by receptors that, considered as sense organs, initiate sensations with strong affective tone.» (Sherrington 1906, XIV, Lecture V; Cf. too the index in the 1920 reedition). Tone (from *tonos*) was a proper physiological term of medieval origin that appeared to Sherrington of good use for arguing about a quality of the nerve, which, in expense of its own predisposition to perceive, this is, to be excited by external agents that occasioned tonalities in its nervous activity, evoked a precise modality, in this case, pain it was, a tonal nervous reaction of a painful reflex. Ideas were mixed once more in the tradition of qualitative conduction (Cf. the 3rd part of QIII, §1 for more historical connections about pre-experimental concepts in the 18th-19th Centuries).

Along with Sherrington’s nociceptors, different affective concepts were introduced into pain theory making following the century, indirectly responding to such feature: the characterisation of pain from its induction, and the

consideration of its affective tone. H Head’s (1920; 1922; 1923-1924) works coupling mental and bodily diseases for understanding sane states, met a quite innovative psychiatric import: that pain can be modulated by mood and attention (by dispositions towards pain), and that the very distribution of noxious sensations not just only depends upon receptors, but as well of inner organs (vegetative pain) and mental conditions (sorrow, cheerfulness, grief) and pathologies (psychogenic pain: depression, conversion, psychosis).

Head alone and with psychiatrist W Rivers, proposed one of the first ideas of pain in terms of an evaluation: not a mere reflex, pain shall involve a central ordering of energy for it affects and is affected by mental, complex states of experience. In this sense, their clinical division between central pain and spatial pain persists until our days: triggered from Head & Rivers’s (1908) experiments on nerve rehabilitation, they accomplished to divide haptic undeterminable pain from located regionalised pain, introducing the nowadays common difference between protopathic sensing and epicritic discrimination. This elicited the physiological connection between the skin and the NS itself, not just as for receptors as such, but for brain and skin development. It is visible in what are now called ‘dermatomes’, relating visceral-cutaneous projections (skin regional pain manifested as a transference of inner, visceral pain; also known as Head Zones after his research), and in the fact that both the NS and the epidermis come from the same embryological origin, the ectoderm. It is to mention that with Head and Rivers, the concept of pain-being-felt took a lucid movement towards integrativism: it started to be conceived not as a manner of division from the noxious world that affects the body, but as a manner of connection, self awareness and as

a process for understanding the integrity of the body itself, from which are subsumed memory, emotion, social interaction and self-beliefs.

In the 40's, a newer intensive approach was provided: Livingston's (1943) Central Summation Theory supported Goldscheider's Intensive Theory, but in this case fear and anxiety were taken as the central emotional cycles to which pain responded and of which the theory had a physiological description. The Central Summation Theory considers that, given tissue damage, nerve fibres ascending towards spinal internuncial neuron pools, develop in intense excitations, abnormal reverberations, self-exciting neuronal shoots in loops until, by summation, they exceed multisynaptic projection cells, from where their multipolar neurites extend input salience towards regions of higher complexity in the brain, assumed to participate in affective and behavioural dispositions of fear-avoidance, risk-taking, anxiety, etc. Pain, in conclusion, was of a critical ethological importance: it seemed to help to explain animal conducts as case-by-case behaving, decision making, memory elicitation and learning.

Yet, running the mid-century, several works (Weddell, Sinclair & Feindel 1948; Weddell 1955; Sinclair 1955) announced the most alluring intensive-summative attempt: the Pattern Theory. It proposes that pain is not acquaintable solely by the action of nociceptors, but from the summative activation of other non-pain-specific receptors too given a stimulus that intensively affects spatial and temporal dimensions of bodily recognition (somæsthesia), thus generating a recognisable pattern that will be modified and extended to the brain, and evaluated like a pain experience as qualitative aftermath. The idea recalled Nafe's (1929) Qualitative Theory of Feeling which postulated that every somæsthetic elicitation shall be explainable as the enco-

ded product of neural firing rhythms (Cf. Nafe 1934 on different modalities). Historiographically read, this was an approach supported by Lele, Sinclair & Weddell (1954), as Moayedí & Davis (2012) reviewed, and later defended by Patrick Wall too, as related by C Woolf (Cf. his discussion thread in Basbaum 2012).

The theory gained a progressive acceptance, later reinterpreted in the light of Torebjörk's & Hallin's (1970) experiments with unmyelinated fibres. Results pointed out that pain spots (as thought of nociceptors) were not present in a point-like fashion, but in extended innervation areas known as 'receptive fields', where connected spatially and temporally to free nerve endings, can approach multimodal sensations in different patterns (Cf. Messlinger 1996).

By the end of the first half of the century, the inspection of nerves and their heterogeneous conduction patterns resolved in useful conclusion (see Chart 1, *infra*): Erlanger, Gasser & Bishop (1924), Erlanger & Gasser (1930), and Gasser (1941) suggested that the continuity of action potentials through the nerves, and the differences found in each of them in the return to their baseline (after potentials), justified the separation of PNS's fibres in three groups: A, B and C, groups that will subdivide according to a component that describes the peak of their intensity into A-alpha, A-beta, A-gamma, A-delta, B and C fibre classes. Gasser & Erlanger (1927) ratified the relationship between the velocities of each intensity and the thickness of the fibres, that lead to the classification based on such correspondence by Lloyd (1943) in relation to muscle reflexion. Remeasured versions of both are used in current times (Cf. Manzano, Giuliano & Nóbrega 2008). With new evidences, it appeared that specific and summative theories had an appropriate historical circumstance to merge.

## ■ Chart 1 — ‘Fibre Comparisons’

Summarised from Kiernan & Rajakumar (2014, 23).

Arranged by Gasser-Erlanger Classification (in parenthesis Lloyd Classification).

<i>Fibre Class</i>	<i>Diameter (µm thick)</i>	<i>Velocity (m/s)</i>	<i>Role in Pain</i>
A-alpha (IA)	12-20 µm	70-120 m/s	
A-beta (IB)	10-15 µm	60-80 m/s	Myelinated Modulation
A-beta (II)	5-15 µm	30-80 m/s	Myelinated Modulation
A-gamma	3-8 µm	15-40 m/s	
A-delta (III)	3-8 µm	10-30 m/s	Myelinated Mediation
B	<3 µm	5-15 m/s	
C (IV)	0.2-1.5 µm	0.5-2.5 m/s	Unmyelinated Mediation

### III — *Second Half of the 20th Century: Mediation & Modulation*

Pain induction is related with the organic performance at peripheral levels (leaving apart neuropathic pain, which develops through proper nerve malfunction, infection, or surrounding cellular disfunction), while pain transduction is understood to refer to the continuation of the action potential once the primary afferent neurons land in the spinal cord towards the brain. The factors that support such enaction are called mediators; the ones that inhibit or help to inhibiting it, modulators, and the second half of the 20th Century was mainly dedicated to find and explain how those processes were carried out.

The contribution that opened the next wave of research was born in Uppsala, at the time that B Rexed (1952) worked on the cytoarchitectonic definition of medullar areas in comparative anatomy with the cat. His investigations allowed modern neurophysiology to move forwards in the identification of nerve afferences landing into the spinal cord, and so some grounding concepts moved beyond the historical direction of peripheral induction. Instead of the classical vision of dappled, scattered nuclei that formed difficultly intuited aggregations of ascending pathways, Rexed identified areas of

cytoarchitectonic familiarity, also known as laminae, where cells resembled to have distinctive inner organisations and formed too different connections with incoming nerves, from dorsal to ventral to medial. The task supposed one of the most valuable achievements for further theorising and experimenting in the 20th and 21st Centuries.

With these tools, a new physiological model of pain transduction appeared to reunite some of these modern ideas: the Sensory Interaction Theory. Proposed by W Noordenbos (1959) in Amsterdam, with the idea of multisynaptic modification (pain signalling modulation), the theory makes use of a prior distinction: Head's difference between protopathic and epicritic discrimination (Cf. Wall 1990). His recognition of temporal summation in fibres enaction led to separate those in small and large, fast and slow afferents, both from PNS and CNS. Interactions between these fibres would render an image of how fast ones blocked slow ones, which was to be a very ecological conception of transduction patterns. The difference between two afferent systems was conceived in this manner: one with slow unmyelinated fibres (now C) plus myelinated but small fibres (now A-delta), which together result in pain emergence, and another one with fast myelinated fibres (now A-beta) associated with other somatosensory conductions

(see Chart 1, *supra*). The first ones connect with dorsal horn roots, cord-to-brain, where by mediation its summation triggers salience and, once integrated by the brain, corresponded to pain experience. The latter are found to inhibit through signalling competition the action of small fibres, preventing summative input, and then collaborating into pain modulation, breaking the signal (as introduced by Noordenbos's 1959 main configuration).

Within this correlation, the seed was planted for developing what is esteemed as the current identification of pain transduction and integration: the Gate Control Theory. Launched in the 60's by Melzack & Wall (1965), the initial hypothesis was preemptively deemed by Wall's (1960) experiments with cutaneous pain sensitivity in kittens, evidencing that harmful perceptions were to be inhibited with vibromassage at the same skin spot of injury: results appointed that inductive electrical damage could be modulated pre-encephalically through a mechanism quite similar to that of Noordenbos's interactive transduction, and that the identification of subjective pain feeling was due to the CNS recognition of the patterns mediated and modulated from the periphery. At the same time, Melzack's (1961) experiments in cordotomy with A-to-E spinal nerves (later generalised with capitals and Roman numerals), and DO Hebb's conclusions on neural-behavioural learning models, benefited the scenario. Hebb was leading the research in the laboratory where Melzack worked in Montréal, so that many new ideas on neuronal reinforcement, memory and artificial induction of experiences would have arrived to the niche of investigation from a wide range of fields, from physiology and neurology, to psychology, logic, and computation, plus the experience in later laboratories in Italy and Massachusetts. In the next year, neurophysiologist P Wall, and psychologist R Melzack (1962) kept a combinatory research assessing both, summative and specific attempts at identifying pain systems, which led to propose the bonding approach in 1965 with a severe focus on transduction (spinal areas). This was enri-

ched by Melzack & Casey (1968) developing the current 3-fold interactive dimensional characterisation of pain: sensory-discriminative, affective-motivational and cognitive-evaluative (spinal-encephalic areas).

The Gate Control Theory unifies, in its own manner, Noordenbos's interactive understanding and Rexed's laminae in a lucid hypothesis that is being confirmed by the latest explorations in immuno-histochemistry (*infra*). The theory suggests that at the arrival of these two afferent classes of fibres (A-delta plus C, and A-beta) into the dorsal horn of the medulla, different chemical exchanges occur between incoming afferents and in situ interneurons, which will afterwards synapse to a projection cell bringing the energy flow upwards to the brain. In addition, both classes have an excitatory synapse with the projection cell apart from interneurons. Interneurons in substantia gelatinosa (Rexed lamina II) are molecularly disposed with inhibitory neurotransmitters; they are suggested to be dynorphinergic, enkephalinergic (two of the main three families of endogenous opioids) and GABAergic (gamma-aminobutyric acid, voltage depressor, present in this environment in glial astrocytic bodies too); thus, when A-delta or C fibrils synapse the interneuron, stopping its inhibiting effect to the upcoming projection neuron, they increase the possibilities of such projection cells to fire, which are detected of N-methyl-D-Aspartate (NMDA) receptors (glutamate, voltage activator). When the A-beta fibres synapse with the interneuron, exciting its inhibitory potential, they lessen the possibilities of the projection cell to fire. In consequence, it is the unbalance of C, A-delta and A-beta combinatory fire rates which ultimately could stimulate projection neurons or not, making A-beta (A-beta IB and A-beta II, and plausibly A-alpha afferents too) to cease energising pain-associated cord-to-brain systems related to C and A-delta fibres activity (spinothalamic, spinoreticular tract and parts of the supplementary dorsal columns) and, in turn, to activate pressure-vibration-related cord-to-brain systems (dorsal columns, medial lemniscus).

With the discovery of myelinated fibres reacting to mechanical noxious stimulation by Burgess & Perl (1967) recalling A-delta fibres, and unmyelinated afferents by Bessou & Perl (1969) for C fibrils, the model appeared to benefit of increasing support.

In the 60's, pain modulation was at least concreted for spinal fibres through medullar interneurons, although not very well defined in terms of descending pathways (brain-and-brainstem-to-cord). By the 70's, Reynolds (1969) and Akil et al (1972) found that specific neurons in the brainstem evoked general analgesia during artificial electrical stimulation. Pointing to the role of endogenous opioids and their receptors, works like Pert et al (1974) opened the door during the 80's to a series of discoveries of opioid families (enkephalins, beta-endorphin, dynorphins, etc.), along with the later found action of another neurotransmitter, serotonin, contributing during stress circumstances to nociceptive suppression (Milne & Gamble 1990; Fields et al 1991).

A model appeared to observe that some collateral ramifications, from afferents in the spinomesencephalic pathway, actually excited inhibitory neurons in the brainstem that had an effect in several downward levels of the spinal cord. Besides the action of C and A-beta fibres in the Gate Control Theory, Le Bars's et al (1979) Diffuse Noxious Inhibitory Controls Model identified this descending modulation, reacting brainstem-to-cord through endogenous opiates and other inhibitory chemicals excreted by neurons in the periaqueductal grey matter, and nucleus magnus Raphé plus locus caeruleus —the Reticular Formation—. The endogenous opiate system detection, as the identification of central nuclei modulatory pathways (anterior cingular cortex, amygdala, etc...) were of many uses in psychiatry: with pain neurochemistry entering psychopharmacological therapy, newer forms of analgesic experience, bodily-dissociative psychotic fabrications, comorbid psychiatric pain, and other conditions could be studied. For these fin de siècle views, a modern chemical attempt was clearly empowering

dynamic anatomophysiology for the times coming. A major conclusion emerged, for all such pathways, when energised, would make substantial changes in the internal and peripheral contexts of cells, irritating, reshaping, and reorganising their biophysical circumstances of communication among each other, thus, affecting the tissues's metabolic chain, and, at last, behaviour.

#### IV — 21st Century Approaches: Complexity

It is difficult to summarise the quantity and value of contemporary pain research during these two decades, and certainly the following track is not to be considered but a mere recension of the main lines of investigation, not exhausting them. Some studies (Yizhar et al 2011; Mar, Yang & Ma 2012; Carr & Zachariou 2014; Christensen et al 2016) identified molecular-specific variations at dorsal laminae neurons that appear to explain the morphological transduction of fibres from PNS to CNS through interneurons in Rexed lamina II. Also recently, Braz et al (2014) could subdivide into three pro-innervation layers this lamina. The findings of Duan et al (2014) helped to evidence how A-delta and C afferences reach indirect projectionality to further nuclei through intersynapses with somatostatin-related neurons in lamina I, and with its heterogeneous ramifications in lamina II ventral sublayers and the II-III laminal border. It is observed that interneurons conduct a somatostatinic excitatory potential as well as a dynorphinergic inhibition, thus, building the 'gating effect' a more complicated system, with plenty internuncial protagonists, affecting mental conditions too in the relation of enkephalins with stress, plasticity and analgesia (Henry et al 2017). In its neuropathic derivation, the exploration of the inner organisation of C fibrils and their accretion into Remak bundles (Murinson & Griffin 2004), provided or not with Swann cells coverage, has been an useful identification for understanding neuropathies.

Comparative neurophysiology introduced a new perspective: tracing possible evolutionary



roads for common sensing fibres, it has been revealed that afferents in vertebrates occur to be subsumed to the development of marine-to-terrestrial fibrogenesis of peripheral thin nervous cells and their roles (Sneddon, Braithwite & Gentle 2003), C fibrils being found in teleosts (bony fish), amphibians, reptiles, birds and mammals, but not in more archeotypical vertebrates as elasmobranchs (cartilaginous fish). A reason for this would be the difference between gravitational, gaseous, and temperature conditions on earth in relation to the liquid milieu (Sneddon 2004).

Some experimental features from the previous century on induction were critical for new research on transduction: recalling Ochoa & Torebjörk (1989) experimenting with intraneural microstimulation of C fibres; Häbler, Jänig & Koltzenburg (1990) discovering 'silent nociceptors' (whose high intensity-related thresholds maintained exposition provoked a very lasting effect on sensitisation); or Woold & Chong (1993) reaffirming that patterns of low intensity PNS induction correlate to low-threshold sensitive fibres, while patterns of high intensity PNS induction correlate to action potentials generated through high-threshold sensitive fibres, leading to conduction of further pain-related sensations. This would show that clinical research advanced by shifting the focus from inductive to transductive lines of work, more attractive for pharmacodynamic experimentation and theorising, and for the understanding of adequate peripheral signalling integration through central inhibition-integration (Li et al 2010). This perspective is also most suited for surgical interventions with psychiatric orientation, as in cardinal regions like the anterior cingulate cortex (Boccard et al 2014). Nowadays for example, cingulectomies, with the purpose of eliminating painful sensitisation and evaluation of overflowing harmful events, are radiologically practised in chronic-acute cases; patients for whom pain-kindred provocations would not be correctly evaluated without managing information through these specific cortical projectionalities. The correlation is now there to be interpreted in more depth than before in the 40's.

Another innovative aspect of 21st-century research comes with neuroimaging, especially of some morpho-functional biopaths of pain transduction and their reflections in the CNS (Yuan et al 2013; Davis & Moayed 2013), which in the brain express the preponderancy of some regions with clinical import including the habenula, the hypothalamus, the amygdala and specific cortical regions (Apkarian et al 2005; Farmer, Baliki & Apkarian 2012), with significance the medial and subgenual anterior cingulate cortex (Gao et al 2004; Pereira et al 2013; Fuchs et al 2014), and the insular cortex (Starr 2009; Baumgärtner et al 2010; Peltz et al 2011; Hauck et al 2015; Lu et al 2016), which are critical for considering pain interpersonal transcendence (Iannetti et al 2013), and its psychiatric development.

New doors opened with the understanding of the roles that ion channels play in thin fibres's terminal bud porosities: the first channel was found through non-selective cation channels exploration with capsaicin (Oh, Hwang & Kim 1996), soon being cloned in TRP vanilloid 1 (Caterina et al 1997) forming a recognisable family, the so-called TRPs: Transient Receptor Potentials (Cf. Venkatachalam & Montell 2007). Among others, TRPV1 has been a centre of surprises, given its relation with depression, been found in hippocampal interneurons (Gibson et al 2008), its chemical mediating role in thermosensitivity, and its association with patterns of glutamate-related interneuronal asynchronicity, which led to pharmacological targets (Peters 2010).

The relation between pruritogenic and algogenic biopaths has also been studied (LaMotte et al 2009; Liu et al 2011) leading to detection of Mrgpr receptor family positive neurons (Han et al 2012; Liu et al 2015) and the proposal of a promising integrative perspective for the combined transduction effects of afferents related with both, pain and itch. Sun et al (2017) speculated the so-called Leaky Model for Pain and Itch, which observes that medullar CNS integration through specific interneurons will be determinant for pattern-coding peripheral common signals that will portray a later characterisation

in the brain as of itchy or painful sensations. In recent studies, according to different responses to histamine by C fibres, Song et al (2018) developed a labelling of two signal pathways of itching sensations: namely, the histamine-dependent (histaminergic) signalling pathway, and the histamine-independent (non-histaminergic) signalling pathway, both of which coalesce in the spinal cord through interneurons in Rexed laminae I and II. These pathways are reviewed to be mediated by different interneurons in contrast with those of pain transduction patterns, being a model which blends descriptions with the Gate Control Theory.

A final important remark is the empowering of glial bodies's research, that are believed to be critical in pain chronification and neuropathies (Ji, Berta & Nedergaard 2013). From the most vital to the most trivial activity of innervated organisms, they have been observed to be more than brain's glue (Slezak, Pfrieder & Soltys 2006; Sherwood, Stimpson & Raghanti 2006; Allen & Barres 2009; Kettenmann et al 2013). They intervene from metabolisation of the commonest neurotransmitters to fagocitation, from memory and self-location perception (Nishiyama et al 2002; Claudel 2006; Kim et al 2011: works regarding the advances of the Japanese discovery of glial protein S100beta's effects on mnesicoception) to psychological and neuropsychiatric diseases where some glial-based failure happens to occur (Cf. Shapiro, Bialowas-McGoey & Whitaker-Azmitia 2010 for S100beta's effects in Down syndrome and Alzheimer dementia).

#### . Closure & Implications

Some discrete thoughts are to be offered in regard to how clinicians assess present theory making. A cardinal obstacle is being pointed out in contrasting information: both the average found in non-reproduced and non-reproducible experiments (Cf. Shamliyan, Kane & Jansen 2010; Iqbal et al 2016), and the lack of interfield strategies used in explanatory needs (Darden 2006; Cowan & Kandel 2001) are two major indicators of this fact, which is also im-

bricated with how interdisciplinary requirements are managing interpretational reasoning and explanation. As Martin (2002, 702) put it for neuropsychiatry, the success of its endeavours «will increasingly depend, as [...] already implied, on interdisciplinary, interdepartmental research». This point is critical, for interfield strategies seem obliged to make use of interdisciplinary shared explanatory efforts, while single field's explanatory attempts, instead, come to put the focus at overflowing issues through unitary, parcelled, even clinically isolated views if contrasted with pluralistic information. The extension of theorising about overflowing topics will be reviewed in QIII, §3: this is, as put by criticism from ethnographic and anthropological studies, exemplified by what Timothy Morton's (2013) examination calls 'hyperobjects' in ecology, or by Stefan Helmreich's (2016, 90) analysis of monotopic theories, with the epistemic concept of 'overflowing theoretical objects'. Both ideas shape a description of general scientific explanatory strategies in unitary fields.

For instance, in the case of pain sensing research, it appears a trend for inductive experimentation to manage general explanations about the physiological puzzle by sticking to peripheral induction concepts, avoiding any more complex centralised connectomic attempts, which seem in turn parcelled to cognitive physiology. Nonetheless, as the arborisation of knowledge makes increasingly more difficult to connect multidisciplinary trends and results, it appears that the dream of an unitary, monolithic theory is finally disappearing (Galison 1996; 2004; 2008; Weinberg 2001; Keller 2003b; Haraway 1991), so that pluralistic reinforcement will surely come in modern years as expected from plural and naturalised epistemologists (Cartwright 1983; Giere 1999).

A final remark on epistemic competition and conceptual rivalry concedes integration an opportunity for action, as it is possible to consider that neither the grounding arguments of the different main ideas exposed above during the text are contradictory, nor their identifications complete: on the contrary, they reveal to

be served by the same founding characterisations, and mutually required for a detailed view of the entire process, being the specificism of reception through fibre conduction redefined in present years for a whole-like explanation of the entire experience, away from its receptive univocal roots (quality conduction and qualitative continentality), as reviewed historically in the previous chapter.

A promising pluralistic characterisation of pain experiences can actually be featured through integration, maybe opening a door, beginning an era of integrative causal explanation, or at least to better descriptions. Recent attempts brought us the epi-phenomenal interpretation of emotions, experiences, memory and consciousness (rather examples in Damoiseaux & Greicius 2009; Gell-Mann 1995; Thagard 2005; 2010), which, applied to pain, might lead to interpreting the issue not as a sole phenomenon of the experimental physiology at hand, but as an epi-phenomenon of the whole organism occurring along the performance of physiological and neuropsychiatric tenets, with further transcendence in self-beliefs: ie, the construction of our experiences by our biography. The fate of such a direction is, naturally, not to be decided here, but to be assembled by a good many future scientific communities and their relatively present theoretical navigations.



## QIII, Chapter § 3

### Sounding the Limits of Materiality & Over-Attribution: On Pain Fibre Specialisation.

(In Niche A — Framing Neurophysiological Characterisations)

☛ 319 —323

—

#### Parts

. *Introduction*

I — On the Difformation of Descriptive Strategies

- . *Explaining the Shift: Difforming Qualitative Contents into Qualitative Continents*
- . *Exploring Unitary & Interfield Strategies of Agency Attribution*

II — On Physiological Reductionism

- . *Considering Over-Attribution in Theorising Fibre Specialisation*
- . *New Approaches for Pain: Epi-Phenomena & Integrative Alternatives to Perception*

## . Introduction

This chapter reviews some of the major epistemological factors that led to form the historical shifts on the material attribution of agency and roles to fibres and regions of the nervous system in relation to their role on pain conduction, as presented in the previous chapters. Putting the issue in Williams's (2012) analytical terms, it will be exposed how the historiographical thread presents a 'difformation process' that affected the underpinning considerations from which each historical and localised scientific context produced its interpretations on materiality, very often implying physiological reductionism.

Reductionism comes mainly through the attribution of evaluative (qualitative) agency to fibres, pathways and regions of the nervous system, decontextualising the roles that microcosmic parts play in facilitating agency that is proper just to macrocosmic wholes: as pain is an attribution solely applicable to the agency of the whole organism, once it evaluates the state of its integrity as an organic entity. However, when applied just to fibres, this frames a material over-attribution of evaluative qualitative agency that results fallacious in multiple senses, which in the case of pain physiology has been introduced through the arguments of fibre specialisation, discerning what stressor is the fibre specialised towards. Pre-evaluative reasoning demands, for this identification, morpho-functional characterisations that do not inform about any particular experience as proper to the fibres that argumentation is characterising, but proper to multiple central evaluations along the organism as a whole.

Problems on over-attribution, thus, of overall agency to specific parts of the system are to be exposed historically, epistemologically, and interdisciplinarily by this text in two parts. Part I will focus on the descriptive strategies that historically came to difform unitary theories (oriented through unique original scientific fields)

conclusions on pain conduction into interfield's (Darden 2006) interdisciplinary research conclusions in more modern times. Part II will extend the epistemological exploration on physiological reductionism in material attributions, and expose alternative ways for characterising pain experiences through integrative dynamic physiology, considering neural systems as non-unitarian and non-statically regionalised theoretical contexts, as an attempt at resulting more applicable to neuropsychiatry (Berrios & Marková 2002; Martin 2002) or experimental therapy (Cowan & Kandel 2001). The analysis will close supporting the use of interfield explanatory strategies to help alleviating the epistemic regress pain theory making is suffering nowadays (Apkarian in Basbaum 2012).

### I — *On the Difformation of Descriptive Strategies*

The historical and ethnographic explorations on the neurology of pain exposed in the previous chapters (QIII, §1-§2) have been pointing out how physiological identifications matured in their meeting psychiatric suggestions (affective, attitudinal, attentional, maladaptive or dysexecutive patterns in such physiologies and in proper organic overall identifications). This scenario frames a broader depiction of what pain can be described as. 18th-century unitary theory making —theoretical characterisations informing of a singular perspective of the puzzle, and voluntarily situating the theory on the standpoint of a unique field of research— has been a very straightforward and dominant fashion of extracting conclusions and interpretations from an unitary guided collection of experiments. Neuropsychiatric influence from the 18th Century and the 19th fin de siècle has been exposed to medical materialism through different material principles, attributing men-

tal or global properties to specific, regionalised, statistically supported, and not for this reason more complete, instrumental parts of the organic, material being (Cf. Berrios & Marková 2002; Martin 2002). This material impulse has been especially significant in attributing narrow features to specific parts within wide scenarios and problems (Cowan & Kandel 2001). Coming to internationalisation of scientific topics and multiculturalisation in research programmes, 20th-century scientific methodologies, practices and views express a movement towards neutralisation of terms in language, exhibiting a pragmatic utilitarianism in scientific language in an attempt at facilitating global comprehension that showed how different communities of researchers interacted and adapted to a global economy of ideas (with all the implications that conveniently or inconveniently this involves). In more current times, 21st-century interdisciplinary research appears to be set to propose new alternatives that gather multiple fields (Darden 2006; Apkarian in Basbaum 2012), and that come with descriptive solutions, explanatory helping tools, or experimental anatomic-comparative and evolutionary approaches framing pluralised interfields that benefit a decentralised conception of pain, where the centre of explanation or description relapses into several disciplines instead of an unitary singularised niche. This movement is not new to historiographic documentation, however what is new comes with the consequences of having involved interconnected explanatory or descriptive strategies into extended, wide matters of study (producing objects of research that overflow their own theoretical niche, in which they were proposed and identified) in a fast, international, dynamic and open to debate moment of history. This hyper-contextualised climate of scientific characterisation grows new as proper to the 21st Century, and should a fruitful panorama be obtained from this, pain characterisations would require to adapt again.

Using Lambert Williams's (2012) voice of historical analysis, 'difformation' gives a working term suitable to identify those processes of shifting and re-shifting on theoretical contents through a very useful analogy with how morphologies (given a theory, a model, a scientific interpretation put as a form to variate) reshape in different ways, conditioned by specific stressors of the time and circumstance, interacting with their environment, valuing and re-valuing certain theoretical traits on account of social, historical, cultural aspects: difformation occurs, thus, framing nuances of those theoretical grounds, and can be understood as an epistemic process that points out the dynamics of the lacks of conformity with certain pre-existing standard at each context.

Epistemological research can help to explain the movement from qualitative contents (early pneumatic to cartesian theories) to modern models on qualitative continents (Müllerian proposal, qualitative fibres), to contemporary alternatives on fibre specialisation and central integration. The contemporary building of knowledge is affected by how anatomophysiology understands pain experiences, requiring pre-evaluative characterisations for sounding the role of preganglionic fibres. Such a pre-evaluative reasoning demands morpho-functional identifications that do not inform of any particular experience as proper to the fibres that they are characterising, but proper to multiple central evaluations along the organism as a whole. Problems on over-attribution, thus, of overall agency attributed to specific parts of the system are to be exposed historically, epistemologically, and interdisciplinarily.

The following sections will briefly comment on two factors that stress from this complex scenario the understanding of modern theorisations coming from the models and the qualitative shift studied in the previous chapter. The first (1) factor relates to the shift on the institutionalisation of 19th-century 'qualitative' theo-

retical conceptions about pain; the second (2) opens the commentary on the existence of unitary and interfield explanatory strategies that are to frame a new shift from 19th-20th-century 'evaluative understanding' of pain affecting arguments on fibre specialisation, to 21st-century pre-evaluative alternatives on nociceptors and the integrative role of central systems for emerging with pain as an epi-phenomenon proper to the whole organism. Discussions on the second matter will be centred in Part II of this writing.

*. Explaining the Shift: Difforming Qualitative Contents into Qualitative Continents*

In its physiological characterisation, the historical exploration of pain can be observed as an example of a linear-to-non-linear difformation process. Putting the issue in Williams's analytical terms, difformation can be understood as an epistemic process of «divergence in form or lack of conformity with some pre-existing standard reference point, practice, mode of institutionalisation, or body of knowledge.» (Williams 2012). In the case of pain conduction, as 18th-19th-century theories abandoned pre-scientific pneumatic, cartesian entelechies, they moved their descriptive and explanatory strategies towards a new form of institutionalisation in scientific experimentation: qualitative reception. So the concept difformed from explaining experiences through conducting qualitative pneumatic spirits to explaining the qualitative experience of pain as a result of exciting the very qualities of the matter that allowed such conduction, the channels that nerves and later fibres resulted to be for epicritic discriminative sensations. By ascribing upper-complex characteristics of emergent phenomena (the living singular experience) to basal phenomena (cells excerpted from their global frame of reference and action) the difformation pops up as a decontextualisation of what is being observed,

giving form to an artificial but experimentally required, thus, instrumental characterisation of pain: an universal pain, a pain of the laboratory, a pain that is the object of the study, and that is felt by no agent in toto. This conception of a universal pain institutionalised in modern physiology and biochemistry, anatomy and pathology in some scientific communities through an experimental tendency, the signature-finding method. This makes conclusions to be extracted from experimental satisfaction, nonetheless, conclusions are limited to the proper limits of the scientific experimentation, and should interpretations follow beyond this boundary, epistemic problems appear. One of those strong problems arises in the clinical application of psychiatric, psychological, therapeutic characterisations of pain, which is even more visible in a liminal science as neuropsychiatry is, where fundamental definitions lack of coordination with those of physiology, and where the individually clinical characterisation faces the collectively medical interpretation. Liminal sciences, thus, interfields (Darden 2006), are perhaps because of this unrelenting difficulty, better equipped for solving the rigma-roles produced.

By following a drift of specificism in experimentation, the shift to modern views made a parallel translation of its interests on pain as referred through the interests that experiments followed in 19th-century terms and, in a general sense, the idea of perceptual induction: ie, that specificity of perceptions is induced from peripheral nerves, thus resting significance to central evaluation, which, at the extent of the scope of those interpretations, is a basis for reductionism, an attempt that avoids or in some degree obviates the complexity of the phenomenon of study by weak inference.

Considering the scene, a problem of over-attribution was parked as a reductionist strategy. By ascribing upper-complex characteristics of emergent phenomena to basal phenomena,

entelechiial metaphors were maintained within modern versions of explanatory practices. Should it apply to experimentation, a qualitatively metaphorical and intrinsically utilitarian tool arrived from pain induction to pain transduction experimental interests. The quality transposed to the fibre, over-attributed of an overall qualitative role decontextualised from its locus in the system, and baptised 'nociceptor' under the argument of specialisation: a fibre specialised towards noxious events. This strategy inevitably framed a physiological reductionism propelled to a mereological fallacy (Cf. Bennett & Hacker 2003; Machamer & Sytsma 2009, *infra*: next Part II) on account of an evaluative inference developed through naming: the event is recognised as noxious at overall organic and central levels, and peripherally, evaluative terms fall under a classificatory characterisation away from their order of complexity.

The utilitarian handling of metaphoric terminology arrived from the theories of induction to those of transduction by the 19th Century. Later, a next step to institutionalisation of the qualitative continent theoretical conception had to be taken from the 19th fin de siècle towards 20th-century physiologicism. Terms (labels and relationships of their qualitative taxonomies of an organic cell classification) along with the use of justificatory and descriptive strategies diffomed into a modernised view for the 20th Century, that stablished and remained as an article of faith by the 21st Century. Utilitarian strategies involved in this process of institutionalisation as interfield practices internationalised, influenced by the plural context of languages, which required a general theoretical principle of continent conduction. This introduced the arguments of fibre multimodality (a precision that is not explanatory but merely informative upon the behaviour of the fibre) and fibre specialisation (why the fibre gets excited by which stressors and by which it does not). These are deep questions that are currently de-

manding new explanatory strategies, and that however are treated through previous historical decontextualised versions of the theoretical contents scientific communities studied. One reason among the many appears clear observing the hypercontext of scientific communication, of mutual linguistic understanding and of common interaction, which necessarily adapted by neutrally adopting a strategy of naming, tagging and attributing led by experimentally useful theoretical vectors (instrumentalism, utilitarianism) and easy to conclude (at the expense of deeper wide-range complex explanatory strategies).

*. Exploring Unitary & Interfield  
Strategies of Agency Attribution*

Unitary sciences, niches of pre-interdisciplinary branches, develop slow until their objectives, agenda, social, political, economical and contextual goals shift from a previously related archetype or standard of observation to another (Cartwright 1999; Kitcher & Salmon 1989; Longino 1990; 2001; 2006; Kitcher 1993; 2003; 2004; Giere 1988; 1999; 2006ab; Galison & Stump 1996; Mitchell 2004). Biomedical theory making is not far from being a socially compromised act, and as different goals grow, unitary sciences start to split into plural disciplines that end up merging into interfields (Darden & Maull 1997; Darden 2006). Different demands of explanation or description reshape standards and reform disciplines. Explanatory interpretations, and the general trends in concluding experimental results, shift too with the drift of scientific theory making, and reductionism is an explanatory strategy as the shift from one observational advancement to another is still to come. This has been the case for physiological research on neurological advancements parallel, but many times immiscible, with a psychiatric, behavioural or therapeutical company, a multiple strategy that would have served as re-



vision in coordination. Neuropsychiatry in this sense is an example of intentional pluralism in a practice that requires complex explanation and description strategies.

Without an interfield compromise, Martin (2002) bewares that «much of what we do today will in 10 to 20 years seem foolish, naive, oversimplified, and self-promoting.» (Martin 2002, 702). Reducing the ultimate components of an explanation to the standard of observation up to a given date, is an almost mandatory strategy for practical fields as medicine or clinical practices: this instrumentalism of explanation is an alibi in order to prompt solutions, even partial, into heavy problems that come with healthcare requirements and their political substratum. To the extent of the convictions in this text, no critique shall be undertaken on common and current misinterpretations or fallacies in speech and logical discourse, that usually lead to vague confrontation, but on their grounds, and on the proliferation of complex dilemmas that are carried on from a past scientific unitary locus, affecting nowadays plural strategies of explanation and characterisation.

The tendency in pain-related physiological theory making has been shown to lead to compose its explanatory principles on its matter by filling with 'white void' (a theoretical *inconnue* that parches explanations: instrumental theory traits, names, elements of a classification, relations among those elements, etc.) the gaps that could not have been filled with the history of biological development. Because there is no immediate continuity of evidential methods, as each method generates in its own time and conditions (Stump 1992; Kitcher 1993), explanations variate depending on the degree of observational limitations, hence that the few clues that are excerpted, are reduced into principles often without guarantees. It is noticeable that the lack of guarantees is proper to instrumentalism, for these explanatory principles face a scale of complexity that becomes increasingly

high. As the topic of interest overloads its scientific locus, conclusions overflow such locus (following the analogy in complexity and biological theory of 'overflowing objects'; Cf. Helmreich 2016, 91). The overflowing topic now requires a pluralised theory making approaching from different angles and with distinct explanatory goals to achieve. Any different scenario would lack a proportional context as time goes by.

Martin (2002) comes to the role of reductionism at scientific grounds: reductionism as an explanatory strategy for biomedical research «has been a powerful and enormously fruitful one. But in the 21st century [...] sciences at each of our institutions and at a national and international level must work to break down the barriers between disciplines to remove the obstacles to fuller collaboration and integration. We must move beyond the turf battles of the past to a recognition that the ground we are now breaking in the science of brain and mind is common ground.» (Martin 2002, 702-703). That introduces the point of integration, of these different theoretical grounds, for epistemological ethnography to the very positive fields (Cf. Cowan & Kandel 2001) and the beginning of a naturalised and socially relevant epistemology of science facing along with the same problems scientific dispositions face to (Fehr & Plaisance 2010).

This enclave focuses how such strategies deal with the attribution of agency by the claims scientific communities make and defend. The problem of 'nociceptor nerves' is a problem of qualitative labelling affecting such attribution. Sherrington criticised that 19th-century theories identified pain perception in a very instrumental way in behalf of their commitment to pain re-ception.

The fact that Sherrington, as the introducer of the term tried to overcome this problem is sympathetically encouraging. He wrote: «It is preferable, however, since into the merely spinal and reflex aspect of the reaction of these nerves no sensation of any kind can be shown to enter,

to avoid the term “pain-nerves”.» (Sherrington 1906; 229). Nevertheless, this turn to reflex reactions by proposing the labelling of ‘nociceptive nerves’, actually embeds the fact to the same intentional problem that he was reviewing: it is making basal-complex parts of a higher-complex organism responsible now of a noxious reaction (in the sense of threatening, committing to damage) through basic fibres. Several limitations can be put: why injure, threat or menace is less affectively intentioned than pain in the labelling of the fibres? Terming ‘lesion’ to a general phenomenon of organic injury is an evaluation of the state of the organism, then how would be the nerve ‘aware’ of such evaluation before the organism as such composes the evaluative frame through the sensation of pain? It appears that a personification has been orienting the labelling process; not just at partial levels, but also among the levels: how is this characterisation related to pains that do not refer to the parts of the organism that are threatened but that coordinate through referred pain (the case of dermatomes embryologically re-structured when the organism grows is a good example), or a pain that is not induced peripherally through the so-called nociceptors, but centrally induced from critical brain areas of psychiatric interest in tactile, thermal or algologic hallucination, or a pain that is mnesogenically (through memory elicitation) emerged as fabulative, psychogenic pains?

An answer to the general question could be that when experimenters prodded their subjects, it was a pain-reflex what identified the disposition of the fibres they were looking for, because in physiologically researchable circumstances, there is the believe that just the outcome would be able to manifest the function. Under these conditions, an epistemic problem appears, for this result is not to justify nociceptive fibres but the very context of the reflex arousal: the result is assumed under the practice of its experiment. It involves a performative inference. Labelling

‘nociceptive’ the fibres that are thought responsible for the induction of pain actually created an intentional over-attributed pain-reception, as pain is what appeared exciting them. However, as far as it can be concluded, a factitious attribution, for the case is that neither pain nor threat nor even an injury is what they are receiving (as pain-receptors or noxious-receptors that they are said to be). Attributing pain to an organism in a general frame will require to assume that it is something the whole organic inter-system entanglement is performing, an answer that does not exhaust in peripheral reception. The same case repeats with evaluative characterisations on neurotransmitters: it is not frenzy what dopamine transmits, but energy flows through continual depolarisations of cell membranes, which contribute to maintain the action potential (ions balancing a voltage) together with a particular chemical ambiance, that affects by irritation to their homeostatic-allostatic equilibrium and, in turn, the whole state of the organism. What fibres receive from stressors in the process of pain induction needs not be thought through intentional evaluative terms: pain would thus be what finally emerges as the epi-phenomenon of integrating these previous processes dynamically at central levels.

As Churchland puts it, these forms of reduction are achieved «when the causal powers of the macrophenomenon are explained as a function of the physical structure and causal powers of the microphenomenon. That is, the macroproperties are discovered to be the entirely natural outcome of the nature of the elements at the microlevel, together with their dynamics and interactions.» (Churchland 2002, 29-30). This dissociation among different levels of complexity comes to langue in the metonymic figure of speech synecdoche, making by the name of the fibre reference to macroproperties beyond the scale of the element being named (this is specifically defined with microcosmic synecdoches, Cf. Burke 1941; Enelow 2011; Bureman

2013). When ascribing this fashion in a scientific environment, the rhetorical movement is identified: a microcosmic synecdoche in the figure of a ‘pars pro toto fallacy’ (eg, the hand opens the door — the hand = the person) reifies pain into the peripheral ambiance, over-attributing agency of pain to the cell by defining it nociceptor neglecting that the actual nociceptor is to be meant the organism as a whole for being the agent in perceiving the noxious event or feeling pain.

Modern literature has investigated how 19th-century instrumental metaphors of the living still appear instrumental for collective understanding and easy communication in today’s scientific models (Cf. Haraway 1976; Keller 1995; 2003ab; 2005; Helmreich 2016), and this may be one of the contradictory factors that contemporary interfield conditions introduce: at the same time the level of complexity and number of advancements grow, expanding the topic of study to an overflowing object, too the international ambiance hypercontextualises and requires fluidity, simplicity and adapts with instrumental and utilitarian strategies in answer to the multiple and dynamic demands of explanation. It is not a problem unitary fields could revoke, but can become a socially responsible circumstance to change by interfield strategies.

## II — *On Physiological Reductionism*

The following part will deal with how rhetorical instrumentalism in scientific language affects interpretations of morpho-functional nature, that have an even more critical role in identifying the ontological nature of dysfunctions with neuropsychiatric tenor: pathologies arrive at certain explanations in aetiology on account of functional irregularities projected against a standard, and this process of ascription needs to be complex, full and skeptic of being definitive as sciences advance in comprehension but as well in their limits of observa-

tion. Reductionism in physiological interpretations does not benefit such ascription process in neuropsychiatric evaluation by understanding materiality as the ultimate form of agency following a highly refutable conclusion guided by microcosmic logical fallacies.

The next two sections will centre the exploration about over-attribution of overall agency to C fibres and central spinal interneurons, examining its epistemological consequences and some alternative approaches for characterising pain physiologically in a plural sense.

In this attempt, the second section will interpret pain as an epi-phenomenon proper to the interaction of multiple systems of the organism, in lieu of a reified universal experimental pain ascribable to a reduced material portion of the organism.

### *. Considering Over-Attribution in Theorising Fibre Specialisation*

Reductionism in basic research characterisation of anatomical regions and of clinical ascriptions has been approached in literature by numerous neurophilosophers. Bennett & Hacker (2003) have informed about this argumental solecism in physiological explanation through what they called the ‘mereological fallacy’: contrasting it with the arguments of evaluative and pre-evaluative attribution given in the previous section, the classification of morpho-functional parts in organisms, when bearing an attribution of ‘qualitative’ (evaluative) functionality to morphologies (that are installed in pre-evaluative functionality ambiances), constitutes a mereological fallacy in the sense that «neuroscientists’ mistake of ascribing to the constituent parts of an animal attributes that logically apply only to the whole animal we shall call ‘the mereological fallacy’ in neuroscience.» (Bennett & Hacker 2003, 73). To give an example of words usage, compare this excerpt from Harley’s 18th-century characterisations:

«Since therefore sensations are conveyed to the mind, by the efficiency of corporeal causes... it seems to me, that the powers of generating ideas, and raising them by association, must also arise from corporeal causes, and consequently admit of an explication from the subtle influences of the small parts of matter on each other, as soon as these are sufficiently understood.» (Hartley 1949, v 1, 11).

Machamer & Sytsma (2009) expose in their work how argumentations are impinged by historically contextualised logical grounds and explanatory strategies manifest so: theory makers tend to reify in the matter of study the underpinning theoretical ideology and historical and social mentality of the context's theoretical expectations. From a social epistemological perspective, theoretical expectations are precisely the main factor that variates and gives form to every scientific project, and through it is that historiographical work can evidence the traits of its historical and cultural production (van Fraassen 1980; 1994; 1997; 2008). Reification through materialism is, in an ontological identification of physiological properties, however criticisable, historically unavoidable.

«The basic problem is not in talking about experiences or even conscious experiences and their properties, but in taking all descriptions to refer to kinds of ontological entities and assuming that physical or material descriptions can only refer to fundamental particles and forces. The problem lies in generating incommensurable ontological pictures of the world from our descriptions of it. But there is no obvious reason why physiological explanation must be incompatible with first-person descriptions of one's experiences, despite the fact that they have different grammars.» (Machamer & Sytsma 2009, 365).

A rather similar form of over-attribution has been approached by the arguments about cellular specialisation in neurophysiology. In the case at hand, the question on what is a fi-

bre specialised towards can be subject to bear reductionist claims too. Regarding the fact that specialisation in C fibrils is overwhelmingly wide to pain, itch, numbness, temperature, friction, caresses, tickling, gentle touch and dermal sexual arousal, specialisation argumentation has also put in vogue the concept of multimodality, which in framing no explanatory solution, stops the characterisation at a merely descriptive step on the numerous affairs the fibre is excited by. This instrumental alibi is a problematic consequence of such 19th-century evaluative metaphorical naming of fibres.

The specialisation argument follows that since cell development tends to class-divide fibres, then pain, itch, numbness and further on shall be no exception of such specialisation, falling into a renewal of ancient reductionist physicalist ascriptions of experiences as individual natural kinds. However such theoretical direction comes opposed to multimodality. Multifarious specialisation appears to face an opposition between explanatory and descriptive strategies: the first direction (explanatory strategy) orients the theoretical content to a specialised stressor explaining the fibre's excitatory pattern following natural kind tracks in medical history as exposed in the previous chapters; the second direction (descriptive strategy) points towards multiple stressors, for these fibres are described to be excited by multiple agents. In one point of the theoretical procedure either certain form of eliminativism is required to act as a selector, or the theoretical presentation should retrace its steps and return to a more basic account of the problem.

The following is an example (pace Han et al 2012) of how introducing specificism on particular fibres as an explanatory strategy uses an overall agency (evaluative) attribution to a reduced part of the body (that shall be pre-evaluative), neglecting upper central nervous complexity, thus involving a physiological mereological fallacy.

«The specific itch behavior that we obtained by selectively activating only the MrgprA3 positive neurons provide direct support for the applicability of Muller's 1826 doctrine of specific nerve energies to a submodality of cutaneous sensations, namely the sensation of itch. That is, the quality of sensation evoked by a stimulus depends on the specific neuronal pathway that is activated, regardless of the nature of the stimulus. In this case, if only MrgprA3 positive neurons are activated by a stimulus, the sensation should be itch even if the stimulus is noxious mechanical, heat or chemical.» (Han et al 2012, 8).

The argument orients multifarious unspecific stimuli at induction peripheral areas (C fibrils stressed by heat, friction, etc.) and specific qualitative evaluation at central medial (spinal) interneurons, MrgprA3 positive cells at transduction phase. In avoiding C fibrils specificist problems, this claim extends the mereological fallacy to central subregions. It seems easy to decontextualise such neurons, attributing qualitative properties to a channel in experimental conditions, but the channel itself without further interaction does not provide of information enough to conclude the quoted interpretation.

As the argumentation favours that the stimulus is unspecific, it over-attributes spinal medullar pathways of specificism of a qualitative overall agency (pain, itch), however this argument is impossible to extract from just spinal areas, as evaluation of those specific attributions requires overall systemic and meta-systemic complex integration at upper cortical areas and downwards regulation-modulation interactions. Spinal areas may be specific, developed in contextual specificity to certain stressor and thus the pathway contributing to the whole experience, nonetheless the specificity cannot be an evaluative one, pain or itch. In this argumentation there appears no justified theoretical element that actually serves for explaining nor describing the contextual roles and agents at the physiological pre-evaluative scenario without

falling into a mereological fallacy. Moreover, without the whole system, the voltage-irritatory wave flow would never be felt at all by the specimen, inevitably implying no positive differentiated conclusion (pain or itch, or any other specific experience) could be extracted *e silentio* and attributed to any low-complexity part of the organism. It also obviates that central induction (atopic induction, occurring at central levels, as for example pain tactile hallucinations, mneseogenic pain, fabulative pain, etc., in neuropsychiatric ambiances —as it happens with the rest of specificities) is not contributed via spinal excitation, implying that the evolutionarily infrastructure necessary for experiencing the feeling involves evaluation along the entire nervous physiology, not just at peripheral or medial central (spinal) levels. This is, thus, a reductionist strategy. It also neglects the evolutionarily stressor-resistance principle that gives its theoretical sense to the role of a particular cellular development being 'specialised on x stressor': such 'stressor x' excites the cell in such a particular pattern not in vacuum, but in a contextual interrelation that has its manifestation in such cell specialisation development being diachronically (evolutionarily) exposed to the constant effect of such 'stressor x' existence and activity, to which there must be proof of both, an organic sensitivity to it, and a resistance modulatory tension towards it (the case of olfaction, a very primitive system and thus morpho-functionally well established and adaptively highly organised one, is an example of this principle; as pain is too via the resistance tension through opioids). Defending multimodality through unspecific induction but specific transduction, still being such transduction specificity at spinal levels a qualitative attribution, does not improve at any extent the burden of the fallacy, nor the degree of the over-attributive process.

To the scope of its justification, this is an instrumental interpretation, not a causal nor explanatory characterisation of the taxonom-

ic classification of the qualitatively attributed fibres. Neurons positive in MrgprA3 marker, indeed appear to transduce into Rexed lamina II contacting with GPR positive interneurons (Sun et al 2017, following the Leaky Model), then projecting to ascending pathways in specific nuclei in upper CNS, which also modulates this interaction in the I-II laminar barrier through endorphins (mu and especially kappa opioids in Rexed lamina II) and inhibiting dynorphinergic neurons (Kardon et al 2014). However a grounding central sub-recount of fibres is experimentally associated with itch as an outputting behaviour, qualitative characterisation (as the text presents) is not justifiable of being grounded on spinal, nor even pre-ganglionic afferents in behalf of the argument of specialisation. Specialisation is just a condition to the system to function, not to the reception as a qualitative originality of fibrils. The discovery of MrgprA3 positive neurons made an enormous contribution to clinical research through physiological identification, nevertheless in relation to explanation (pace Han et al 2012) the qualitative interpretation follows an example of utilitarian explanatory strategies for exposing the character and nature of the fibre's developmental affinity to itch. The relevance of the finding is not transposable to the relevance of the interpretation.

The argument of specialisation cannot be used to justify the responsibility on agency of afferent cells in induction or interneurons in transduction as properly perceptive, which is a qualitative characterisation of their morpho-functionality that would constitute an over-attribution by reification of a distinctive sensation (pain or itch) directly present in transduction. Cellular taxa therefore do not receive a clear input whose object is direct to that of a perception of a natural kind, as clear as olfaction with proteins in the mucosa that exhibit action potentialisation to the decomposition and fitting of molecules from the outside,

exquisitely differentiated (~200 types of reactive molecular stressors have been isolated in human olfaction). In the case of pain, itch, numbness, or tickling, specialisation of fibres cannot be explained as a development of recipient to noxious, itchy... natural kinds: noxious events are but productions, evaluations of further complexity.

If what the fibre receives is not molecularly itchy, a decontextualisation of terms (metaphorical instrumentalism), and neither is qualitatively itchy the channel (as if it was a metaphorical envision of a quality materialised through the fibre), there appears the right question on what is supposed to be the stressor condition beyond?

Through a dispositional perspective two arguments fundamental for explanatory strategies are suggested to be taken into account: (1) the identification of morpho-functional specialisation as by-product of a diachronic (evolutionary, adaptive) exposition to a specific sustained stress; and (2) the illegibility of partial biosignatures in experimental conclusions.

(1) *Morpho-Functional Specialisation as a Diachronic Product of Sustained Stress*: fibrogenesis with its specific development comes as a part of a morpho-functional disposition of the organism developed by virtue of an evolutionarily-maintained contactual exposition to a particular stressor. This fact is what conforms specialisation: under the condition of a maintained exposition to a particular stressor cell-specialisation emerges. The further recognition of the stressor by the organism is undertaken because of the expositional adaptation, which has a relevance not in the function of a particular type of cells (evolved), but in the whole organism. Specialisation is thus the recognition formalised through the system, in multiple steps, and in multiple regions of the organism. If we reconstruct the characterisation just of the receptor, we miss the whole sense

of the morpho-functional adaptation. When we approach the fibre as a ‘channel for a quality’ the fallacy takes place, because unintentionally we are characterising the basal function of the morphology as a hallway of an upper function of the organism itself, which would frame an entelechial characterisation in multiple senses. On account of the problems that identifying C fibres with so-called ‘nociceptors’ introduces, an alternative pre-evaluative attempt at presenting specialisation is suggested through integrative dynamic anatomo-physiology in the next chapter, the RIF (Reciprocal Inflammatory Fibrogenesis) Interpretation —that focuses not solely on peripheral ambiances, but takes into account transductive, integrative, mediating and modulating phases, as evaluative and regulating phases proper to the multi-systemic interactions attributable to the whole organism.

Another important remark on specialisation processes makes the case for the definition of the stressor not as a singularised actor, but as a dynamic and shifting, adaptive context that acts as a condition to the organism, where theoretical identifications can apply abstract concepts like gravity and its implications for collision, and further psychological organic behaviours (like fighting behaviours), or time-dependent concepts, ascribing a particular stressor under the conditions of its activation pattern, which may change and thus variate the stressor’s effect and activity (for example the pattern recognition applicable for friction can variate depending on the time context, speed and lapses, to which dermal areas present different reactions: eg, erotic evaluation reaction can present through a friction C fibril pattern very different from a scratching evaluation reaction pattern). Adaptive behaviours may not be the only factors present in the scenario. Erogeous-identified areas, mostly topic-dermal, involving C fibrils facilitating erotic-kindred experiences, caresses and gentle touch as aroused in specific conditions, could have been developed sen-

sitised to friction as an exaptive instead of an adaptive process, making use of peripheral C fibrils in mammals presenting such adaptation and renewing part of its morpho-functional role into a newly required condition with a similar stressor ambiance: nuances of friction patterns.

(2) *Illegibility of Biosignatures* — when certain microcosmic parts of the macrocosmic whole are interpreted as specialised-in-pain (qualitative over-attributed), the notion of a Q-fibre (substitute ‘Q’ by any other qualitative concept) would serve for measuring such quality Q through the activation or de-activation of the Q-fibre as a biosignature (a material marker). This movement is fallacious. In experimental contexts conclusions may be extracted from interpreting what occurs if the Q-fibre is not functionally active (eg, via genetic ablation), then implying its role as a biosignature for Q. By Q-fibres ablation (eg, the previous itchy attribution through MrgprA3+ neurons) is followed that an absence of reflexes and behaviours related to the specific Q at hand (itch) shows Q-fibres being functionally itchy. There appears a circularity: if Q-fibres are off, no Q-behaviour emerges, then positive Q-behaviour is explainable in behalf of fibres following quality Q are present, because Q-fibres are explainable in behalf of Q-behaviour, since the experimenter uses behaviour as a paradigm of standard:

$$\begin{aligned}
 (-Q_{fib} \rightarrow -Q_{beh}) & \rightarrow (+Q_{beh} \mid +Q_{fib}) \\
 & \rightarrow \exists(Q_{fib}) \text{ iff } \exists(Q_{beh}).
 \end{aligned}$$

The circularity manifests in part because it is an argument e silentio, in part because of an illegibility of the attributed quality through the biosignature, that was previously fallacious. For the case of Q as pain, it would be impossible to conclude these fibres are qualitatively-specialised or not since pain-behaviour, guarantor of these, would not appear if they stopped

at pre-medullar or medullar phases, or were modulated by upper CNS neuronal opioidergic fields, appearing unconscious to the organism and thus not exhibiting a pain-behaviour. The significance of their conduction is not within themselves, it is in their systemic role as facilitators for later integration at the central levels. There are no guarantees that these fibres are legible as specialised qualities in pain, but that their conduction is valuable to interpret that at the central level its integration with multiple networks facilitates an evaluative painful response. The probatory sample is that if such upper contact is inhibited, pain is not elicited (illegible signature), and multiple examples give reasons why to think this way (thalamic dysfunctions, cingulotomy, traumatic and degenerative problems in insular cortex, de-memorisation in somatotopic cortical areas SI-II, etc.: Cf. Gao et al 2004; Pereira et al 2013; Fuchs et al 2014; Boccard et al 2014).

As was it the core idea that lead to von Bertalanffy's (1950ab; 1955) Open System perspective, it is somewhat unjustifiable to reduce the life-arrangement of an organism's integrity in terms of a mere mechanical process, as neither is such reduction justifiable in terms of entelechies, inner organisers proper to biological systems, forces that unify and characterise living organisms as alive because of their having such particular vital force inside, for it occurs that both attempts commit an explanatory regress that results to be non-responsive in the long run (Cf. von Bertalanffy 1966 for the Open Systems view on the problem of biological entelechies and psychiatric explanation). Applied to pain, neither is justifiable to characterise an organism's experience of painfulness as painful (high-scaled complexity question) because of its perceiving pain as a noxious outsider quality that can be received through the body (external reification), nor through bodily envisions of such quality through the nerve being qualitative (internal reification). Since the experience

of pain events comes as individual recreations of the proper organism, its having a particularly qualitative nerve oriented to the recognition of pain, threat, itch or caresses would come to a low-scaled complexity answer.

Recalling Koch & Laurent (1999), reduction and atomisation will not probably lead to a fundamental understanding of brain working from a complex systems perspective: each brain is a tremendously heterogeneous patchwork, «understanding the function of any of its parts requires a precise knowledge of its constituents but also of the context in which these parts operate.» (Koch & Laurent 1999, 97-98). The question seems to be not just a business of over-attribution of epi-phenomenal characteristics to basal phenomena, in so doing the arguments would follow the present diffamation of entelechial reasoning, historically inherited metaphors without solid ground, basal qualitative specialisation, and utilitarian terminology that actually self-promotes the usage of instrumental explanatory univocal theory making strategies as Part I of the text reflects on. The question seems also a business of complexity in biological explanation (Cf. Bechtel & Richardson 1993; Heylighen 2000), of understanding a growing mereological problem that overflows a pivotal locus of classification (Cf. Valentine 2003; McShea 2001), of classifying and arranging more and more adapted living morphologies from an evolutive point of view (Cf. Lane 2006; Zylstra 2002; Pavé 2006) and of understanding the evolutionary characteristics emerging from these complexities (Cf. Eldredge 1985).

. *New Approaches for Pain: Epi-Phenomena  
& Integrative Alternatives to Perception*

Two main conclusions would help explaining the problem of classifying nociceptors as a historical practice of diffoming a definition through utilitarian usage. A conclusion driven by several studies on causation in science is that



the very usage of classification factors is meant to stress-conduce analyses to elaborate kinds, classes, types with a presupposed idea about the contents they are classifying (Mayr 1982; McCauley 2009; McCauley & Betchel 2001; Thagard 1999; 2005; 2010; 2012; Craver & Betchel 2007; Racine 2009). Another main conclusion of historiographic, ethnographic and epistemological reviewing, points out that such contents of analysis are at their end point, in fact, not pure reality but a documented fabrication, contents of belief, believed by scientists (Cf. studies on pluralism and naturalism: Cartwright 1999; Fehr & Plaisance 2010; Harding 1991; 1993; Mitchell 2003), contextualised in their time and era (Hacking 2002), and endorsed by communities of belief (Longino 1990; 2000) which obviously make use of some instrumental, metaphorical thinking that facilitates their reasoning (Kitcher 2003; 2004; Giere 1999; Keller 1995; Galison 1987; 1996; 2003; 2004; 2008).

As biodynamic anatomy grows in discoveries, a contemporary integrative view is gaining influence: in the assumption that the frame from which to interpret pain is not the proper phenomenon, but experiential, an epi-phenomenon emerging from the activity of system's integrative action, some approaches view the case of emotional manifestations as pain an issue of biological complexity. The reason grows merely because it is not justifiable to infer that harmfulness, a qualitative-intentional phenomenon, is acquainted by an organism before the very organism evaluates it. At all instances for mammals, pain experiences cannot be consistently justified when conceived away from central nervous integrations (not just induction, not just transduction) and multi-systemic epi-phenomenal inferences (evaluations).

In the aim of avoiding not biological complexity, contemporary epistemological interpretations elicit the assumption that experiences, emotions and bodily self-judgements (as those as pain) are epi-phenomena that appear to

emerge in synchronicity from multiple organic activity, once modulated after medullar transduction, through several encephalic integrations affecting memory, sentimental pairings, individual organisation, and thus involving psychiatric traits (Cf. Damoiseaux & Greicius 2009; Gell-Mann 1995; Thagard 2005; 2010; Corlett et al 2010). In the same sense, emotionality, the role of memory and self-construction endorsing affective beliefs needs be taken into account as a form of cognition (Duncan & Barrett 2007). Indeed, pain events show their cognitive evolutionary sense in community-creation, social recognition and self-differentiation. Diachronic adaptation and social organic interactions cannot be de-contextualised away from physiological argumentation. As historian of pain Joanna Bourke exposes, «pain events are inherently social and, therefore, integral to the creation of communities [...] precisely because pain-communication could resurrect de-stressing memories, elicit imaginative forms of identification, and risk extreme responses, it could similarly profoundly influence and facilitate social interaction.» (Bourke 2014, 46).

Pain as an organic interpretation of multiple-faced tensors, including cognition and pathological affectivity, is no new idea (Cf. Tracey 2005; or Melzack & Casey 2008 three-fold dimensional model), the audacious point is that describing pain with a dimensional account of cognition and emotion does not exhaust the characterisation of its evolutionary complexity, and does not stop the physiological solecism following reductionism and over-attribution.

From an integrative epistemological point of view, pain can be exposed taking in consideration the factor of biological integrity, which is actually what prompts complexity as a manifestation of an organism being adapting to not just functional integrations (summation), but morpho-functional developments, in an evolutionary sense. Interestingly, Sherrington's (1947) major contribution was addressed to integra-

tion, to functional integrity, for which all actions of the NS are oriented to coordinate competing flows of energy from the different parts of the body until salience of some of them is achieved. In regard to pain identification, the alternative interpretation as exposed in the next chapter suggests to surpass the qualitative conduction as reception, and to approach the issue from the pre-evaluative process of fibrogenesis that made conductive a system, being the epi-phenomenon of physiological integration what shows qualitatively as pain, proper to the organism as an agent, and being microcosmic specific parts identified as ‘facilitators’ with a diachronic role in such integrative effort. This would require to approach pain through the whole systematisation of the organism as an integrative manifestation (morpho-functional realisation) of the scaling complexity that is exhibiting as it develops. The reorganisation of biophysical circumstances, through particular changes in body tissues, appears to be biologically, evolutionarily coherent through a process of integration of diachronic actions along the whole organism. Is such coalescence of diachronic actions that come to be present altogether in a big-picture scene of fibre activation, not only focusing the specialisation of such fibres, which can be explained by an evolutionary adaptation through a maintained contactual stressor-climate, but the rhythms of salient impulses, what resembles an assessment of the current state of the capabilities of the organism.

P Wall’s (1979) statement that pain experiences cannot be thought apart from an organism being reconsidering its possibilities, by healing (immune reaction to pathogens, rebuilding of injuries) or preventing itself from more pain (inflammation), bears this relationship. The assessment —reshaped by the organism’s past encounters with similar event-patterns (biography)— may emerge, thereby, as an epi-phenomenon of such integration: the very experience of pain, an emergent consequence

of the overall activity occurring diachronically. Pain thus would not be characterised as a perception *stricto sensu*, but as a developmental accomplishment of the circumstantial need of integrating an ambiance of different stressors (which explains specialisation of particular systems and different cell bodies) empowering an escalation of complexity that leads to epi-phenomena, feeling, experiences. The term ‘nociceptor’ would be no longer justified, faced against multifarious stressors, multimodality, and pre-evaluative requirements in an attempt at avoiding fallacious interpretations.

Explanatory alibis are used in the entire process, and as Machamer & Sytsma concluded, their value needs not necessarily be coming with absolute comprehension of ontological ultimate dogmas; partiality of description can be of valuable interest if put in context:

«The value of neuroscientific explanations can be recognized and accepted without rigid ontological commitment to the entities that frame them; likewise [...]. Explanations do not invoke ultimate ontological entities with a corresponding apriori metaphysical status. Explanations are historical phenomena that are context, theory and purpose relative. Explanations need to be seen as our attempts to understand the world, to predict its course, and to intervene in the furtherance of our interests. Some explanations are more useful than others in a given context. Usefulness does not require that an explanation uses a is really only description. Reductionism in the strict and philosophical sense has no place in science or in philosophy.» (Machamer & Sytsma 2009, 374) .

This examination can explain some of the difficulties that clinical and basic research on pain is dealing with, a form of regress that Vania Apkarian has compared with visual neuroscience, «where knowledge of brain mechanisms is perhaps a century ahead of that in pain research.» (Cf. Apkarian in Basbaum 2012). It can be seen why the accretional drift of experimen-

tal documentation is orienting contemporary multidisciplinary research by adopting utilitarian and accessible terms for explanations, which accidentally avoid contemporary complexities in modern characterisations of pain, revealing problems of decontextualisation, and exhibiting a lessened contact among the different interfields justificatory strategies in relation to interpretative fields as neuropsychiatry, or clinical practices like therapy.

. *Closure*

Putting the historical frame together, the dogmatic interpretation is suggested to come from an entelechial inspection of the nervous system that tracks back to a pneumatic tradition of intentionality, transcribed to modern physiology by Müllerian interpretations of qualitative nerve conduction in the 19th Century. This interpretation does not correspond with current developments in the 20th, nor the 21st Centuries, not just because the justification of universal pain is under discussion, but because the definition of pain as a *stricto sensu* perception of a natural kind as such is trivial, and is being open to debate in modern times (Cf. Dalenbach 1939; Boring 1942; Moayedi & Davis 2013; Cardeña 2018).

The historical comparative analysis holds the argument that modern physiological characterisations of pain induction seem not yet to come with a contemporary non-utilitarian identification of pain-related fibres proper to the 21st Century, and continue working with inherited analytical specifications of the 19th Century. This conceptual environment explains why it seems that physiologists, psychiatrists, psychologists and therapists are talking about different matters when they talk about pain.

On the one hand, physiologists infer their data based on the thin identification of pain that the method is able to report, an epistemologically questioned method for biosciences that falls under artificial evidence (Mitchell 2003; Longino 1990; 1996; 2001; 2006; Cartwright

1983; Giere 1988; 1999; 2006; Kitcher 1993; 2003; Stump 1992; Fedigan & Fedigan 1989; also Cf. Boddice 2012 for a historical review of the cultural development of vivisection methods through the 19th Century). It is the pain of the laboratory, the universal and factitious act related to the response, the pain as a reflex, the pain of an animal, *in vivo* or *postmortem*, from which anatomical, physiological, pathological, pharmacological, evolutionary models are generated, but restricted to them and often difficult to translate to humans (eg, the very spinothalamic tract from rat to human models). Again, this involves as has been argued the epistemic problem of realism in science and natural kinds in biological and medical classification (Dupré 1981; 1993; Hacking 1986; 1998; 2002), and the insisting use of metaphors inherited from 19th-century explanations (Cf. Keller 's 2003 work on this precise topic).

On the other hand, psychiatrists, psychologists and therapists infer their own data according to a clinical, emotional, evaluative identification of the singular and private experiences of a human being, usually a patient, not an animal of another species. Obviously, their interpretations need to face with underpinning definitions, classification and explanations coming from the previous fields. When those are not suited for the other, a basic epistemological problem for cross-research pops up, as it is customary for what Darden (2006) terms interfield disciplines. In neuropsychiatry, where investigations deal with mental pathology in between, when it comes to issues such as fabulative pain, the biochemistry of grief, social pain, the disappearance or the anagenesis of empathic pain... there emerges an annoying discoordination in the characterisation of pain. It would be interesting to coordinate in the characterisation of pain at all levels, and it is an exercise of responsibility for medical epistemology too, in its making of a naturalised socially relevant analysis of scientific attainments (Fehr & Plaisance 2010).



# QIII, Chapter §4

## Pain Physiographies: A Contemporary Image.

(In Niche A — Framing Neurophysiological Characterisations)

☛ 323 — 328

—

### Parts

. *Introduction*

. *Note — On the Physiographical Presentation of Experiences*

### I — A General View

. *Immune Performance, Inflammation & Peripheral Induction*  
(Chart 1) *Inflammatory Chemical Ambiance*

. *From Upstream Central Transduction to Downstream Modulation & Regulation'*

(Chart 2) *'Mediating Fibres with Origin at Laminæ II & II-III Barrier'*

(Chart 3) *'Mediating Fibres with Origin at Lamina X'*

(Chart 4) *'Mediating-Modulating (Evaluative) Central Integration & Regulation'*

(Chart 5) *'Modulating Fibres with Origin at Laminæ VII & VIII'*

(Chart 6) *'Modulating Multi-Cyclic Stressor-Resistance Tension'*

### II — Contemporary Advancements on Transduction

. *Sounding Transduction: Rexed Laminæ & the Discovery of Interneuronal Matrices*  
(Chart 7) *'Overall Transduction Matrix Chart'*

. *On the Role of New Proposals in Understanding the Gate Control Theory*

(Chart 8) *'Gate Mediation Chart'*

(Chart 9) *'Gate Modulation Chart'*

### III — Physiographical Inputs, Further Interpretations

. *Reciprocal Inflammatory Fibrogenesis Interpretation*

(Chart 10) *'Reciprocal Inflammatory Fibrogenesis Interpretation Chart'*

. *Closure*

## . Introduction

Physiographies are consistently used in medical explanation and description. Charts, diagrams and images exposing, analysing, annotating physiological and anatomical matters of study, map and summarise clinical data while working as simplified instrumental scientific models. In managing different scales of complexity, such schemata show an immediate tool to face biological morpho-functional entanglements.

This chapter sums a general image of contemporary physiographies approaching pain induction and transduction, involving bottom-up projection maps (from peripheral induction to spinal mediation, to central integration), and top-down projection maps (especially central downwards regulation and medial-spinal modulation). The text is divided in three parts with a total of 10 charts. Part I offers a general view of the scenario, from Induction (peripheral and central), including the inflammatory chemical ambiances and their impact on master pathways of overall salience, to cortical Integration and Evaluation, and downwards Modulation. Part II deepens in contemporary advancements on Transduction, at medullar levels, including central spinal transduction and interneuronal matrices at Rexed laminae, analysing their role in achieving a contemporary reading of the Gate Control Theory. Part III closes outlining a final interpretation presenting the evolution of nociception-related biopath systems as fibres that would have developed sensitive to immune reactivity, especially inflammatory processes, analysing fibrogenesis of C fibres in organisms from a systemic biological standpoint, involving a Principle of Integrity on the basis of recognising the organism's unity as an integrity, a cellular cooperative coral environment that is self-sustained on account of its interaction with a medium that provides mutual variations in a reciprocal relationship. This departure point

would serve to building a Reciprocal Inflammatory Fibrogenesis Interpretation for pain-linked fibre specialisation, in the hope it can serve to help explaining problems on specialisation of these fibres, in the attempt at avoiding the over-attributive problem identified by QIII, §1, and §2, and extended in QIII, §3.

### Note — *On the Physiographical Presentation of Experiences*

From a connectomic, biodynamic anatomical perspective, maps focusing epi-phenomenal experiences present fragmented experimental reconstructions of a broader overall reaction within the context of a highly conditioned clinical intervention: the limits of scientific experimentation. This means that physiographical maps are relevant to such context recognising they present partial information to be completed from other sources, perspectives, and points of interpretation for arriving to an actual understanding of individual maps.

Reductionist conclusions on the role of the different biopaths extracted from interpreting physiographies can seriously affect how arguments are delivered on behalf of inferring the weight of a single biopath's role into the overall organic system. This extension of the significance of the role of a particular biopath or certain nuclei within the Nervous System (NS) especially comes to mind in perceptive and cognitive aspects, assigning general agency to particular pieces. To overcome misunderstandings, such an agency shall be interpreted as proper to the whole organism, at the time that 'facilitation' or 'coherence of dynamic activity' can be applied to the different positive particulars. The exploration in the present text uses terms in language like 'master nuclei', acknowledging that these nuclei (organisations of neuronal aggregations of cellular nuclear regions usually

conforming grey matter) characterise physiographically not agency in toto but facilitation or coherence of dynamic activity, and that are aided by glial bodies in the majority of occasions. Master nuclei are, thus, typically assigned to functional specific, perceptive, locomotive or cognitive performance, however no argument is to be applied for them characterising agency towards what the organism feels, but to characterise them as ‘facilitators’ or key ‘orchestrators’ in order the organism to be able to feel whatever function associated with such nuclei the agent is feeling —as analogy of the action and the instrument, a key inside a door works as a facilitator for a person to enter a room, the agency of entering is not attributable to the key, but to the person that receives the burden of being the agent of the verb ‘entering’ the room.

For the case of pain experience, the concept of nociceptor (C fibrils and A-delta fibres working as nociceptive cells) can extend this agency misunderstanding through the question of specialisation, for the cell is not the agent of pain perception, neither is pain being received from the outside. The experience is proper to the organism and, should the context of the observations allow to interpret so, pain is an evaluation of stressor conditions, thus, a cognitive experiential complex nervous creation, an epi-phenomenon of such actions. Following the scenario depicted in the previous chapters (QIII, §1, §2, §3) exposing the epistemological problems inherited by the 19th-century tags ‘nociceptor’, ‘nociceptive fibres’, for the scope of the present overview, an attempt has been made to put the physiographical morpho-functional relationships with such master nuclei and master pathways eliminating over-attributive agency.

The problem with defining nociceptors is not a trouble of being linguistically fussy with naming. It is a characterisational problem that affects the ontological recognition of what the fibre does, the proper understanding of how it evolved, and of the stressors it undertook spe-

cialisation towards. The problem with nociceptors triggers a final interpretation that will be delivered at the end of this text. Considering that such master biopaths are not defined as assigned to pain —for nociceptive fibres as commented elsewhere also bear the burden of facilitating multimodality on gentle touch, erotic touch, caresses, itchy experiences, tickling and numbness—, there appear at least three right questions on (1) what are thus these fibres sensitive to, (2) how those fibres specialised —eg, embryological, genetic and anatomical studies (Cf. Patel et al 2000; Marmigère et al 2006 on TrkA+ sensory neurons migrating from the neural crest) point out how very early in life, nociceptors and proprioceptors are not yet fully specialised, and several branches of prior general fibres appear to exist and further on differentiate, heterotopise and migrate—, and (3) what was the evolutionarily niche and requirements for these fibres to exist, be adapted and generate.

How overall frame interpretations are handled solving these questions affects the physiographical presentation: the ending interpretation offers a plausible workaround, an alternative way of conceiving of these fibres as to assigning them a connectomic relevance of their role in sensing immune reactions (the case of inflammatory phases is introduced). In this sense, the proposal results in a Reciprocal Inflammatory Fibrogenesis (RIF) Interpretation, outlining that RIF fibres would act in answer to a reciprocal interaction with their contextual cellular milieu given destruction of a Principle of Integrity: ie, these nervous cells are interpreted to be prone to excite when the organism disintegrates, involving mutual interplay with immune, hormonal and vascular systems.

### I — *A General View*

The following section summarises overall physiographical work on pain experiences, informing about 7 constitutive phases: (1) In-

duction (departure phase, at topic and atopic regions), (2) Transduction (exchange from peripheral fibres to interneuronal central fibres), (3) Integration (generally encephalic and mainly cortical, and at certain extent Evaluation, for Integration involves competition among different focuses of dynamic activity of master nuclei and pathways for achieving salience between excitatory and inhibitory neural firing), (4) Evaluation (cortical cognitive and metacognitive assessment of the physical integrity of the organism through salience outcome of the previous integrative performance), (5) Regulation (inhibitory response to Induction at cortical level, involving affective, cognitive, attentional, mnemonic and experiential colouring), and (6) Modulation (inhibitory response to Induction at medullar-medial-spinal level) triggering (7) a Downstream Resistance Answer (via inflammatory reduction through hormonal plus inhibitory neural regulation-&-modulation gating effects).

. *Immune Performance, Inflammation  
& Peripheral Induction*

Inflammation seems to start the underlying processes by which pain facilitation is outlined physiographically (Cf. Chart 1: 'Inflammatory Chemical Ambiance', *infra*). This phase provides of several factors and substances for exploring the departure point through a material principle satisfying that pain as studied physiologically is proper to the contributive action of an overall reorganisation within the NS of an organism (for this case, human and analogical mammalian NSs will be considered). From these factors, many triggers act as stressors outside the NS, other factors imply directly the NS fibres as stressors of non-NS cells, like immune mast cells and blood vessels. This scenario further on initiates a cyclic and continuous stimula-

tion of the NS. Immunological stress at tissue levels is a major facilitator of nociception and algocation. The inflammatory ambience is the main niche of Pain Induction. It is to be noticed that the inductive phase can also occur under no peripheral ambience (eg, at brain level), however inflammation may still be, as many new reports are increasingly evidencing, a paramount inception for induction facilitation even at central and proper-nerve levels (Abbas & Lichtman 2009). As a general description, the physiological stages of the chemical ambience involve a set of cycle recognitions among four major actors: cellular tissue that has been exposed to disintegration (especially membrane rupture generates the pathological scenario), several neurite pods of thin nervous fibres (peripheral receptors: eg, a C fibril), free immune cells (mast cells), and blood vessels.

The factors that contribute to depolarising the fibre generally start via damaged tissues that filter intracellular chemicals to the extracellular common ambience. When this situation is to exceed a critical threshold, and adjacent cell bodies contact the broken chemical equilibrium due to membrane rupture of damaged cells, the general damaged and non-damaged cells conforming the tissular scenario settle in a chemical extracellular reorganisation. This can be properly understood as tissular deterioration (for example in neuropathic pain, the very nerve cells), tissular damage (under probable reconstruction or cellular healing), or destruction (following necrosis and toxin flow under sepsis).

A prior initial step is the breach of the cellular walls (caused for instance by an injury), releasing parts of the internal cell chemical settings into the extracellular milieu, of special significance adenosine triphosphate (ATP), a basic energy exchange marker. Potassium, capsaicin, and acetylcholine also act on ligand-gated cation channels contributing to fibre depolarisation. Trypsin (Trp) and tryptase also activate G

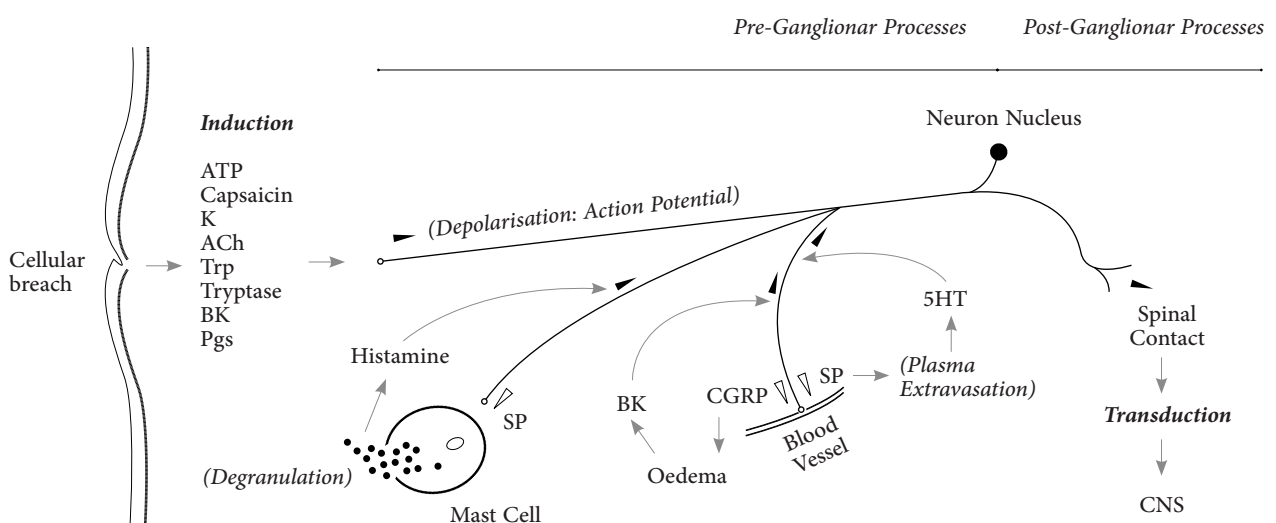
protein-coupled receptors, as bradykinin (BK) and prostaglandins (Pgs, both PGE2, PGI2) are released, affecting the fibre by depolarising its membrane, generating voltage conductance. Irritation also comes to place, as the fibre reacts to the presence of ATP, BK and Pgs corrugating, filtering out glutamate, Substance P (SP) and calcitonin gene-related peptide (CGRP). SP and CGRP frame a cyclic impact on mast cells and blood vessels: SP promotes plasma extravasation, and affects mast cells orienting degranulation; in the granules of the mast cells high levels of histamine concentrate which, being released by the action of SP, end up affecting the NS fibre back; CGRP widens blood vessels, prompting an oedema proper to what is topically visible at inflamed areas. As a result, the oedema contributes the damaged tissue to keep releasing BK, which keeps depolarising the fibre. Histamine has a clear facilitator impact on pain induction but also on itch induction through shared peripheral biopaths via C fibrils, as studied by the Leaky Model in relation to the Gate Control Theory (Cf. Sun et al 2017); histamine from mastocytes also has a vasodilatation effect, supporting the oedema (Komi et al 2017). From the aggregation of platelets in blood vessels serotonin (5-HT) is also released, filtered to the extra-

cellular milieu and sensitising the neurite pods of the fibre in turn.

Since some of these actors are nervous (SP, CGRP, glutamate), the cyclic nature of the process as a result of voltage-irritative performance has come to be named neurogenic inflammation —this is one reason why in cases painkillers may not work as required, non-steroidal anti-inflammatory drugs (eg, naproxen) can contribute to ease neurogenic pain (to the extent of the process, neuropathic pain too).

Reached this point, the scheme marks the initial movement towards a protective re-equilibrium affecting multiple and different further biological processes which manifest a proper allostatic reshaping of the functional relationships between damaged cells and not damaged cells. Coming to the NS (should peripheral fibres be spotted), as terminals get triggered by the immunological picture resulting in cyclical depolarisation of the neuronal membrane, following the fibre's neurite pod they proceed from, the product of such performance would present a voltage-irritatory wave that will reach the spinal cord and track forward to upper central nervous fibres. The wave-exchange from peripheral to central nervous ambiances initiates the process called Transduction.

■ **Chart 1 — ‘Inflammatory Chemical Ambiance’**





This original triggering process conforms Peripheral Induction, and this is consistent with NS fibres being activated by the chemical ambience of damaged cells, without NS cells being damaged. There are other forms of induction in contrast to this standard: for instance, neurotrophic pictures would present NS cells being damaged and producing self-perpetuating inflammatory ambiances (neuropathic pain is one case, as commented elsewhere in the previous chapter), or progressively neurotrophic scenarios in which the NS cells are constantly exposed to inflammatory ambiances, producing overreactive multisignaling. Other terminals may be not peripheral, thus assuming pain induction is centralised (eg, spinal injuries, damage or dysfunction of descending inhibitory pathways, or brain signal integration dysfunctions): fabulatory pain (eg, in psychotic events or in pain hallucinations) could serve as an example, where the initial phase of the pain experience does not regionalise into peripheral tissue, but in master nuclei, and are overall networks or dynamic aspects of the activity of such networks or parts of such networks what seems to be originating a cortical, evaluative pattern proper to a central recognition of pain as an experience felt by the organism as a whole. In this sense, a problem that appears within the context of the central integration of nervous waves at brain level, appears too parallel to induction-within-the-brain —up until the present day the multiple etio-pathogenic causes of central induction, that mainly affects population affected by psychiatric conditions, is unknown.

*. From Upstream Central Transduction  
to Downstream Modulation & Regulation*

After Peripheral Induction, fibre branches proper to the Peripheral Nervous System (PNS) synapse into Central Nervous System (CNS) interneuronal matrix fibres through the dorsal horn into the medulla via the Lissauer tract. This

process is generally called Central Transduction, starting from spinal (medial) cordal specific areas (physiologically mapped through the Rexed laminae appointed in the previous chapter) that will finally arrive to multiple medial (yet spinal regions) and upper (general encephalic, and further specific brain regions). When the multiple voltage-irritative waves coming from the induction focus are maintained and reinforced by the nervous network, the process would come to be called Mediation (positive conductance, forward excitation). If the voltage-irritative waves activate inhibitory interneuronal enclaves in their path, working as a backstop, certain wave signals would be interrupted (resulting in an overall decrease of the wave salience reaching central upper levels). This process is to be called Modulation, and generally acts at spinal levels through descending inhibitory fibres coming from medial regions, especially from Raphespinal areas and Spinomesencephalic-Periaqueductal areas. These operate through specific chemical inhibitors, generally endogenous opiates, peptides constituting the main limitation to the overreactive wave from the induction focus. The chemical families, including the newly discovered opioid peptides in the 90's, involve enkephalins, dynorphins, endorphins, nociceptine and endomorphins, observing their receptors in multisite spinal and central areas (modulating transduction), and even in peripheral level areas (induction focus). When the inhibition comes through a reorganisation of key brain networks (integration networks, evaluatory networks: cortical areas, especially cingulate gyrus, amygdalin complex, long tracing interconnective pathways, and insular cortex), the modulation of the voltage-irritative waves ascending from the induction focus are said to be regulated, involving Regulation as top-bottom descending inhibitory backstop, which incorporate emotional, memory, attitudinal and conscious management of pain. Central Transduction, considered as a whole via

ascending and descending pathways, consists on multiple interneuronal Mediation-&-Modulation salient milestones, that compose a complex supporting grid that variates dynamically individual by individual, moment by moment, and that is constantly reshaped by contextual stressor conditions. The supporting grid has multiple pathways, much of which are currently known through consequential experimentation: perturbation methods consist of acknowledging an initial excitation focus, and an ending reaction consequence, while intermediate steps performed by the wave are unknown, as these do not present to observation. While perturbation still introduces a methodological obstacle, multi-species analogies (generally rodent models) are being conducted and approach a general understanding of human and by extension mammalian pain central transduction pathways.

Interneuronal matrix transduction occurs at the point of wave exchange between pre-ganglionic PNS fibres and internuncial CNS fibres collected within specific spinal laminae. At this phase, the Gate Control Theory, along with new data supporting interneuronal mediating-modulating matrices, serves a good tool for mapping the interrelations of the waves's ascension and the blocking of their salience through inhibitory descending fibres. As a general picture, the map can present the following pathways considering the departure point of transduction at different Rexed laminae and their role in Mediation or Modulation. Charts 2-6 show such pathways:

— *'Mediating Fibres with Origin at Laminae II & II-III Barrier'*

C fibrils, mainly present in Rexed lamina II and the II-III laminar barrier, would transduce inductive waves via lamina V and scaffolded areas of lamina IV. A-delta fibres are showed to contact interneuronal projection fibres too at lamina I and II, from which a low percentage

of them return to interneurons projecting to lamina I, and others deepen into lamina IV and follow on to lamina V. From the consequent new branch of transduction fibres from Rexed V, two separate groups will project transduction patterns towards the thalamus.

The first group (immediate projection fibres) will cross the medial line into the parallel hemilateral region, through this spinal decussation fibres ascend via Spinothalamic pathway (in ventral orientation), and arrive to the ventral posterolateral nucleus of the thalamus (VPLN). These collect with C fibrils coming from the trigeminal nerve, gathered via Trigeminothalamic pathway (anterior) arriving to the ventral posteromedial nucleus of the thalamus (VPMN). From the thalamus fibres transduce to somatotopically ordered Somatosensorial Cortex (SI and SII), and further on to parietal areas from both SI and SII, provoking further integrative reorganisation at cortical levels with dynamic information waves from different origins.

The second group (deeper projection fibres) from Rexed V will project to Rexed VII and VIII. At such phase, deeper in the medulla than the first immediate group, fibres would cross into the parallel hemilateral region, following the Spinothalamic pathway (in reticular orientation) constituting the Spinoreticular ascending pathway, interrupted at the reticular formation (RetF), and finally arriving to the gigantocellular central zone, into the intralaminar nuclei of the thalamus (ILNs). From ILNs fibres will transduce to cortical areas, some to the insular cortex (IC), related to thermal and topic-critical salient experiences, and to the less clearly studied vegetative responses to pain, intervening physiological basal responses like heart contraction frequency, sweating, numbness, etc. Other ILNs fibres will transduce to cortical areas related to complex experiencing, anterior cingulate cortex (ACC), and other memory-impact affective cortical areas peripheral to ACC,

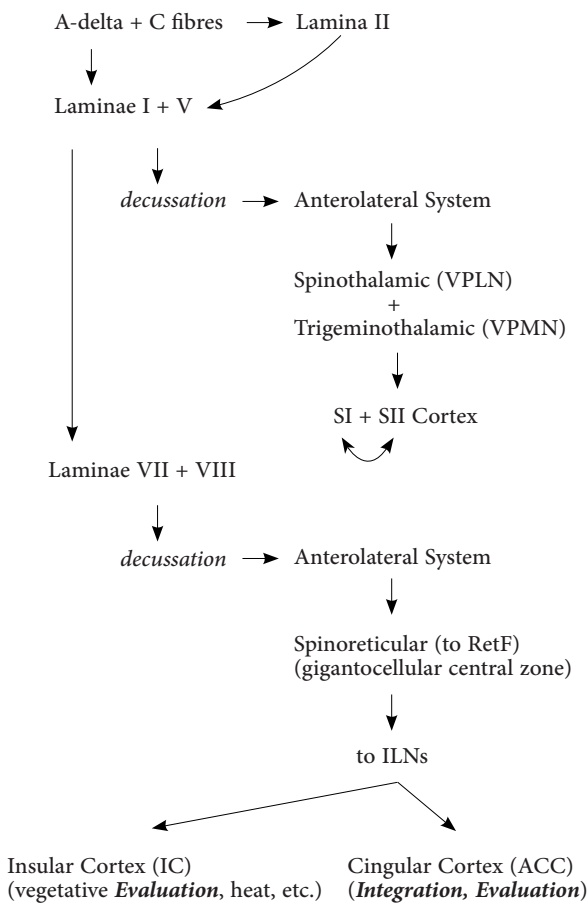
provoking further integrative reorganisation at cortical levels with dynamic information waves from different origins.

— ‘Mediating Fibres with Origin at Lamina X’

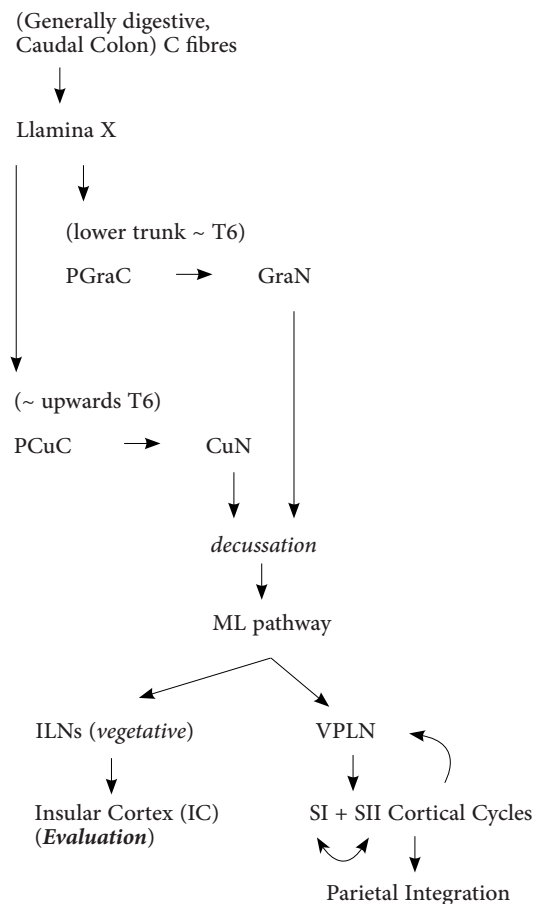
These fibres are generally related to vegetative pain, which introduces significant disturbance in psychiatric patients understanding chronic and fabulative pain due to poor cortical integration or to evident neurological dysfunction. Very thin peripheral C fibrils come gathered mainly from the digestive tract (the caudal portion of the colon).

These PNS waves ascend via spinal pathways through the posterior root, and contact by the tract of Lissauer into the CNS neuromatrix, deepening the medulla and transducing at Rexed X to central regions. From Rexed X interneuronal fibres, projections will reach two different systems depending on the spinal level of transduction: from the lower trunk (until T6), fibres will gather from Rexed X towards the gracile nucleus (GraN) through the Posterior Gracile Column (PGraC). Upwards T6, fibres will gather from Rexed X towards the cuneate nucleus (CuN) through the Posterior Cuneiform Column (PCuC). Both PGraC and PCuC ascending fibres will cross laterally and

■ Chart 2 — ‘Mediating Fibres with Origin at Laminae II & II-III Barrier’



■ Chart 3 — ‘Mediating Fibres with Origin at Lamina X’



follow the Medial-Lemniscus pathway (ML) towards the thalamus. Here fibres contact two main thalamic regional systems.

The first regional system is endorsed by general gross medial fibres, that arrive at the ventral posterolateral nucleus (VPLN) and project to the somatotopically ordered Somatosensitive cortical area SI. In cycle certain fibres will return to the thalamus, and another group of projection fibres will contact the somatosensitive cortical area SII. From SII further cycle fibres return to SI. This spiral process of cortical reverberation gating patterns is presented by integrative theories to have a role in refreshing the location of regional body contexts, with significance in adapting movement, and is related to a proper sense of awareness of induction focuses. From SI and SII transduction waves will enter further cortical integration via parietal posterior areas, related with spatial exploration and location-locomotion awareness.

The second thalamic regional system comes with less studied thin vegetative fibrils, which come through the medial lemniscus and contact the thalamic ILNs, projecting to IC which, further on, is assumed to integrate transduction waves with other cortical areas of different origin.

— *‘Mediating-Modulating  
(Evaluative) Central Integration  
& Regulation’*

ACC, and projective fibres peripheral to the cingular cortex (Villemure & Bushnell 2002), are significantly related to integration of complex experiences, decision making attitudes, attention and distraction, and emotional colouring of the relevance of the pain that is being felt. ACC presents very specific neurons (von Economo neurons, VEN) identified in complex organisms favouring cognitive dysfunctions when affected. VEN are characterised as proper to the ACC, IC and the dorsolateral prefrontal cortex (Fajardo et al 2008), in evolutive theories

associated with the requirement of fast processing of multifocal integrative information, generally implying animals installed in social contextualisation, including non-humans species, from which cetaceans have been contrasted in recent years (Butti et al 2009).

Excitation in ACC by intensity of pain, reactivity to pain and counter-reaction (obviation of pain) are also associated dynamics to cingular regions. ACC projects towards the main descending regulatory pathway, exciting from a top-bottom orientation the periaqueductal grey (PAG) matter, which is reinforced by the action of the amygdalin complex into PAG (the second main regulatory descending upper pathway). PAG will reach the medulla at medial spinal levels in consistent waves influenced by the ACC, inhibiting through opioid action the inductive wave, further on helping lessening the inflammatory reaction reinforcing hypothalamus-hypophysis hormonal anti-inflammatory effect at induction and topic levels. ACC also brings multiple connectomic reorganisation of cortical dynamics, reshaping memory scenarios and enhancing a better understanding of the causes and consequences of stressors associated to provoke pain experiences. This mnesic recognition is key in affective learning through the limbic system.

ACC also allows memory consolidation by relating memory scenarios of specific topics of attention (objects, sensations, people, etc.) with long-projecting neuronal networks associated to different perceptive colouring of events, including odours, textures, light and colour, etc., which favours precision in memory consolidation, distraction and prevention, linking future processes that involve the present aspects linked to the pain event as being felt by the organism (Posner & DiGirolamo 2000; Valet et al 2004; Orr & Weissman 2009). ACC is thus a critical biographical connectomic master region in the balance of ascending sub-cortical waves and integrative descending cortical waves.

Exploring the limbic dynamisms linking pain to cortical integration, chronic pain has been characterised as a neuroplastic shift pattern that shows reorganisation of cortical limbic patterns, pointing out how sustained pain experiences affect anatomically master evaluative brain areas, readapting morpho-functional neural developments involved in emotional reactions that generate and help to provoke affective comorbid unbalance. This reorganisation, fomented by continuous exposure to pain related stressors, ends up featuring bad responses reaching disequilibrium at reward and anti-reward systems (Fields 2006; Apkarian 2008; Hashmi et al 2013).

Insular integration will favour complex connectomic implications, being a master area related with evaluation of critic assessment of salient pain episodes. IC's repercussion on proper self-conscious pain experience is associated with its contribution to the general emotional colouring of rejection, and its implication in central regulation initiating a top-bottom descending inhibitory cascade hindering ascending pro-inductive and pro-transductive excitatory waves. IC is specifically active during thermal acute and chronic pain-kindred experiences.

A critical region for the hormonal modulation of induction is the amygdalin complex. This nuclei are also indicated to affect the insular integration of transductive waves at cortical levels, and are associated with the emotional colouring of scare, rage and immediate withdraw motion. Observed as an important neuropsychiatric area, its projections form critical accesses to the ventral tegmental area (VTA), the tegmental lateral dorsal nucleus (LDTN) and locus cæruleus (LC), niches for dopaminergic, noradrenergic and adrenergic neurotransmission, and for glucocorticoids projection. All compose a chemical ambiance associated with bodily responses to stress factors and anxiety. The relation between the hormone cortisol, pro-

duced via suprarenal cortex, and this ambiance, specifically for glucocorticoid projection and its role in blood dynamics, starts with its synthesis: the amygdalin complex affects the hypophysis (effect in the anterior portion), which in turn releases ACTH (adrenocorticotrophic hormone) stimulating glucocorticoids projection, that impact the blood barrier and filter to the blood stream as a result of organic inductive stress. Glucocorticoids projection affects the scope of this exposition since their presence in blood and finally cells at peripheral levels provokes a strong anti-inflammatory response. This reshapes via top-bottom orientation the whole process of pain induction, especially reorganising the inflammatory chemical ambiance at overall levels and topic levels, lessening the concentration and biochemical function of leukocytes, of import basophils and lymphocytes, and of immune free cells, mast cells.

In addition, at peripheral inflammatory regions, glucocorticoids increase the levels of phospholipids, decreasing prostaglandins, which has a significative impact on inhibiting immune response provoking alleviation of peripheral overreaction on C fibrils neuropods and, in turn, decreasing induction.

Noradrenaline projections also relate to reorganisation of cortical dynamics in connectomic significance for triggering memory scenarios, which is another effect of the amygdalin action. The amygdalin complex also projects to the hypothalamus, involving further responses from the autonomous nervous system. The hypothalamus is also reached by projections from the habenula, in modern times characterised as a master hub for neural interaction functionally associated with motivation and decision making. Dysfunctions in the habenular connectomic patterns have been neuropsychiatrically associated with depression (Ranft et al 2010); depressive population shows decreased medial and lateral habenular volume; and with emotional anaesthesia, exhibiting response to ket-

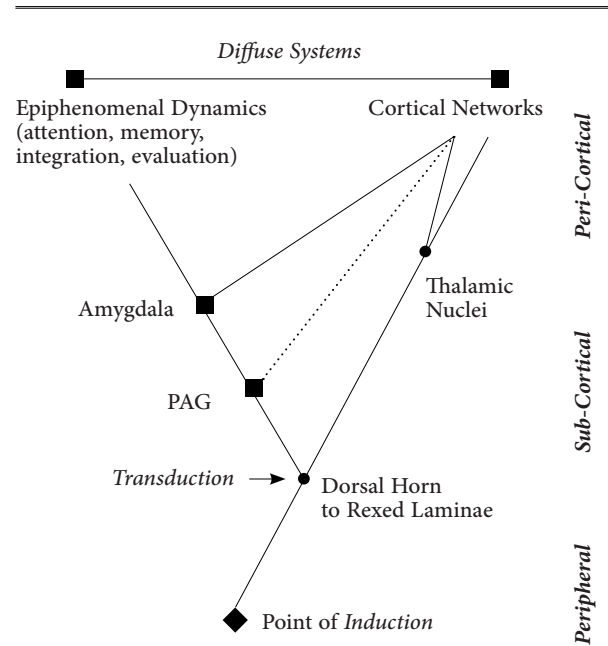
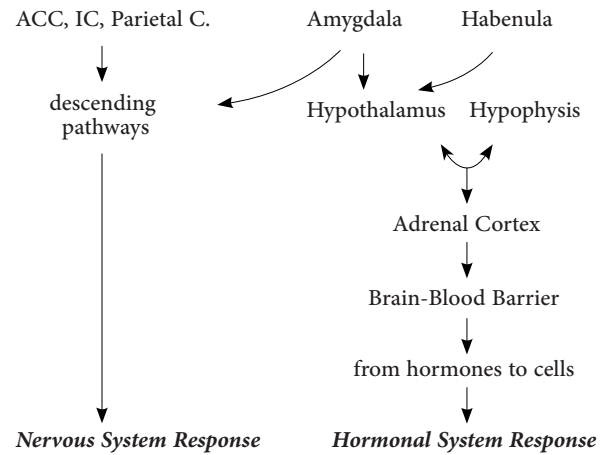
amine, thus used as an experimental therapeutic niche for facing depression (Serafini et al 2017).

On the connectomic interpretation of long connective entangled fibre processes, from master nuclei and master biopaths, and their role in emotional integration and evaluation, recent perspectives orient the topic to infer that differentiated emotional experiences cannot be spatially mapped into specific brain regions, falling into a reductionist localist approach. Instead, master areas appear to be dynamic, requiring time-specific cooperations with other areas, involving special orchestration (neural synchronicity) through cortical and limbo-cortical entangled networks operating through emergent properties that are proper to the interaction among such networks and not of any specific singular region (Lindquist et al., 2012; Sporns et al 2004; Roy, Sohamy & Wager 2012; Hashmi et al 2013). This understanding of dynamic morpho-functional master actions benefits the epi-phenomenal interpretation of pain experiences as exposed in the previous chapter.

Implications for neuropsychiatric studies are direct. Interdisciplinary literature (Baldeweg et al 1998; Pezard & Nandrino 2001; Behrendt 2003) has pointed out a critical feature for understanding the integration of different waves along the cortical areas, inferring how mobility (of neurons and glial bodies altering wave integration and interactions), disorganisation (of neural firing patterns and cellular dysfunctions affecting at overall levels) and reorganisation (of anatomical functional areas) may introduce markers for better defining and identifying behaviours neurotypically associated with psychiatric conditions. Applying network chaos theory, given its use in explaining such behaviours, a rebirth of oscillatory theories on thalamocortical integration of irregular wave patterns has emerged, proposing that psychiatrically-compromised patients seem to present interferences in connectomic fields that, when synchronised

chemically and biobehaviourally in disproportionate rates, provoke overall patterns clinically identifiable with psychiatric symptomatology.

■ **Chart 4 — ‘Mediating-Modulating (Evaluative) Central Integration & Regulation’**



— ‘Modulating Fibres with Origin at Laminæ VII & VIII’

Returning to Peripheral Transduction, certain stages at spinal levels are reached by the regulatory actions annotated above via top-bot-

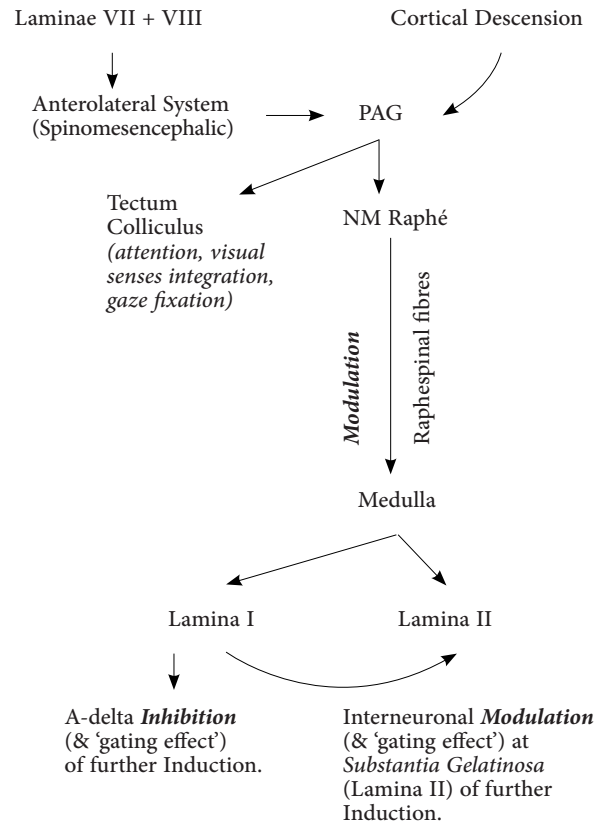
tom opioidergic pathways. However they affect inhibiting transduction via descending neurons blocking pro-inductive incoming waves. Such processes are excited by multiple specific ascending fibres with a main origin at Rexed Laminae VII and VIII and different further branches that happen to trigger medial medullar, pontine, mesencephalic and cortical downstream modulation and regulation reinforcement.

These fibres begin from Rexed Laminae VII and VIII and cross the medial line, ascending through the Anterolateral System reaching mesencephalic CNS regions. Fibres contact PAG via the Spinomesencephalic pathway, which gathers them with fibres from the cortical ambiance (of special import ACC downward regulation projections following the Corticomesecephalic pathway). PAG enacts the tectum, generally related to optical spatial and strategic attention, which can be also contacted by the hypothalamus via autonomic nervous signalling in relation to stress (Cf. results in zebrafish physiological models in Heap et al 2018), framing attentional attitudinal contributions to visual experience and gaze fixation through the colliculus (Avitan et al 2017).

A different branch of fibres from PAG enacts descending modulation by reinforcing the inhibitory opioidergic action of fibres from NMR, at pontine level. PAG contributes to NMR modulatory projections to spinal areas via Mesencephalopontine (etiam, Mesencephaloraphé) pathways, which will finally deliver inhibition through Raphespinal pathway fibres in posterior position arriving to the medulla at Rexed I (suggested to inhibit A-delta fibres that however reach laminae VII and VIII) and Rexed II and the II-III barrier (suggested to inhibit C fibres too).

In anterior position raphespinal fibres do not hold a role in pain induction inhibition, but in movement and locomotive performance (as cerebellum contributes) and in cardiovascular functions through the thoracic intermediate area.

■ Chart 5 — ‘Modulating Fibres with Origin at Laminae VII & VIII’



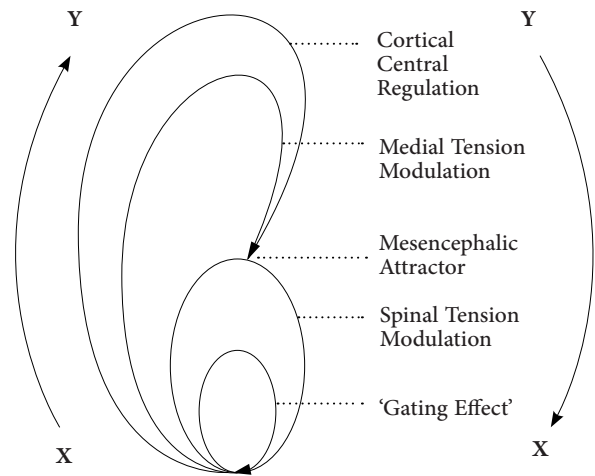
— ‘Modulating Multi-Cyclic Stressor-Resistance Tension’

To the extent of the exposition, a theoretical framework can be applied to explain what happens when PNS and CNS fibres contribute to pain modulation, involving stressor-resistance tensions. The stressor-resistance tension model informs about an organic development to stress, a morpho-functional development: given a bioevolutionarily framed tendency to face a present specific stressor (ie, presence of tissular deterioration, damage or destruction, pro-induction conditions unleashing inflammatory chemical ambiances), the organism reacts generating resistance tensions (ie, allostatic dynamics that prevent stressors from deforming the organism’s homeostatic equilibrium; Cf. the

notion of ‘physiological regulation’ in Ramsay & Woods 2014, where is suggested that homeostatic-allostatic models will be surpassed in a future by contemporary understanding on sophisticated, intricate sensor-effector relationships; Cf. Sterling 2004 and Peters & McEwen 2012, for understanding the historical premises that helped allostasis to be proposed as an active process, vs. homeostasis as a reactive feature given its reliance on reaction towards stress, a post-hoc response).

The stressor-resistance tension model can offer a shape from which to interpret the multi-cyclic activation patterns observed in CNS inhibitory contributions to modulation. Introducing a graphical analogy, the model illustrates the pattern of responses using the image that geometrical cardioid figures form (see the graphic ‘Cardioid Tension Model’, below), which is proposed to serve as a tool for describing and helping to interpret the responses to induction the multiple PNS and CNS fibre connections perform. The framework assumes two theoretical tensions (two conditions) that will serve to accommodate the orientation of the different pathways understood by neurophysiological studies up to date: an Upstream Tension, involving cycles actualising multiple ‘bottom-top resistance calls’; and a Downstream Tension, involving cycles actualising multiple ‘top-bottom resistance deliveries’.

■ **Graphic 1 — ‘Cardioid Tension Model’**

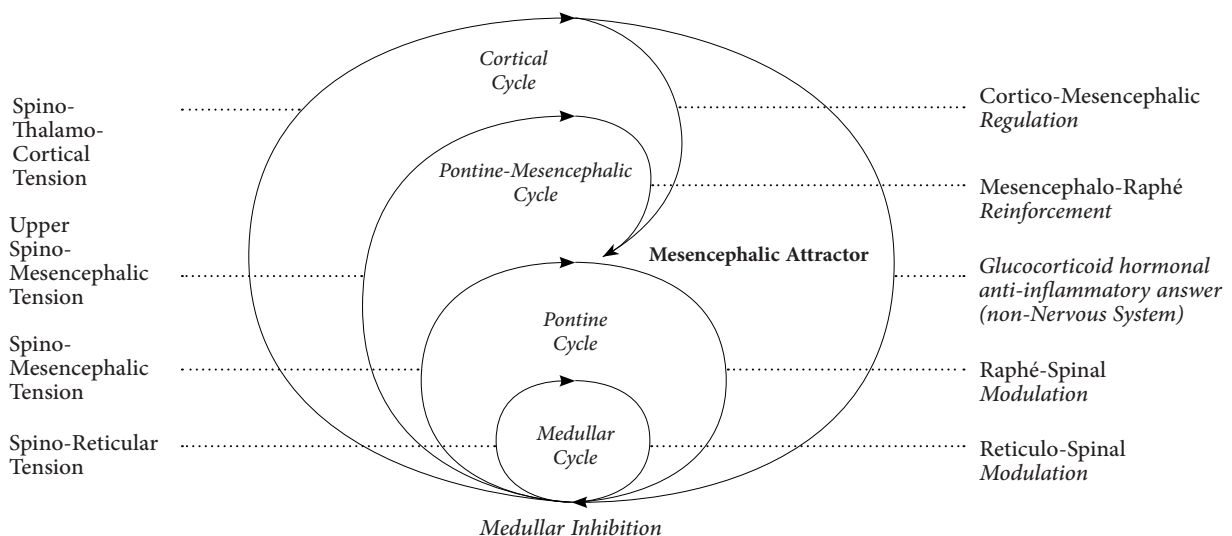


X—Y: Multiple bottom-top resistance calls.

Y—X: Multiple top-bottom resistance deliveries.

Both tensions configure a series of channels proper to the voltage-irritatory inductive and modulatory waves (upstream and downstream conductions). These channels are oriented within several central transduction and integration lapses or levels, which communicate via different fibre tracts. This communication and the overall connectomic dynamism generates functional and active pathways as summarised in the graphic ‘Multi-Cyclic Tension Patterns’, below:

■ **Graphic 2 — ‘Multi-Cyclic Tension Patterns’**





Here follows an outlining physiography on the multi-cyclic patterns produced by such tensions (Cf. Chart 6) exposing what this previous image overviews:

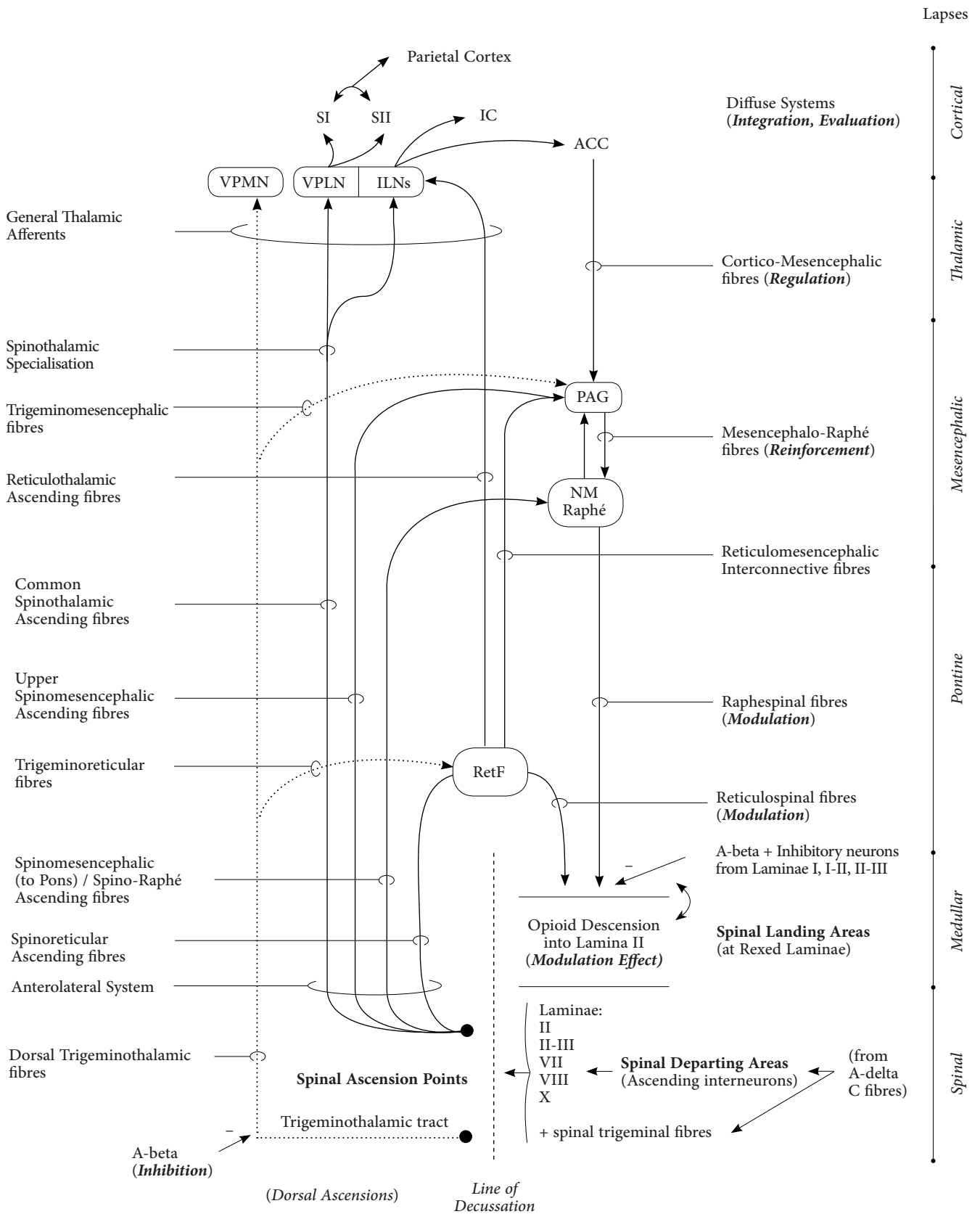
The Upstream 'Calling' Tension introduces a requirement of resistance, which is oriented bottom-up framing several cycles, several calls for feedback, being the feedback opioid inhibitory reaction for the incoming inductive signal, and further anti-inflammatory hormonal action. The fact that the resistance response towards induction is both of nervous (via opioids) and of anti-inflammatory (hormonal) nature, favours the suggested RIF Interpretation (*infra*).

The central transduction and integration lapses cover the following levels: at spinal medial levels, this tension implies ascending fibres that excite upper parts of the CNS, especially at Rexed laminae VII and VIII; at medullar levels it implies the activation of the RetF spinoreticular projections; at pontine levels it implies the main activation of Raphé's magnus nucleus (NMR), and LC, following spinopontine upward activation; at mesencephalic levels it implies the excitation of PAG via ascending spinomesencephalic projections; at thalamic levels it implies distribution to cortical regions via spinothalamic and reticulothalamic afferents, then projected to somatotopically ordered somatosensitive cortical areas SI and SII following VPLN of the thalamus, and ACC, IC, etc., via thalamic ILNs; at cortical levels it implies integration, salience evaluation and signal competition-contribution through cortical complex connectomic interrelational projections.

The Downstream 'Answering' Tension affects those projections destined to inhibitory action upon induction, vectorising the required feedback from a top-bottom orientation. The central transduction and integration lapses cover the following levels: at cortical levels, this tension will imply a reinforcement cycle returning to PAG via downwards corticomesecephalic projection from ACC to upper pontine-mesen-

cephalic regions —this projection from cortex to mesencephalic areas comes to be Regulation (affective, attentional, personal coloured interference)—; at thalamic levels there is no major cyclic reinforcement, neither downward projection of opioid nor anti-inflammatory hormonal action —which would serve to answer the resistance call of the previous Upstream Tension from spinothalamic origin, creating a point of avoidance through monodirectional non-downwards-specific projection answer (one possibility is that the calling tension does not actually 'call' the thalamic environment to answer, but to resonate the call disseminating it throughout cortical regions given the expansion of cortical tissue in the CNS)—; at mesencephalic levels the tension implies activation of PAG through cortical return, which reinforces NMR downwards action via mesencephalopontine projections —this downwards projection is of modulatory nature reinforced by cortical regulation (at this point the model comes to the central bulb of the cardioid shape)—; at pontine levels it implies NMR being reinforced to deliver inhibitory opioidergic resistance on voltage-irritatory induction waves via raphespinal projections —this downwards projection is of modulatory nature reinforced by PAG modulation, and of cortical regulation nature, which endows projection by multiple previous cycles of central salience contribution (as emotional affective tenor, memory scenarios, attention, etc. will cortically help to vary ascending waves, PAG will contribute too to reinforcement, meaning that dysfunctions in any of those master reinforcements will bring dysfunctions at further pontine and spinal levels)—; at spinal levels this tension implies the 'gating effect' blocking induction as suggested at work by the Gate Control Theory via both A-beta fibres and endogenous inhibitory modulation (this ends the second bulb of the cardioid model).

■ **Chart 6 — ‘Modulating Multi-Cyclic Stressor-Resistance Tension’**



## II — *Contemporary Advancements on Transduction*

Transduction has been the battlefield of pain electrophysiology during the last century (Cf. QIII, §2), producing a vast quantity of models trying to explain the interactions between peripheral and central nervous activity. By the end of the 20th Century, W Noordenbos's interpretation achieved a major acceptance, being re-elaborated and worked on by PD Wall's (1960; 1979) and R Melzack's (1961) individual works, and joint work (Melzack & Wall 1965) focusing transduction mediating-&-modulating firing patterns in a model that was finally theorised as the Gate Control Theory, conceiving of specific medullar areas gating the mediating or modulating performance of the internuncial neuromatrix of fibres connecting PNS with CNS. Entering the 21st Century, the conception was reprocessed and deepened by immunohistochemical studies pointing out where precisely at the different Rexed laminae of the medulla this internuncial transduction is performed. What follows is a physiographical review of the advancements on this matter.

### *. Central Spinal Transduction: Rexed Laminae & the Discovery of Interneuronal Matrices*

Modern optogenetic, immunohistochemical and electrophysiological studies (Yizhar et al 2011; Mar, Yang & Ma 2012; Carr & Zachariou 2014; Christensen et al 2016) have finally identified some molecular-specific variations at neurons in the dorsal laminae of the medulla. However assessed by rodent models, analogies may work with limitations for human pathways. Two populations of spinal dorsal neurons (Duan et al 2014) tracked right interest along international scientific communities: somatostatin-related excitatory neurons (SOM), and dynorphin-related inhibitory neurons (Dyn). These have been offered as evidences of in-

terneural connection from Rexed II to further projection neurons. The former are proposed to gate mechanical somatic pain through an internuncial cyclic circuit. In recent literature other classes of spinal neurons were found with different functionality (Krashes et al 2014; Rossi et al 2011), marked by their genetic load: the pre-prodynorphin gene, the neuropeptide Y gene, the choline acetyltransferase gene, and the pre-proenkephalinergic gene, mainly disposed to coadjuvate in inhibitory and homeostatic processes. This indicates that the medulla's chemical environment has a highly heterogeneous origin of intermingled GABAergic, glutamatergic, and opioidergic neurons among other peptides and receptors, among psychiatric interests cannabinoids can be included.

In regard to the role of Rexed I, new research has revealed the significance of its molecular instantiation for upstream projection and downstream modulation, a milieu for ascending-descending encounters framing a portion of the neuromatrix. Through immuno-histochemical biomarking, it has been evidenced that the expression of NK1R-antibody (the neurokinin-1 receptor, a metabotropic G-protein coupled receptor), seems to identify a vast fraction of ascending projection neurons located in Rexed I (Todd 2002; 2011). NK1R is also known as the substance P receptor (a tachykinin found in ambiances of tissue damage with a fundamental role at fomenting inflammation as reviewed in the previous section).

Immunohistochemical and electrophysiological biomarking evidenced that ~37% of neurons in Rexed I-III exhibits pre-proenkephalinergic (Penk) genes (Harlan 1987; Chen et al 2014; Liu et al 2015). These opioids are judged to have a role mediating pain thresholds and are desired to benefit chronic pain therapies in a close future, however their full mechanism is yet not well understood (François 2017). As an example, enkephalin degradation is known to enhance pain tenure, in turn, inhibitors of en-

kephalin degradation can reduce pain-salience transductance (Schreiter 2012; François 2017), which is related to the weakening, at modulatory medullar levels, of exciting upstream reinforcing waves from inductive inflamed tissue, caused by excitatory and pro-cyclic chemicals like Pgs, histamine, 5-HT, BK, and the neurogenic response to them through SP and CGRP.

Opioids's genetic expression is related to medial and upper central instances, mainly NMR, descending in medial and dorsal position, and the RetF, excited via PAG and Tectum. These medial and upper instances are centrally primitive, ancient, and morphologically more diffuse regions, associated with modulatory and homeostatic basic processes. This supports suggesting that a plausible genesis of such chemicogenetic ambiance in the dorsal and rostroventral medullar horns could have had its origin in a downward homeostatic-allostatic answer, expressed through a migration from those primitive central modulatory cores to the very afferent dorsal landing: through parallel diachronic evolution it can be suggested that now-pontine neurons migrated, with their chemical family, innervating now-lower medullar internuncial laminae (specifically Rexed I, and the II-III barrier).

A downward trend of morpho-functional progressions orienting a pontinospinal direction of evolutionary fibrogenesis can be proposed following two paradigms: (1) that C fibrils present later in evolution, proper to organisms of terrestrial milieu as pointed out in QIII, §2, (and *infra*), thus stressor cycles from newly morphological regions could have required a resistance answer tension, then reutilising opioid chemical ambiances proper to more primitive morpho-functional homotopies, like the mesencephalo-metencephalic areas, and expanding through the midbrain towards the medial and lower medulla via myelencephalon with thin long heterotopic intermingled fibres as are observed now reaching the laminae and forming the gating modulating effect that can

be observed today in mammals. The mesencephalo-metencephalic chemical opioidergic ambiance would have migrated to spinal bases following this direction and accompanying the nerves. And (2), the resistance tension as explained in the previous section is always activated through a preceding upstream resistance call: this implies that the very process of induction engages both, transductance mediating pain facilitatory dynamics and modulating firing patterns of inhibitory dynamic. The latter, which are always oriented downwards, are 'called' by the former ascending firing patterns, thus 'answering' through evolutionary progression downstream. Should this pattern be taken as a biological response, this factor may favour the pontinospinal (downwards) inhibitory fibrogenic interpretation.

Coming to how this opioidergic modulating effect performs transduction, Rexed II has been in modern times the common theoretical battlefield for finding the niche where interneuronal synapses relate afferent dorsal C fibrils and A-delta with projection neurons in the medulla to upper brainstem-and-brain regions. Recent works (Braz et al 2014; Todd 2002; 2011) have been able to differentiate Rexed II as subdivided into three pro-innervation layers:

The outer layer (IIo) is innervated by CGRP+ peptidergic dorsal afferent neurons (ie: neurons that are molecularly disposed to react through calcitonin gene-related peptide dynamics). A deeper dorsal layer (d-IIi) is innervated by dorsal afferent neurons molecularly disposed through isolectin B4 (IB4), a kind of glycoprotein that has been judged of value since the 80's as a cytometric biomarker for labelling endothelial cells with an extended use in identifying neurites and glial bodies. Another sublayer of interest for transduction towards projection neurons, the ventral inner layer (vIIi), is relatively defined by interneurons that express the isotype gamma of protein kinase C (PKCgamma). PKCgamma has been identified

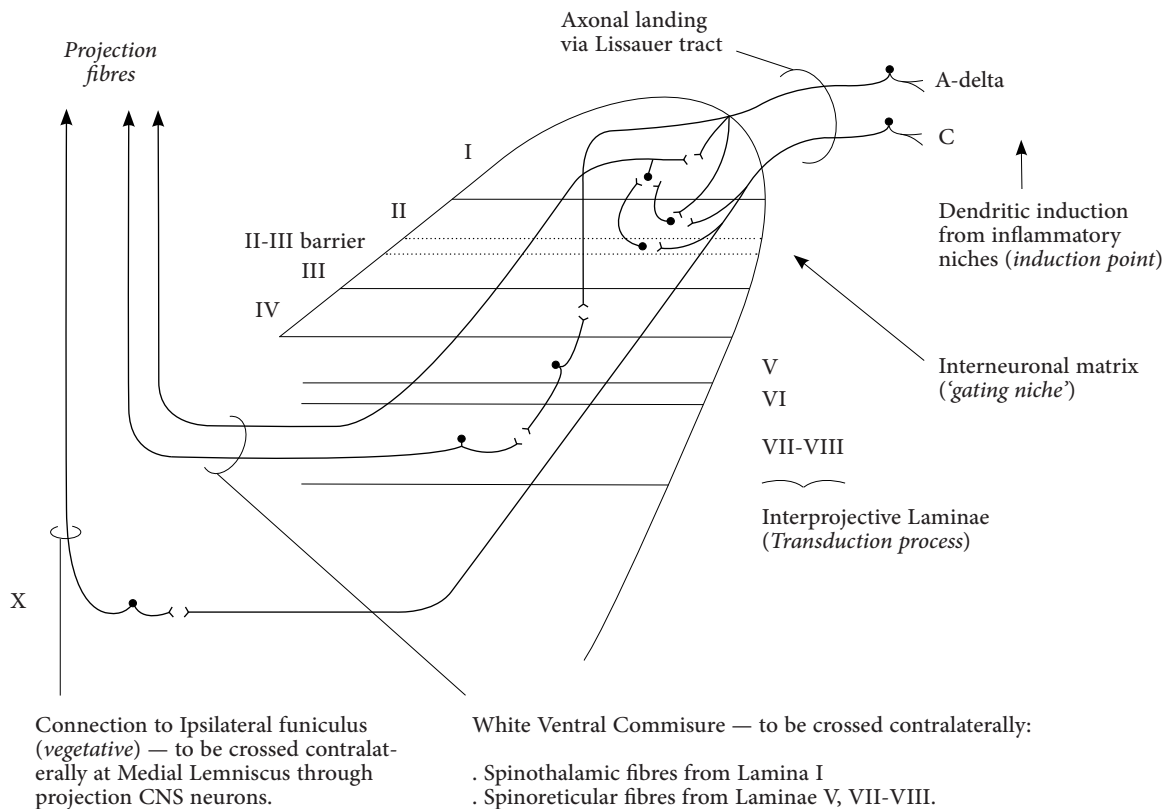
as a pro-signal transducer with selective location in the brain and spinal cord, especially in cerebellum, hippocampus and cortex. Given a scenario of PKCgamma deficit, this has been related to affect spatial and contextual agency, coordination or attenuation of opioid reception (Saito & Shirai 2002). PKCalpha and beta have been found decentralised (peripheral), therefore PKC central expression suggests a profuse relation to upper regions, functionally implied in overall adaptive responses in common with spinal areas, cognition and sense of stability. It is noteworthy that the relation between learning, memory, motor reaction and pain experience has a marked ethological significance.

Duan et al (2014) showed recently how somatostatin-related neurons are intermingled with CGRP+ terminals in the outer IIo layer of Rexed II, and with IB4+ terminals in its dorsal inner layer dIIi. The ventral limit of dense somatostatin-related neurons joins with dense PK-

Cgamma+ neurons in the ventral sublayer vIII. As an overview, although somatostatin-related neurons appear to be circumscribed to Rexed II, its heterogeneity happens to scatter them throughout Rexed I, III-V, and present differentiated excitatory patterns. This helps to find the relation between such neurons and homeostatic dynamics in Rexed I, and the very projection to upper areas in the medulla (mainly, Rexed V). Findings of vesicular glutamate transporters in somatostatin-related neurons (Fremeau et al 2004) show that a majority of them are excitatory (Yasaka et al 2010). This frames mediation in transduction.

The findings of Duan et al (2014) help to explore how A-delta and C fibres reach indirect projectionality to further thalamic nuclei through intersynapses with somatostatin-related neurons in Rexed I and with its ventral heterogeneous scattered morphologies at Rexed II-III.

■ **Chart 7 — ‘Overall Transduction Matrix Chart’**



*. On the Role of New Proposals for a Sound Understanding of the Gate Control Theory*

As described in literature, virtually the 100% of somatostatin-related neurons in Rexed II receives C afferents, with 50% of them reaching output, while 18 out of 22 somatostatin-related neurons at the Rexed II-III border receive C fibrils input, with barely 30% of them reaching output. As for A-delta fibres landing in Rexed II, a 50% reaches somatostatin-related neurons, with almost 20% of them attaining output. The fact that proprioception-related low-threshold fibres (and generally A-beta fibres) also appear to land in Rexed II ventral sublayers and the II-III border, as recent findings depict (Abraira and Ginty 2013), might hearten as well the question about how to interpret the specialisation process, in an evolutionary sense, of C fibrils from other non-pain facilitation specialised fibres like A-beta, which would frame the distinction between proprioceptive and nociceptive fibres. Following that a diachronic adaptation could have taken place with C and A-delta fibres from primitive pre-existing proprioceptoid fibres, further on undertaking their fibrogenesis via evolutionary characterisation growing under the effect of terrestrial conditions (especially inflammatory environments as the interpretation at the end of this text suggests), thus, characterising them as what now-nociception-linked fibres are to be observed, somatosensory and visceral fibrils, peripheral and multisensitive modality (pain, tickling, numbness, itch, temperature threshold salience, caresses, gentle touch and erotic touch).

From this perspective, their being tagged 'nociceptors' loses validity: an alternative, different argument is required to be proposed focusing the stressors through which these fibres came to exist, and the stressors that are now exciting them answering to the question on what are those fibres sensitive (specialised) to. There is also the point of debate in noting that the

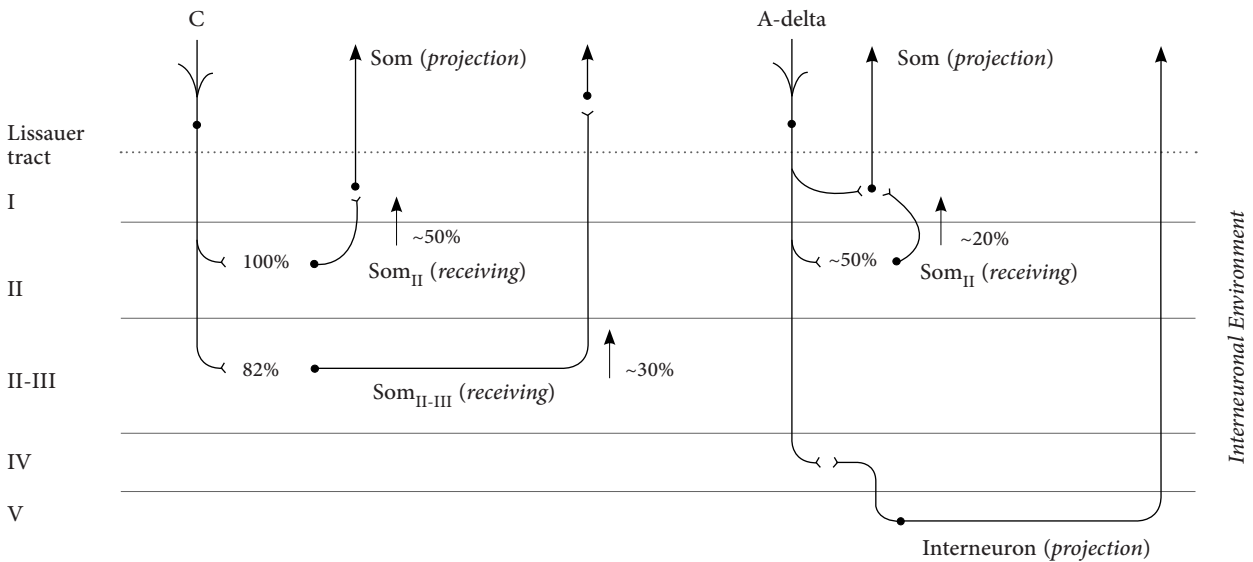
answer to those two questions might not be the same stressor. As for the role of proprioceptors in the Gate Control Theory, the assumed relay mechanism between interneurons, that is appointed to gate the transductive mediation and modulation through excitatory-inhibitory neurons, introduces the presence of A-beta fibres' enriched diameter landing into almost a 70% of somatostatin-related neurons in different firing patterns. Monosynaptic A-beta patterns produce output, while fast A-beta connections develop a counterstrike inhibition (Duan et al 2014). Somatostatin-related neurons receiving A-beta fibres are associated with GABAergic inhibitory processes, and are found mainly in the II-III laminar border, with a weaker presence in Rexed I. Results tend to hypothesise that somatostatin-related neurons act as a relay for A-beta afferences from the II-III border towards Rexed I, which projects from this point to the upper Spinothalamic tract. Another finding is that dynorphin-related neurons (regionalised in Rexed I and II, and subsidiary in Rexed III, IV and V) act as inhibitors, mediating mechanical pain as they express synaptic GABAergic and glycinergic behaviour against somatostatin-related neurons in both Rexed I and the II-III border (Duan et al 2014; Sardell et al 2011). More experiments on different forms of physical pain need be performed and interpreted. Dynorphin-related neurons (because of their heterogeneous position, or in response to other cells) also happen to gate inputs from A-beta myelinated thick fibres coming from Rexed III to somatostatin-related neurons in the II-III border: as A-beta fibres excite inhibitory dynorphin-related neurons, they continue favouring the propagation of their action potential until inhibiting somatostatin-related neurons in the II-III border, impeding them to excite projection neurons in Rexed I-II, that in turn thus not go further via upstream pathways to upper central integration areas. This manner, proprioceptive A-beta fibres from tendons, tonic muscular

spindles, hair follicles, Ruffini, Meissner and Pacini skin corpuscles, inhibit directly through the former process, and indirectly through dynorphin interneurons the transduction of pain. The fact that A-beta and C plus A-delta fibres compete for salience may be a theory making factor in understanding how newly formed C fibrils, consistent with the interpretation that these come from proprioceptoid primitive fibres, arrive at mediation niches in a very similar way to A-beta fibres, and are modulated by opioidergic inhibition at the same niche, putting in value overall psychobiological homeostatic-allostatic conditions (Cf. Karatsoreos &

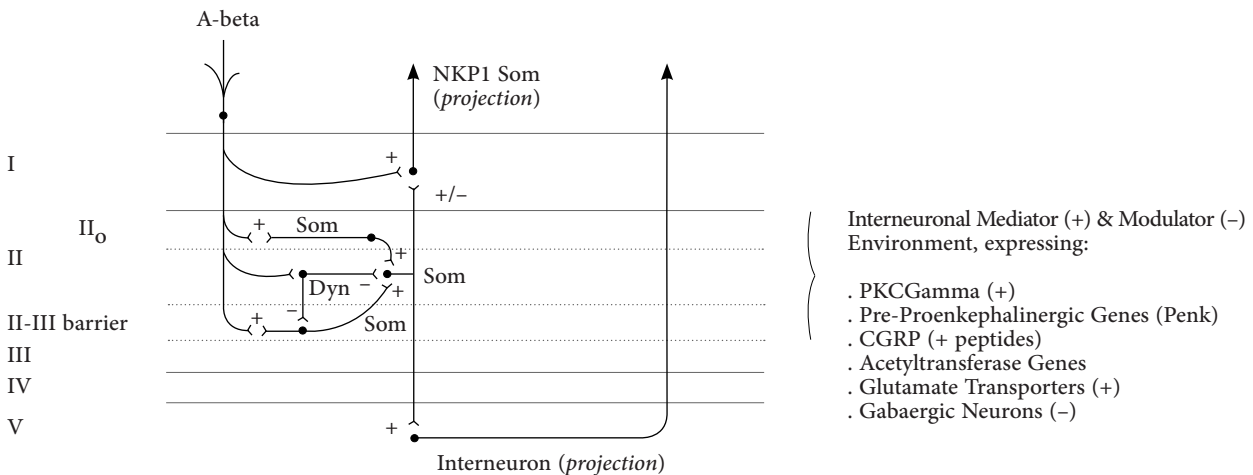
McEwen 2011). In conclusion, excitatory somatostatin-related neurons in outer and dorsal sublayers of Rexed II, and dynorphin-related inhibitory neurons in heterotopic regions of Rexed I-V, synapsing C and A-delta primary afferents plus gating A-beta proprioceptors, are generally interpreted by contemporary literature to be acting as interneurons connecting peripheral waves towards projection central neurons in Rexed I and V (Todd 2002; 2011). This supports and completes the Gate Control Theory in a general standpoint.

Chars 8 and 9 expose this scenario visually:

■ **Chart 8 — ‘Gate Mediation’**



■ **Chart 9 — ‘Gate Modulation’**



### III — *Physiographical Inputs, Further Interpretations*

Physiographies are appointed to unfold relevant connections given a specific goal in their plan —goals that may be implicit and related to the case of study (eg, ‘showing a general image of the connectomics among x systems and event y’), or explicit, indicating a hypothesis relating multiple parts of a system reviewed through a particular frame. Understanding the motivations behind the design of such physiographies may serve to deliver shortcut models clarifying the relationships among different focuses of interest with an applied and instrumental use (evident examples are surgical physiographies, developments of pathological processes, anatomical models, etc.).

These images are oriented to such goals, and therefore are required to be interpreted as delivering on information proper to the epistemic boundaries of their time and context. In the case of pain studies in humans, much of what is known on the paths that present these physiographies is limited by bioethical impossibilities and incompatible analogies among human physiology and other species, both conditions result in developing incomplete although progressively advancing maps of experiential phenomena.

Accordingly, conclusions extracted from examining physiographies must receive meticulous treatment, for further hypotheses will inherit those such limits. These maps are useful for conceiving of evaluative interpretations, which apply to physiographies as they serve to contrast among alternative theoretical proposals and experimental specific outcomes. Scientific interpretations are at the opposite end of scientific hypotheses, in the sense that hypotheses provoke initiation of experiments and interpretations emerge from comparing and contrasting conclusions from results analysed after hypotheses are experimented.

Comparative work can walk along the same argument, delivering useful physiographical interpretations. This third part will expose an integrative attempt at interpretation. ‘In-system interpretations’, proper to the organisation of such physiographies, can serve to gain wide-range perspective as they collect particular conclusions, and thus, being aware of their instrumental and pragmatic nature, their scope will come too conditioned by the relevance of their theoretical use: in contrast with common ‘constative-performative hypotheses’, that are proper to experimental scenarios (claims presenting hypothesised contents to be the case should the performance of experiments does not refute such claims), ‘in-system interpretations’ are proper to the physiographies prepared on the basis of the outcome abstracted from such previous experiments, and do not claim beyond such system but within the very building process of the system. In other words, the orientation of scientific interpretations is not towards the fulfilment of any experimentation, they are oriented to proposing a view regarding the general picture embracing the development of studies on the topic of analysis. In-system interpretations are thus evaluative in the sense they outline, actualise or debate the ‘conception behind the contents of hypotheses’, engaging a meaningful collection of relevant data and a contrasted evaluation of bibliographical backgrounds, generally presenting historical, comparative outlooks, for they are the product of demands for integrating specific experimental conclusions into a broader theory making, which forms not a theory *stricto sensu* but an interpretative claim.

#### *. Reciprocal Inflammatory Fibrogenic Interpretation (RIF)*

Specific proposals have been recently suggested on transduction patterns as reported by the previous section; also new hypotheses point



out to cortical connectomic dynamic orchestration as a key factor for engaging synchronicity and expressing epi-phenomenally a framework for studying organic experiences. Taking the previous considerations into a physiographical general picture, the present section suggests an interpretation facing the problem outlined at the beginning of this text on why C fibres need a reconstructive re-reading regarding which stressors provoked its genesis and what stressors they are specialised to, having being evolutionarily differentiated from other topic similar fibres, like proprioceptors. The problem with nociception triggers questions on (1) what are pain facilitatory fibres sensitive to, (2) how those fibres specialised, and (3) what was the evolutionarily niche and requirements for these fibres to exist, be adapted and generate.

One plausible interpretation applying the previous physiographical evidences suggest that Rexed I chemoactivity is implied in homeostatic-regulatory performance, maybe driven through an evolutionary parallel genesis alongside inflammatory responses to tissue damage, whose activity radiates constant firing cycles towards these matrix-gate-shaped medullar interneurons. Therefrom, a replying regulatory system could have been developed in response to inflammatory-related progress in the synaptic internuncial area among afferent dorsal fibres, firing-gating interneurons, pre-projective areas in Rexed I towards III, V, VII and VIII laminae, and modulatory descendent neurites (with special attention to endorphins, mainly the enkephalin family of endogenous opioids from the gigantocellular raphespinal downward system). Concerning the origin of the presence of this opioid in laminae, little is known, nonetheless the previously presented theoretical development has been oriented to an evolutionary downward-migration of pontine modulatory chemical ambiances to the medial medulla as a diachronic response to the continuous evolutionarily reinforcement of neural excitement

due to inflammatory activity. Evolutionary studies have pointed out how the liquid-to-terrestrial milieu shift affected dyachronic fibrogenesis, nonetheless identifying a niche variation put as a description of the factors that engaged organisms to adapt to a new environment does not favour a critical explanation of how the new stressors conditioning the organism reorganised into the modern morpho-functional NS physiographies we can observe today in mammals.

Stressors, and the organic resistance to them, require theoretical substantiation. To this extent, pain signatures have been identified through Bateson's (1992) criteria in mammalian, amphibian and bird systems (Cf. Lynn 1994; Willenberg & Stevens 1996; Gentle 1992). These criteria include the organism having nociceptors, specialised brain structures, upstream pathways towards such brain structures, opioid receptors and opioid substances active in specific downstream areas, and analgesic effect when at experimentation performance analgesics show to reduce nociceptive response. Modern literature (Henry et al 2017) has informed about how enkephalins present a therapeutic use for treating stress resilience, connecting opioids effect on different central levels, of significance those of integration and cortical reorganisation, interpreting that the enkephalinergic dynamism acts not alone in downstream projections but also in upper central areas. In addition, biobehavioural tenets must be present, including avoidance through learning (mnestic, cognitive and metacognitive scenarios) and finally the suspension of normal behaviour (informing about critical rest needs).

Pain exhibition in animals is thus experimentally limited to these conditions for a scientific understanding as decided by the common acceptance of these criteria. These criteria are synchronic, ie, static, framing the animal as how it is at the present in its exposition to experimentation. Accepting such criteria for diachronic explanations, evolutionary or pro-

cedural interpretations of systemic nature, may hinder explanations on why the animal shows nociceptors, why brain structures are developed the style they are in each taxa, why there are resistance calls to stressors informing such brain structures, why opioids introduce an answer to stressor resistance calls, and why avoidance and learning paradigms are properly common to pain once performed a physiological work transmitting and modulating voltage-irritative waves from induction focuses throughout the previously developed tissue. For diachronic interpretations attempting at facing at least some of these three previous questions a basal pre-specialisation, pre-innervation and pre-learning theoretical agent shall be identified.

Species division from water to land makes a central issue the research of pain signatures in fishes. Both elasmobranchs (cartilaginous fish) and teleosts (bone-bearing fish) have distinguished fibre classifications, being found both classes A-delta and C fibres in teleosts (Sneddon, Braithwaite & Gentle 2003), and just A-delta in elasmobranchs. Two arguments can be applied: (1) pro-myelination gene-related selector process would have been expressed and/or avoided in relation to slower conductance and medium diversification in the evolutionary drift of the different taxa; and (2), in the process of such differentiation, terrestrial stressors (gravity, collisions, acidity, temperatures and gases different from aqueous milieu) could have played a weightier role contacting the tissue's ecological conditions (Sneddon 2004).

This idea is supported by the fact that teleosts, phylogenetically closer to further amphibians and terrestrials, present C fibres, which would have had a more significative fibrogenesis in landed animals because of those reasons. Studies on fish also showed similar evidence as for mammals in the trigeminal nerve but failed to demonstrate slowly adaptive mechanoreceptors, proper to mammalian fibrils. Conduction through depolarisation and afterpolarisation

momentum is slightly slower in fish fibres because of the medium. In regard to brain and brainstem architectures, spinal cord laminae are closely analogical in the vertebrate organisms, teleosts, mammals, birds and reptiles. Afferences ascend spinoreticularly and land in reticular preencephalic nuclei even in elasmobranchs, reaching telencephalic, thalamic and tectal nuclei; spinal projection and medullar transduction therefore seem to be basal for all, proper to a more primeval organism.

Modulatory rhythms through endogenous opioids in enkephalinergic and dynorphinergic paths have been exposed in fish, birds, reptiles and amphibians (Snow, Renshaw & Hamlin 1996; Willenbring & Stevens 1999; Cruce, Stuesse & Northcutt 1999). In fish, these have been shown to modulate too afferent fibres in lamina A, the analogical to Rexed I to II in humans, which provides a bright approach for comparing homeostatic adaptive functionality (Baffy & Loscalzo 2014) in generative morphologies through dorsality, at least in vertebrates, and their relation to the development of pain signatures and the gating effect.

These observations may also have an impact on assessing downwards answers: the more terrestrialised and subject to gravity and collisions the organism is exposed, the more it will face a family of stressors related to peripheral tissue, deformation, concussion, that would fit provoking multiple and abundant calls for resistance in a basic tension against stressors impeding deformation. An implicit primitive principle of Integrity is being identified in such process.

At this stage, the Reciprocal Inflammatory Fibrogenic (RIF) Interpretation can present its claim: C fibrils, proper to a dorsal fibrogenic process, less myelinated, more modern and arborised, and their relationship with downstream resistance answer through inhibitory opioid spinal presence and anti-inflammatory hormonal response, could have been installed in an evolutionary niche of reciprocity between

immune performance, especially through inflammatory chemical ambiances, and the process of nervous fibrogenesis in specialisation to now selected cells (A-delta & C fibrils) that would be facing stressors prone to disintegrity.

This RIF Interpretation suggests that specialised fibres would have progressed from a basal, primitive nervous fibre mesh (an homotopic matrix, adjusted through ganglia) that extended through an early organism, innervating it as an initial facilitator to agency in sounding the outworld from the inside. This homotopy is theorised to express the recognition of the previously mentioned basic principle in organic formation, a 'coral tenet' that satisfies cellular aggregation and specialisation thereafter: accepting a principle of Integrity the organism installs in the recognition of its unity as 'an integrity', an environment that is self-sustained on account of its interaction with a medium that provides mutual variations in a reciprocal relationship.

Such primeval homotopic matrix would need to introduce the following developmental characteristics: (1) development of Topic Extensivity (specific fields in surface or skin: haptic afferences near the dermis and epidermis); (2) development of Inner Projectivity (visceral, capsular, tensional and muscular interoception, fibres that may be not haptic in relation with dermatomal topic afferences, perhaps because the latter preceded the former ones); (3) development of homeostatic-allostatic balancing variables (leading to an immune system and chemically to inflammatory cell cycles associated with tissue stressed to disintegration, like structural deterioration developing dysfunctional cellular environments) which involves an Upstream Tension Resistance Call; and (4) development of a homeostatic-allostatic modulatory system in reaction to inflammatory and other stress-related overexcitement (descending of ultrastructured chemical ambiance from archeotopic, well-intertwined structures, mainly the brainstem) which involves a Downstream Ten-

sion Resistance Answer that could explain the homeostatic-related functions in Rexed I, and the presence of enkephalins in Rexed II, in coadjuration with GABAergic astrocytes as presented before in the text —Cf. the different significance given to the roles of allostatic and homeostatic processes by modern literature since the 90's in Dworkin 1993; Sterling 2002; Karatsoreos & McEwen 2011; Peters & McEwen 2012; Ramsay & Woods 2014; Baffy & Loscalzo 2014.

The initial matrix is to be configured by both, Topic Extensions and Inner Projections, which would remain in the body homotopically oriented (ie, conserving the principle of Integrity), this is, resting in a hushing, smooth topology within the organism as a whole. The use of the characterisation 'homotopically oriented' neural mesh acknowledges a primitive innervation of fibres specialised towards sensing such integrity, however undifferentiated towards different forms and levels of disintegration. Craig's (2002) interpretation for interoception, where fibres are clearly associated with a ventral fibrogenic process, can be contrasted with a dorsal process in the current proposal for RIF fibres. The diachronic theorisation of primitive homotopically innervated organisms additionally connects integrity sensing with the argument of pre-terrestrialised phylogenetically linked organisms. Understanding fibrogenesis following the ossification and terrestrialisation of organisms (following Sneddon, Braithwaite & Gentle 2003; Sneddon 2004), the RIF Interpretation would claim these organisms acquire tissular genetic features proper to the shift of their milieu in their need of sensing their integrity, as recognising the need of qualifying (specialising) and enriching their systems towards the new progressive ambiance. Ambiance shifting presents a good theoretical support for conclusions on diachronic (evolutive) and synchronic (of a determined actual moment) fibrogenesis and fibre variations (Murinson & Griffin 2004; Kisseleva & Brenner 2008). As this basal ho-

motopy deforms, consequence of the action of environmental overall conditioning stressors, like turbulences against a diffuse mesh, a process of heterotopy begins, thus deforming the morpho-functional mesh stability.

Heterotopisation, introduced as a process of deformation affecting and intimately contacting and specialising such mesh, would come imposing variations conditioned from the medium and changes in the medium towards the receptive homotopy. This too reorganises and redefines the agency facilitation of the organism as supported by the fibres in a dorsal fibrogenic process. Heterotopisation would initiate specialisation variables in reciprocal relation between the ambiance and the organism. It would be the case for pain inception that a primitive, diffuse, proprioceptoid homotopy drift might have derived into two fundamental forms of stress heterotopic specialisations, ie, two basic families of fibre response to disintegration of cellular cohesion, following cease of the Integrity principle: one kind of heterotopy affecting the organism's basal de-homotopised fibre topography would happen to relate and install in non-inflammatory ambiances of mechanical and kynetic stress (becoming modern proprioception, mechanoreception and interoception related fibres); a second, posterior regionalised heterotopy affecting the de-homotopised fibre topography would have developed exposed to inflammatory fibrogenic ambiances (becoming modern nociception, algoception linked fibres) where injuries and tissue damage happen to occur as stressors.

The RIF characterisation of such fibres could help to explain the morphological, functional and local resemblances between proprioceptive and nociceptive fields, the fact that both fibre families are not fully specialised at birth, and the fact that given the milieu shift from aqueous to terrestrial media, C fibrils appear later in the diachronic evolution of organisms, thus, heterotopised after proprioception and developed in

response to higher inflammatory stressor conditions of disintegration than in water milieu.

For the case of pain physiodynamics, inflammation presents the initial step of the organism recognising disintegration: de-homotopised, the topography of fibres would be able to get excited in a particular excitatory cycle associated with the chemical expansive inflammation process, a firing patten proper to a chemical ambiance of disintegration. Chemically, in this inflammatory process the tissular ambiance disruption (substances externalised from intracellular to extracellular areas) would affect the primitive homotopy as a constant stressor shifting fibre specialisation to such chemical ambiance in a process of heterotopisation reciprocal to immune inflammatory conditions.

This implies both systems, pain or disintegration sensitivity and inflammation or immune reaction to sensitivity, may have been intimately related in the evolutionary process that gave birth to C specialisation fibrogenesis and immune cellular specialisation. The fact that induction expresses through reciprocal relationships among immune cells, mast cells, C terminals, disintegrated tissue and blood vessels builds a good argument for inflammation being an answer to what could have caused the heterotopic shift from a primitive gangliar proprioceptoid mesh to modern C fibrils and modern proprioceptive fibres. One fibrogenic branch of the system (RIF+ fibres, facilitating pain, itch, tickling etc.) is suggested to be sensitive to disintegration by being installed in an ambiance of reciprocal contact with inflammatory processes, whereas the other fibrogenic branch of the system (RIF- fibres, facilitating proprioception, mechanoreception, etc.) is suggested to be sensitive to disintegration installed in a non pro-inflammatory ambiance (a key fact of these fibres is encapsulation of terminals into corpuscles and spindles, a form of discontinuation that also can be related to be more distant and thus theoretically more dissociated from inflamma-

tory repercussion than bare terminals as in the case of RIF+ fibres). In the case of RIF+ fibres, provided that disintegrated tissue cells and mastocytes refeed the neural dynamic through very specific substances (BK, Pgs, histamine, potassium, 5-HT, etc) that are also reciprocally re-fed by the neuron terminals (via substances like SP or CGRP), the heterotopy would have imported a consistent energising cycloid pattern allowing Induction through fibre projections to grow and specify. This happens to project dorsally, as an upstream call, that is later answered back ventrally by descending inhibition, modulation and gating developments as exposed in the section above.

The inflammatory chemical ambiance, and its concomitant expansive stress against this de-homotopised fibre topography, would act as a reinforcement for the primary afferent neuron until voltage-irritatory salience emerges by summation (in relation to cellular allostatic changes due to inflammation), depolarising further processes allocated in the medulla (especially as studied for mammals). The medullar ascending pathways, through collateral ramifications at the pontine and mesencephalic levels, instantiate the corresponding descending modulation in reaction to inflammation-related overexciting cycles. In more complex organisms, these cycles continue modulating pre-encephalic afferences, until reaching different integrative dynamisms in the brain, which react (moto-cognitive reactions) to the injury, thus exhibiting a macro-behaviour in regard to the previous coalescence of such micro-behaviour in the tissues's heterotopised fibre topography that also can provoke developing learning patterns, cognition, recognition, metacognition, avoidance and rest behaviours.

The RIF Interpretation, this way, puts in value two historical conceptions. The idea of an unspecific threshold (Intensive Theory) becomes partly true as it turns into a computation competition of salience among afferences in

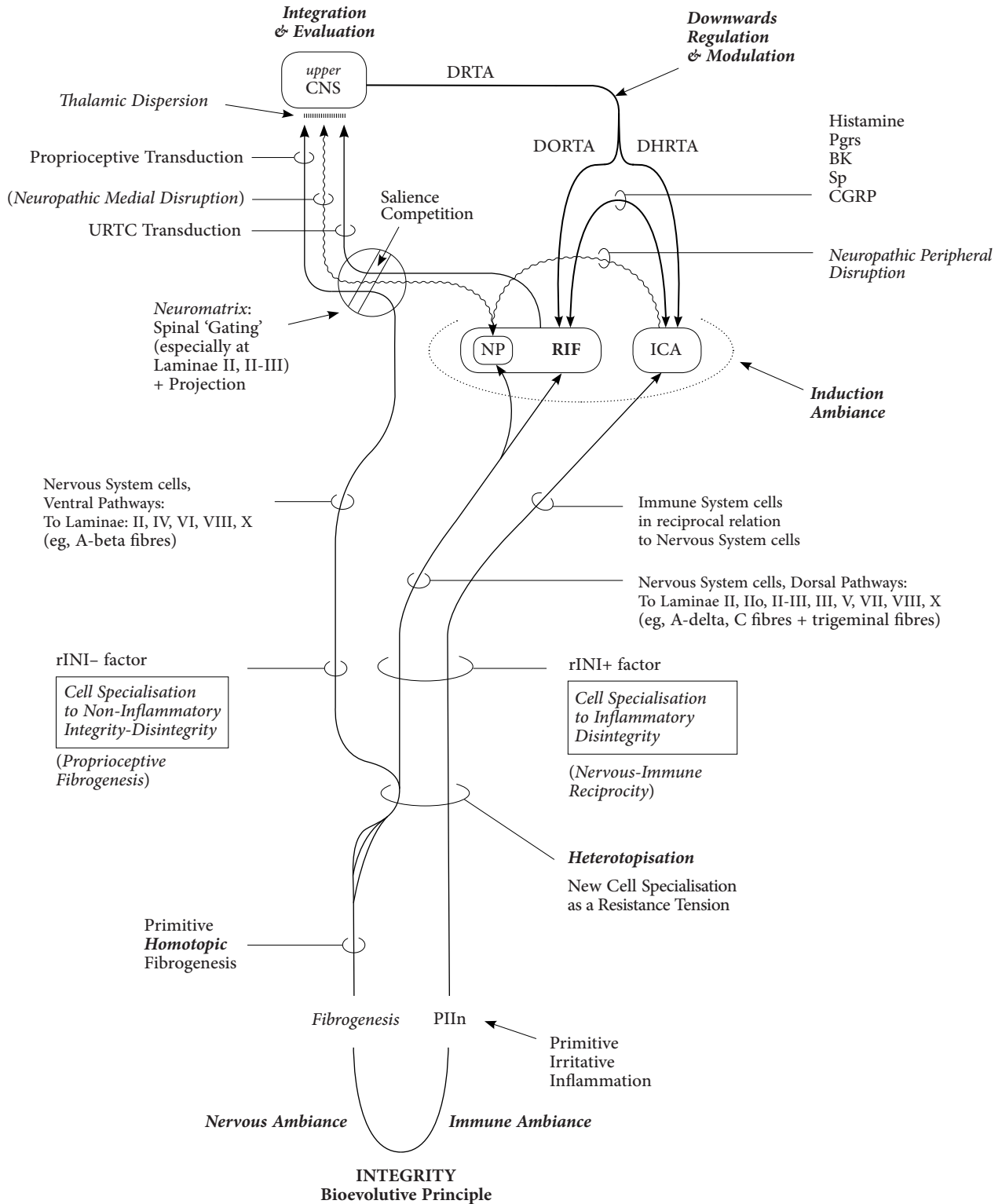
different cycles (stimuli waves, patterns in peripheral topic fields generating induction waves and inner projection areas), and the idea of specific receptors for pain (Specificity Theory) through heterotopisation, that reorganises the theory into a more pre-evaluative concept of cell specialisation, that follows the spirit of the contemporary redefinition of perception from 19th-century concepts (Cf. Kobayashi et al 2006). In this sense, peripheral fibres, C fibres, are thus not over-attributed with evaluative load in argumentation: these fibres do not conduct pain, pain is proper to the whole organism as agency of pain is an evaluative feature of the whole systemic aggregation. These fibres conduct a voltage-irritatory wave that happens to facilitate a more complex integration of neural and immune recognition of disintegration informed by chemical tissular processes, based on stressor chemical ambiances exposed to a continuous diachronic inflammatory de-homotopisation, thus affecting fibrogenesis reciprocally.

Chart 10 'Inflammatory-Fibrogenic Reciprocity Interpretation', *below*, summarises and specifies the elements of the RIF Interpretation.



■ **Chart 10 — ‘Inflammatory-Fibrogenic Reciprocity Interpretation’**

Nomenclature in next page.



—  
Nomenclature for ‘Chart 10’:

<i>BK</i>	Bradikinin
<i>CGRP</i>	Calcitonin Gene-Related Peptide
<i>CNS</i>	Central Nervous System
<i>DHRTA</i>	Downstream Hormonal Resistance Tension Answer (Affecting Induction Ambiance and Immune System)
<i>DORTA</i>	Downstream Opioid Resistance Tension Answer (Affecting Induction Ambiance via Nervous System)
<i>DRTA</i>	Downstream Resistance Tension Answer (General)
<i>ICA</i>	Inflammatory Chemical Ambiance
<i>NP</i>	Neuropathic Pathology (Cellular damage developing signal disruption)
<i>Pgrs</i>	Prostaglandins
<i>RIF</i>	Reciprocal Inflammatory Fibres (Proposed fixing the epistemic problem substituting the concept of nociceptors)
<i>rINI+</i>	Reciprocal Inflammatory Nerve Induction (positive process)
<i>rINI-</i>	Reciprocal Inflammatory Nerve Induction (non-given process)
<i>URTC</i>	Upstream Resistance Tension Call (Cf. Cardioid Model)

—  
***Note on Trigeminal Fibres***

Not much experimental work has been able to produce evidences in humans on trigeminal pain experiences, which given their acute shrillness can provoke and reinforce psychiatric pain-bearing scenarios, and favour overall dysfunctions easily in humans (dysfunctional activity for eating, speaking, sensing flavours, migraines, attitudinal impotence, characteriological depressive traits, chronic passivity, stupor, etc.). Evolutionarily observed, trigeminal areas have reached almost the whole sensitivity of the head in humans, excluding occipital areas and other specific ear regions. An important anatomical neuropsychiatric point of order has been established in modern literature (Cf. Bermejo et al 2017) concerning transcutaneous stimulation at auricular levels (Ramsay-Hunt areas, especially nearby the conchæ of the pinna), areas innervated by lesser trigeminal afferences, but contributing facial, glossopharyngeal, auriculotemporal, vagal and cervical nerves, and that have shown therapeutical targets for symptomatic alleviation of many neurological and psychiatric conditions related with pain-bearing scenarios, including chronic migraine (Straube et al 2015), major depression disorder (Rong et al 2016), autism spectrum disorders (Jin & Kong 2016) or inflammation downstream regulation in vegetative systems (Marshall et al 2015) and Parkinson pro-dementia (Weise et al 2015). The trigeminal nerve has also been evolutionarily ‘filtering’ or acquiring some afferences proper to other nerves at further upper areas, diverting voltaic waves from those nerves to the trigeminal nuclei in their stead; eg, fibres coming from the Ramsay-Hunt auricular area. This may help to explain why pain-kindred experiences with psychiatric evaluatory component may affect central integration.

## **QIII, Chapter §5**

### **Overflowing Morbidities: Pain Reinforcement & the Value of Epiagnosis.**

(In Niche B — Framing Psychiatric-Epidemiological Characterisations)

☛ 329 — 335

—

#### **Parts**

. Introduction

I — The Overflowing Effects on Neuropsychiatric Diagnosis & Pain

. Pain Prevalence: A Tendency that Overflows Diagnoses

. Overflowing Definitions

. Overflowing Classifications

II — Revaluing Prognosis & Multifactorial Assessment: Introducing Epiagnostics

. Closure



## . Introduction

The relevance of comorbidity in diagnosis is experiencing a formal reconstruction in today's 21st-century neuropsychiatry. The coexistence of several pathological conditions in the same patient, whose identification is central to pluralised diagnoses and to his or her clinical assessment, exposes a definitional, classificatory and epistemic challenge that has produced almost fifty years of medical and philosophical discussion, evoked variegated attempts at using comorbidity terminology in daily clinical language, and prompted significant criticisms on the validity of systematic and categorial disease classifications instead of wider person-centredness (van Praag 1993; Feger 2001; Maj 2005; Aragona 2009a; Jakovljević 2008; Cramer et al 2010; Klinkman & van Weel 2011; Goldberg 2011; Hickey & Roberts 2011; Borsboom et al 2011; Anjum 2015).

Tracing back to early research, Feinstein (1970) outlined the term 'comorbidity' accounting for the coexistence of two or more clinical entities that may occur during a patient's clinical course of a prior index disease. Since the 70's, the notion has been exposed to a good amount of transformations, growing a definitional re-attunement to complexity and heterogeneity within medical and epistemic literature that is bringing deep consequences for the entire diagnostic practice and its research activities.

Modern dissertations mainly concern about two arguments, (1) systematic identification and definition of several diseases in different gradations, and (2) classificatory requirements for organising complex, fuzzy clinical entities that produce diagnoses beyond scope (Cf. general discussions in Krueger & Markon 2006; Valderas et al 2009; Jakovljević & Crnčević 2012; Jakovljević & Ostolić 2013; Wurm 2018). Such practices introduce ethical, procedural, ontological and deontological discussions (Goffman 1968; Haraway 1976; Dupré 1981; Thagard 1999;

Schwenk 1999; Hacking 2002; 1998; Darden 2006). Both issues need even wider attention when evaluating pain-bearing populations and/or addressing neuropsychiatric statuses (Fishbain et al 2014), for clinical difficulties accentuate in psychiatric and pain-bearing patients than in non-pain-bearing population.

The gain of pain-associated conditions pairing with an index disease, or the presentation of a previously detected pain accompanied with peripheral diseases and disorders, usually introduce a psychiatric-interpersonal assessment of comorbid states in patients suffering from multiple diseases without a monographic cause (Fishbain et al 2010; Kato et al 2006). These, in the majority of cases, develop in processes of 'pain reinforcement': generally precedent, already indexed diseases manifesting a characteristic distress that reinforces unhealthy experiences (adding, emphasising or enlarging pain), contributing to the worsening of the patient's life quality, personal apperception of harm, and coping strategies. Nonetheless, the opposite process is true for pain-bearing populations, where a preceding pain, usually sustained, is determined to cause-coadjuvate, degenerate or contribute to promote further comorbid diseases, continued crises that foster the common involvement of mental disorders (Breivik et al 2006; Fishbain 2007; Tegethoff et al 2015; Schuh-Hofer et al 2013; Roehrs et al 2006), interfering with diagnostic practices of identification and differentiation of symptoms (Starfield 2006). In neuropsychiatric ambiances, the evaluation of distress and diseases corresponds to a clinical attitude that falls into the definition of complex heterogeneous diagnosis (Anjum et al 2015): non-monocausal, multifactorial, proper to circumstances of an individual patient.

To the extent of this interpretation, it appears that the concept of 'epistemic overflow' shows an accurate tool to assess the blurrisome

problems that analyses face with complex heterogeneous diagnoses of comorbidities in neuropsychiatric studies and pain theory making: Morton's (2013) outline titles 'hyperobjects' to this kind of problems beyond the scope of a singular theoretical perspective, problems that Helmreich (2016) has given the name 'overflowing objects', alluding to typical interpretational affairs of monotopic theories (unified standpoint theories) in transformation to pluralistic models, dappled standpoints assisting in validation and accommodation of new perspectives and cultural practices of theory making: Cf. epistemic pluralism, perspectivism, naturalism: Cartwright 1983; 1999; Kitcher 1984; 1992; 1993; Giere 1985; 2006a; 2006b; Longino 1990; 2001; 2006; Weinberg 1993; 2001). Within this context, comorbidities would present complex heterogeneous diagnostics as 'overflowing theoretical objects'.

This chapter covers the current neuropsychiatric panorama dealing with pain-associated comorbidities, addressing the 'epistemic overflow' introduced by comorbid states into clinical theorising, along with its implications for diagnostic practices, pain assessment, and the organisation of diseases within systematised classifications. Divided in two parts: Part I overviews the prevalence of pain-associated disorders, understood as comorbid or index diseases accompanied with a running index or another comorbid diseases and disorders; moving the issue to an analysis of major debates on defining comorbidity, its usages and pragmatic attitudes; and finally to the discussions the concept launched on systematic, categorial and dimensional classificatory requirements.

Part II outlines the value that an 'epidiagnostic perspective' can present in supporting future proposals improving the work on comorbidity-&-multimorbidity-driven clinical practices. Epidiagnostic practices are introduced to define diagnostic efforts fundamentally directed to determine collateral and correlational factors

to better decide the detection of plausible comorbid instantiations of pathologies in a patient's clinical picture, and primarily aligned to finding the appropriate treatment interventions, informing about prevention and prognosis of further comorbid possible scenarios, given any index diseases under study. This work suggests stressing two characteristics: (1) an attitudinal shift towards prognostic detection, prevention and more accurate intervention, and (2) multifactorial assessment of the plural dimensions of stressors affecting patients's health.

The value of epidiagnostics as a practice lies in how it focuses multifarious, heterogeneous, complex, multimorbid, comorbid circumstances employing mereological solutions through Artificial Intelligence Assisted Diagnosis for facing overflowing scenarios, proposing differential diagnoses for depicting antithetic-polythetic processes, using probabilistic inference for organising plausible hypothesis practicing multiple drafts theory making, and orienting the circumstantial nature of a patient's symptomatology with a clinically significant prognostic account (including concurrent or future comorbid/multimorbid peripheral distress). Contrasting patient's-ambiance information with epidemiological and epidemiographic standards in an open network, the epidagnostic can be an useful tool for a physician for making more critical and educated guests to solve a patient's clinical picture.

#### I — *The Overflowing Effects on Neuropsychiatric Diagnosis & Pain.*

Comorbid states are reported by the 35-80% of general diagnoses internationally (Mezzich & Salloum 2008), which vary attending to the definition of comorbidity instated by researchers, the methods used by each group for collecting and interpreting data, and the characteristics of the coexisting pathologies (Taylor et al 2010). Such systematic identifications and

differential diagnostic practices are guided by national and international catalogues, which usually involve both, neuropsychiatric and internal medicine specifications: eg, the 'International Classification of Functioning, Disability & Health' (ICF), the 'International Classification of Diseases' (ICD10v), the 'International Classification of Primary Care' (ICPC), the 'International Guidelines for Diagnostic Assessment of Mental Health' (IGDA), or the 'Diagnostic and Statistical Manual of Mental Disorders' (DSM5v).

The ways that such definitions, classifications and attributions to patients suffering from comorbid instantiations related to pain and neuropsychiatry are being affected, changed over time and remodelled due to the overflowing effects of hypercontextualisation —as presented in QII, §1 using Helmreich's (2016) terms— are reviewed in the present part.

*. Pain Prevalence:*

*A Tendency that Overflows Diagnoses*

In the presence of pain, patients who find themselves coping with some or many of the wide extended range of painful experiences, rather severe, chronic, long-lasting or cyclical (reappearing, continual) distress, tend to index further pathologies into their general health condition (Fishbain 2007; Tegethoff et al 2015), being stress, panic and generalised anxiety disorders well-known co-occurring psychiatric features of pain-bearing scenarios (Asmundson & Katz 2009), installed in a deeper clinical relationship with pain than depression (McWilliams et al 2004). Usually, a sustained bearing of distress affects these new pathologies incorporating certain degrees of restrain or aggravating them. It appears, however, that in regard to pain-kindred comorbidities, such effect participates of a feedback chain that forces different stressful situations to resonate in the patient's proper apperception of pain, thus reinforcing the link between prior and incoming patholo-

gies, worsening comorbid dispositionality, thus, leading to the development of 'pain reinforcement'. Such a notion comes along with definitional concepts like 'suffered pain', 'felt pain', 'incoming pain', etc., which serve as indicators that guide definitions of subjective, personal experiences in a contribution of any other 'incoming' pathology that reinforces the 'suffering' or the 'feeling' of such a prior pain.

Qualitative research on subject-based self-assessment of pain helps in forming a better identificational claim about this sort of reinforcement, as autonomy, functionality and adjustment disorders tend to reformulate the quality of life in the patient (Sutherland & Morley 2008). Pain reinforcement can be generally declared among three characteristics, it being added, emphasised or enlarged. 'Added', because of external clinical performances; meaning an appended pain, a form of consequential pain of a treatment (iatrogenic pain); or added for it had been favoured through another disease at the same course of time in which the patient was suffering an original pain. 'Emphasised', because another disease aggravates the sensation of pain, the burden and or its bearability by a particular patient. 'Enlarged', because the time span a particular pain runs the patient's life comes to an extension, enlarging its durability and/or the patients's coping process.

Yet QIII, §6 reviews a wider neuropsychiatric panorama of dysfunctional comorbidities associated with pain, the following lines can serve as an overture to its prevalence. Depression, stress, anxiety and fear disorders present the common psychiatric cases of pain-bearing populations, either instantiated along added, emphasised or enlarged pain reinforcement.

A ratio of 2 out of 10 patients suffering from a chronified pain circumstance appears to be diagnosed with comorbid depression (Breivik et al 2006), affecting not just adult bearers but children and youngsters. People in early and advanced growing stages of life show depressive

traits as bearing and coping with pain: sustained distress is related with introjection and personality lacks while a person creates his or her characteriology of social projections, relationships and confidence in the self and others; in this sense, children and adolescents in pain conditions exhibit faster interpersonal disengagement, social abandonment and personal resignation than other non-pain-bearing populations (Forgeron et al 2010; Bullis et al 2014). Interpersonal stress and social contactual dysfunction appears as well a comorbid factor in adolescents growing with an enlarged pain-bearing process (Murberg & Bru 2004), a relation between emotion and sustained pain that accentuates over time for this target group (Collishaw 2015). In addition to neurodevelopmental affective disorders, several niches in the symptomatology for anxiety are detected to emerge widely in pain-bearing patients in contrast with non-pain-bearing people (Burke, Mathias & Denson 2015), including social or interpersonal anxiety (Cox, Fleet & Stein 2004; Gadermann et al 2012), and fear disorders: sensitivity to anxious scenarios rises above the general in pain-bearers, attaining higher scores in measurements for fear of anxiety-related symptoms than the regular (O'Brien et al 2008), and presenting commodious irritability, mood changes and negative affections (Wong et al 2015).

Pain-bearing patients are found to display different somatic neuropsychiatric symptomatology too, among of which sleep problems, fatigue, headache, irritable bowel syndrome, restless legs syndrome and different parasomnias are observable (Fishbain et al 2014). A somatic comorbid impression of import is the common relation between pain and insomnia (Finan, Gooding & Smith 2013): the general inability to attain a proper quality of sleep increases both, evidences of pain reinforcement (Schuh-Hofer et al 2013; Roehrs et al 2006), and of pain reinforcing insomnia (O'Brien 2010), integrated within a cycling tension whereof maintenance is studied to provoke personality, functioning

and employment disabilities in the long run (Lallukka et al 2014). Some of the physiological changes that occur in pain affecting sleep touch the limits of stability for certain liminal mental diseases, generating further psychiatric symptomatology (Monti & Monti 2007), modulating mood, attention, irritability, and reshaping patients's character traits (Busch et al 2012). The clinical burden of pain complicates coping strategies as well: for example, socialising skills are affected in such a way that shame, fear-avoidance behaviours, shyness or self underestimation tend to orient private and common interpersonal projectionalities, ending up restructuring character dispositions to social situations, and re-elaborating personality (Gustafsson, Ekholm & Ohman 2004; Gadermann et al 2012).

Beside socialising and interpersonal facts, pain experience exposes patients to prominent biochemical, physiological changes, usually including weakening of the down-regulating opioid system, inflammatory over-expression, asymmetric resilience to pain (coursing with allodynia or different paraceptive reflexes) and other physical interactions of iatrogenic origin, mostly due to sustained treatment.

The combination of comorbidity and pain is, far from being an exception, a ruling scenario that complicates patients's quality of life, mediates and modulates pain reinforcement, and interferes with diagnostic practices (Starfield 2006; Fishbain et al 2014). The coalescence of comorbid pain and mental disorders, along with the feedback chains that let consequences to develop as well for mental disorders and comorbid pain, suggest that comorbidity is a 'presentation circumstance' for clinical depiction, recognition, comparison and relational inference, a procedure felt by patients that acts reshaping the experiential tenure of distress in their daily life, and a clinical practice of identification that performs in multiple grounds, and involves multiple factors for diagnosis.

Another important remark regarding deontological concerns claims how pain-associated comorbidities are a clinical event that makes diagnoses rewrite biographies. Inadequate classificatory attempts and abbreviated few-dimensional practices in diagnosing patients's health status are shown to have strong collateral effects in statistical medicine and epidemiology (de Groote et al 2003), impeding the clear identification, detection and characterisation of multiple diseases and comorbid instances, further prognostic ideation, treatment and catabasis. In the same sense, the sheer introduction of diagnostic variability, and the extended disordinated presence of multiplied stressors interfering the extraction of a singularised diagnostic attachment, offers the case for pain in comorbid presentation to act as an ostensible example of overflowing diagnoses. This makes pain-associated comorbidities incorporate specific clinical practices into scenarios of diagnostic complexity and heterogeneity (Anjum et al 2015), frames of depicting and reasoning which drive causal theory making and classificatory requirements to overflow the proper definitions of comorbidity in use, as the following section overviews.

#### *. Overflowing Definitions*

The majority of reviews expresses a primary conclusion: there appears to be no consensus in relation to the pragmatic accounts that practicing clinicians in research and medical theorists display for defining the notion 'comorbidity' (Cf. Krueger & Markon 2006; Valderas et al 2009; Jakovljević & Crnčević 2012; Fishbain et al 2014; Wurm 2018). Such consensus is neither visible when addressing standard terminology for entitling the diagnostic specialisation of comorbid diseases.

Uses broadly involve relational terms of proximal meaning families for denoting multifarious symptomatology, valuing emerging words with common characteristics like 'co-

morbid disease/disorder', 'multimorbid case', 'prior disease', 'index disease', 'secondary disease', 'attached diseases', 'spectrum disease', 'added symptomatology', 'symptomatic cluster', etc., titles that impinge on practices of diagnosis, prognosis and treatment with terms like 'concurrent diagnostics', 'dual diagnostics', 'co-existing factors diagnostics', 'multifactorial diagnostics', 'multifarious diagnostics', 'trans-diagnostics', etc., all of which usually end up assisting a general conception of a correlated or extended symptomatology instantiated by a given patient, adding a particular value to the ostensive definition of comorbidity introduced by Feinstein in the 70's for internal medicine.

Pain-associated comorbidities are no exception, as their prevalence has the capability to affect the virtual totality of diseases and syndromic states with peripheral complexities, much of which deal with neuropsychiatric comorbidity indices. Their implications for definitional and classificatory discussions bear similar problematics, some of which have been treated elsewhere (van Praag 1993; Feger 2001; Maj 2005; Aragona 2009a; Cramer et al 2010; Borsboom et al 2011).

The following lines are a summary of the different added values and clinical attitudes these concepts attach to the ostensive definition of comorbidity, from 1970 to 2018.

The term grows from a piece of work by epidemiologist Alvan R Feinstein (1970) exposing the use of 'comorbidity' in application to the coexistence of two or more clinical entities that may occur during a patient's clinical course of a prior index disease under study. During this study, any observable entity (or any observation of a clinical entity) would inform about the general patient's health status, orienting relative prognostic factors and arriving with plausible lines of treatment. This depiction grounds on the consideration that health statuses are monographically driven: ie, they are valid for one identified disease chosen from a clinical system

of diseases organisation. The case of comorbid observable clinical entities presents a complication for this consideration: some would argue that comorbid instantiations in positive particular patients interfere with clinical systemic categories as the former do not exhibit all of the characteristics attributed to the latter ('polythetic characteristics'), or the latter do not exhaust a singular identification of the former ('illness uncertainty').

Moreover, defending the presence of comorbid observable clinical entities entailed the accommodation, or incrustation, of comorbidity itself in the very system of diseases organisation, for its observability would depend on the fact that symptoms of comorbid kind are equally a scientific ascription that depend upon a system of clinical organisation. This means that any instantiation of a comorbid symptom comes to be observable through a patient presenting it, and identifiable through a clinical guide for naming it, like any other recount of a symptom ascribable to an index disease. This has proxied the arrival of criticisms about the factors of classification used in vernacular medical and clinical practices of identification, tagging and attribution (*infra* in the discussion of classificatory requirements). Discussions point out some concluding thoughts, and some report that the observation of a clinical entity would better depend on the situation of specific patients making use of dimensional and multifactorial diagnoses, rather than on just classificatory indices and guiding epidemiological and statistical inventories (Aragona 2009b; 2009c; Anjum et al 2015). Already in value for general practice medicine, the scene complicates the depiction of the health status itself, as comorbid diagnosis can multiply the number of suffered diseases, or make incongruent prognoses and treatments for each of them.

This first characterisation of comorbidity placed some questions that explain why discussions on its definition opened and continue: for

instance, temporal issues interfering with diagnostic practices (which of the different diseases shall be attributed as the index disease: the first one diagnosed, the most durable, the easiest to treat, the most relevant for the patient's general status, the most salient, etc.?), and causal interferences in etiology and clinical reasoning (what is the causal/correlational familiarity, if exists, among the clinical instantiations of the diseases presented? This will differentiate comorbidity from multimorbidity, usually appearing in literature the first of them as a relationship of causal tenure among clinical entities, and the second of them as a mere coexistence of diseases without a clear correlation, but equally affecting, aggravating or impeding treatment among each other). If taking in consideration complexity and heterogeneity, problematics for prognosis materialise too with futuribles and risk factors (how many diseases could be comorbid to an index disease if complicated, understanding the indexical attribution of a disease as a clinical hook for different presentations?), or treatment collateral effects (if focusing treatment on 'disease x' supposes exacerbation or amelioration of 'y' or 'z' diseases, does this suggest 'x' is not an index disease for a particular patient's diagnostic circumstance, or is the contrary true?). On these questions, some authors have given their added value to the ostensive definition.

For example, understanding a 'primary disorder' as independent of 'following disorders' or 'secondary disorders' allows to theorise that if the former affects the latter, exhibiting a worsening effect, secondary diseases can be introduced as comorbid attributions (Feighner et al 1972; Heninger in Maser & Cloninger 1990). A different direction toward identifying diseases presentation is the definition of comorbidity as an 'associated disease' or 'associated disorder' which can simulate a pack of symptomatology in familiar resemblance with a generally interpreted index disease (Kaplan & Feinstein 1974; Piccirillo & Feinstein 1996), implying a recrea-

tive attitude in ensuing two pathologies that are etiologically different but similar in presentation (eg, dopaminergic syndrome caused by substance abuse and fabulatory schizophrenia).

If separating primary and secondary diseases, comorbidity can be expressed as a 'combinatorial reinforcement', entangling a tendency to increase the probability of suffering from reciprocally related conditions, which ends up presenting 'co-occurrence' among different conditions (Boyd and Burke 1984). In a similar sense, another value approaches abiding the symptomatic criteria for identifying a particular disease (inference-based differential diagnosis). A 'diagnostic comorbidity' thus, would afford the definition of a patient definitional health status whenever diagnostic criteria follow non-specific symptomatic patterns, unable to determine a precise morbidity (Heninger in Maser & Cloninger 1990). Within the psychiatric conceptualisation of the problem, primary and secondary diseases have also been invoked as the 'antecedent' or 'concurrent psychiatric syndrome' amounted to a 'principal diagnosis' (Strakowski 1995), a phenomenon that can also provoke system interferences, reorganising or overlapping categories of diseases classification: this, accounted as 'heterotopic comorbidity' (Angold et al 1999), involves disorders arriving into the patient's scene from different diagnostic groupings (eg, major depressive disorder, conduct disorder and personality disorder).

Entering the 21st Century, the expression 'symptom cluster' prospered over some communities. Cluster collections of symptomatic attributes add a differential value to classificatory problems in comorbidity, as comorbid schemas can be extracted by comparing clinical and personal differences in the properties of core symptom clusters, identifications that have functional effects in a patient's health status diagnosed with a prior disease (Dodd, Miaskowski & Paul 2001). Symptom clustering has attracted certain critique of being somewhat elusive (Barsevick

2007): are symptom clusters framing a modification in a categorial disease based on patient constraints, or is rather the clustering strategy introducing a comorbidity to argumentation instead of a categorial, non-modified disease which adds polythetic and/or multidimensional pathological traits into a prior index disease? Is the possibility of continuation of a symptomatology cluster in a ratio of time per population liable to provide an accommodating modification of several categorial classifications of diseases in its application to regionalised, contextualised patient communities? (Hauser et al 2009).

These questions show a theoretical setup that comes from the application of the so-called 'comorbidity reasoning', a form of theory making, a theoretical attitude, that approaches diagnostic feasibility from a multiple working hypothesis standpoint, impartially driven but embedded within the task of finding and excluding fallible or less plausible options from non-faulty or more plausible clinical choices (Oschman 2003).

Comorbidity reasoning applies to general diagnostic practices if the co-existence of two or more pathological conditions, being one of them predominant (Grumbach 2003), in contrast 'multimorbidity reasoning' attitude, in cases where no causal, correlational or interconnecting relationships among the different diseases are exposed. Comorbid and multimorbid states can undergo classificatory requirements beyond categorial interpretations, thus favouring those explanatory attempts which trace the origin of comorbid and multimorbid diseases from various 'clinical dimensions' or 'niches of stressors': the dimensional, polydimensional/multidimensional featuring orients and shapes diagnostics from within the person's habits, concerns and ideas, discerning its epidemiological and aetiological orientations away from a mono-cause model of classification (Musalek & Scheibenbogen 2008). The comorbidity attitude reflects on 'complex diseases' that gain their causal impli-

cations from multifactorial reasoning: by genetic, environmental and lifestyle factors of which clear epidemiological roots are yet unknown (Craig 2008).

Some suggestions made appear those terms installed within dispositions of affinity between time span and presentation, drawn in probabilism and frequentism (Aragona 2009c), and defining comorbidity as the 'frequency-based co-occurrence' of several diseases that present inevitably together, and multimorbidity as the 'accidental co-occurrence' of several diseases that present in no common or expected manner.

In regard to relational uses, some authors have worked with the concept of 'dual diagnoses' for informing about comorbid states emerging in psychiatry, often when exploring complex or contradictory behavioural circumstances of patients, being defined as the clinical attribution of a relationship between symptoms that, in the recognition of a complex or problematic identification of a disease/disorder, re-shapes a generalised diagnostic into two valid, situated and hypothesisable solutions (Sawicka et al 2009), another example of application of comorbidity reasoning and multiple drafts attitudes.

Contrastive reviews of comorbidity and multimorbidity in psychiatric fields have dealt with the very nature of the diseases to relate, presenting a definition of comorbidity-multimorbidity focusing the co-occurrence of mental and physical disorders in the same person, appearing through particular chronology or causal bond (Goldberg 2011), sometimes argued in favour of pain disorders and pain syndromes affecting or being affected by similar symptomatology. In this same sense, some concerns on the nature of comorbid states call attention to the kinds used in classification: are comorbid dispositions attached to an index pathology characterisable as 'comorbid diseases', 'comorbid disorders', 'comorbid conditions', 'comorbid illnesses' or 'comorbid health problems' (Cf. Booth 2006; Klabunde et al 2000; or

Ritchie 2007 in Valderas et al 2009), to which we shall include 'comorbid distress' in the case of pain-associated comorbidities.

Another definitional question is proposed here about the term 'disease spectrum', as some would argue that depression and anxiety disorders are no differentiated pathological identifications if a patient suffers from the two of them at the same time. Patients instantiating both shall not be classified as bearing a co-occurring comorbid display, but a spectrum that relocates two instantiations of two different classifications into one collection that assumes the patient as bearer of one condition in continuation, aggravation or time span extension (Valderas et al 2009). The same concept arrives for pain-associated comorbidities. This idea frames a problem with the simultaneous existence of loosely defined pathologies, and moves forward different critiques about the systematic few-dimensional theory making of diseases organisation (Kaplan & Ong 2007), along with the clinical exigencies for understanding the degree of 'illness uncertainty' in plenty classifications, most of them recurring to neuropsychiatric frameworks (Fishbain, Burns & Disorbio 2010). Illness uncertainty does not prevent comorbidity instantiations to coalesce with different diseases into one, framing a similar theoretical bed to the spectrum attitude, but for arguing this time about another diagnostic possibility, the 'disease clustering' (using other terms as 'causal comorbidity' and 'cluster comorbidity'). Comorbid more than multimorbid states would actualise a plausible cluster of pathophysiological kinship among different diseases, especially for those that share similar risk factors (from an etiological point of view), or similar complications (from a clinical point of view) derived, for example, from treatment, or the lack of it (Schaefer et al 2010).

It has been evaluated how acuteness or chronification of a comorbid instantiation can weight the usage of terms referring to the sa-



lience of different comorbidities. Weighted comorbidities manifest a comparative strategy. The coupling terms ‘hypercomorbidity’ and ‘hypocomorbidity’ have been offered to this extent (Cf. Jakovljević & Crnčević 2012): hypercomorbidity for the association of two or more diseases at a higher rate than expected by chance, hypocomorbidity (instead of the term anticomorbidity) for those that appear together at a lower rate than expected. Given an index disease, and using a statistic or frequentist approach, classifications could take into account this comparative strategy to attach then diseases that are generally hypercomorbid to said index disease and prevent (prognostically) their manifestation by an anticipatory diagnosis of comorbidity (this perspective is discussed in the final section, as the proposal of epidiagnostics stresses preventive prognosis and multifactorial assessment on comorbid scenarios).

Recent reviews and analyses have drawn attention to how comorbidity and multimorbidity reasoning present a difficult-to-assess etiological heterogeneity in correlating differentiated but diffuse diagnostic states (vaguely, loosely drawn clinical entities) that present important ontological, mereological and/or classificatory challenges (Eriksen et al 2013). The same framework of critique is valid for cases addressing ‘complex disorders’ and ‘complex diagnoses’ —with multimorbidities and heterogeneity affecting the causal engine that gives form to a procedural systematic arrangement of diseases (again, much of which is applied from a psychiatric standpoint)—, as these are organisational consequences of having used primarily epidemiological and statistical-quantitative mono-causal methods that attain, in many cases, weak and unsatisfactorily classifications and blur the plural origins of health stressors (Anjum et al 2015).

Observing the diagnostic practice in psychology and neuropsychiatry, some authors have suggested that causal inferences during di-

agnosis do follow the same problems any other clinical practices manifest, evolving concepts like ‘emotional comorbidity’ or ‘affective comorbidity’ attached to index diseases, being or not of behavioural origin, from which pain-associated comorbidities are especially delicate (Wurm 2018). In associating such classificatory kinds with the heterogeneous expressions of diseases by the very patient, clinicians’s interpretation of symptoms may get affected by plenty out-of-reach interferences, like medical singularities, maleficent polypharmacy, false positives, unmanifested genetic predispositions, or hidden psychosocial conditions and habits, involving the need of comorbidity reasoning (Cardeña 2018).

#### *. Overflowing Classifications*

The previous section has exposed some conclusions from different authors on the problems comorbidity terms and reasoning attitudes bring forward into classificatory practices. The present section will address some of them.

In other writings, Feinstein (1967) expressed how categorial and taxonomic structures fundament the methodological and theoretical grounds of clinical practices: ‘diagnostic categories’ inform about the «locations where clinicians store the observations of clinical experience», as ‘diagnostic taxonomies’ point out and arrange «the patterns, according to which clinicians observe, think, remember and act». Accordingly, diseases organisation procedures and diagnostic recognitions form a bond in which classificatory requirements for both of them meet, and their modifications affect to each other.

Medical classificatory requirements put attention to the factors and guarantees in need for a proper classification, as for assessing the reliability of such practice if compared throughout separate periods of time. Guides and manual methodologies (eg, ICF, ICD, ICPC, IGDA

or DSM) assist clinical evaluation to associate tags and kinds organised in a system of diseases and pathological dispositions with symptomatic instantiations manifested by positive, particular patients. Then, taxonomic, classificatory tensions appear concerned by how licitly these things end up actualising relational bonds, by how classes, types and kinds —both in formal considerations about pathological structures, and in clinical entities giving shape to clinical recognitions and diagnoses— are ranked, accommodated and associated with other classes, types and kinds, inside and outside particular medical and physical ontologies. Such a practice introduces ethical, procedural, ontological and deontological discussions (Goffman 1968; Haraway 1976; Dupré 1981; Thagard 1999; Schwenk 1999; Hacking 2002; 1998; Darden 2006).

Regards on classificatory kinds (and to this extent ‘human kinds’, Cf. Hacking 1995) connect ‘suffered experiences’ with the clinical ‘practices of identification and assessment’, and in so doing, classificatory kinds bring together, through common acceptance, depiction and naming, patients and clinicians (Cardeña 2018). Either natural, social, analytical kinds; either pathological, clinical, definitional kinds; clinical practices attune their requirements by producing very specific classifications, decisions of tagging and grouping that affect to patients and to symptoms, collectives, families or healthcare systems (Ballerini 1997; Hacking 1986), and which root their theoretical depth from a tradition of studies in biology, genealogy, botany and zoology, that lead to historically designed structures managed for correlating organic levels of complexity with ecological emergent features (MacMahon 1978; Bechtel & Richardson 1993; Lilienfeld & Marino 1999; Heylighen 2000).

Concerning psychiatric comorbidities, multimorbid states, multifarious diagnoses, dual or multiple, and their reasoning schemata, some critique has been directed to the validity of diseases organisation (van Praag 1993; Feger 2001;

Borsboom et al 2011). The natural co-occurrence of different but specific factors that actualise a non-unitarian definition for a given patient’s disease has been ascribed a flaw of the proper organisational system that correlates epidemiological pathological facts with particular case-to-case suffered symptomatology, attribution that has led to interpret the phenomena around psychiatric comorbidity as an overall indicator of deficient embeddings and clusterings of diseases (Cf. critiques in Feger 2001; Maj 2005, Cramer et al 2010; Aragona 2009a)

Classificatory requirements contributing to the fixation of common diagnostic criteria introduce also a methodological problem arriving to two fundamental strategies in definition and distinction of pathologies: causal inference and family resemblance among clinical entities (Mumford & Anjum 2011). One reason to explain this is that any clinical accommodation of traits, properties and characteristics of pathological evidences inside pathological structures would necessarily specify both, an etiological niche (inferring causal origins, hierarchies, dimensions, priorities, etc.), and a taxonomic niche (inferring relationships among properties, resemblances, familiarities, etc.). The case of polythetic characteristics in disease clustering (ie, having many, but not all properties in common) rises this issue in procedural diagnoses, as Aragona (2009b; 2009c) has pointed out: if some but not all of the required criteria are elicited by the symptomatology of a patient, and if there resolves a lack in severity, continuity, preponderancy, or any other hierarchical or dimensional shaping, it is very reasonable to elicit comorbid, multimorbid or multifarious diagnoses as several clusters and pathologies are being evoked in a partial manner, suggesting co-occurrence or inevitable related presence in between. Coexistence of vaguely defined pathologies argues too for the same critique on systematic diseases organisation (Valderas et al 2009; Kaplan & Ong 2007), as etiological and/

or taxonomic niches of health stressors come up blurred in the patient's health status description.

A common path seems to indicate that either dimensional-functional, person-centered, behavioural, or event-driven models (all of which work informing about psychopathology, pathogenesis, epidemiology and nosology), tend to mingle, one way or the other, causes oriented to some disorders with consequences for others, stressors that act as agents of pathological consolidation with behaviours and habits of the proper patient as an agent deciding or being exposed to the dispositions of his or her own pathology, and developments of previous disorders with temporal origins of further diagnosable pathologies, in most cases iatrogenic.

Worries about the very ideogenesis and motivations behind the construction of these organisations of nosological entities seem actually necessary in today's dissertations, along with the inquests on whether psychopathology, pathogenesis, epidemiology and nosology need be the fundamental tenets for the classification and organisation of diseases being applied to diagnostic medicine, or completely required for grounding clinical practices to ensure diagnostic criteria or diagnostic validity. This is, given the amount of problems with classical statistical systematisations, maybe there are already plausible reasons to build feasible systems and organisations of diseases and conditions without these factors as endogenous classificatory requirements. This acts a fortiori, increasing motivations, when present times can help decidability of complex diagnosis and arrangement of pathological traits and architectures by acknowledging the benefits of using Artificial Intelligence, text analysis engineering and mathematical clinical ontologies as tools for re-understanding nosographies, together with epidemiological collections of data, in the light of case-to-case, patient-centered medicine and care. It is generally formulated that proper classificatory systems hold validity when diagnostic

categories offer orientation for, or attain theoretical satisfaction of, prognosis, treatment/prevention and catabasis (beginning of overcoming processes) upon a given disorder or pathological circumstance. Concerning comorbidity and multimorbidity states, there arises a question of efficiency, about how many separate diagnoses and, in consequence interventions, are necessary to follow on to the patients's recovery, in contrast with affecting, accelerating or reinforcing the proliferation of their given index diseases.

A secondary problem of classificatory systems results in asking how such clinical procedures affect the patient's self understanding and his or her ambiance (family, friends, working contour, etc.), framing a question about the diagnostic consequences of communicating diagnoses beyond the proper attribution of a categorical entity to a person: there exists an entire universe of prejudices entailing a burden, for instance, to the psychiatric patient, that performs as stressors beyond the sheer clinical action, a form of degradation, a social incapacitation or familiar impotence that, for example, a patient suffering from depression or severe anxiety could feel as a diminishing feature of his or her character, favouring different plausible comorbid states redundant with a previous diagnosed anxiety disorder or depressive schemata. These burden-related comorbidities, affective comorbidities (Wurm 2018, Cardeña 2018) worry the psychiatric and social entailments of classifications, and are stressors to include in the proper diagnostic endeavour.

Coming closer to neuropsychiatric comorbidities and their inceptive process, whether the same biological, physiological, behavioural, or any other causal-kindred bonds apply to explain comorbid diseases is a question to answer from multiple standpoints: for instance, alcoholic behavioural processes require of attention within a wide range of psychiatric disorders (put desperation, characteriological, mood, stress, anx-

iety, economic or family related disorders), but to infer that alcoholic processes run through the same physiological or biological pathways that any of these disorders do would be of a harder task to argue (etiology complicates). A plain causal approach is relatively diffuse when actualising the general causes of alcoholism, where different beyond-the-person arguments appear, featuring social, demographic, ambience-related, economic, cultural, even climatological stressors (diagnosis turns multifactorial, and prognosis unclear).

In opposing such approach, when a particular diagnostic is a normal, consuetudinary gateway for a different clinical condition, and there is a clear, plausible connection with a co-occurring multisystemic disease, then, talking about multifarious diagnoses is understood as a positive clinical practice, giving shape to 'trans'-diagnostics (Mansell et al 2009; Allen et al 2012; Linton 2013), and transdiagnostic vulnerability factors (Cf. Wurm 2018). Serve as an example this observation about the Wernicke-Korsakoff Syndrome: the enduring relationship between these two disorders (what was historically split as Wernicke encephalopathy and Korsakoff memory syndrome) is usually taken as an archetype of multifarious-monadic diagnosis, where patients suffering from either diseases, neurological and psychiatric, are usually diagnosed with Wernicke-Korsakoff Syndrome as a singularised monadic entity (Thomson et al 2008). The etiological shared cause that allows a monadic instead of a dichotomic attribution to such disorder is, essentially, a biochemical deficiency in thiamine, a vitaminergic scarcity that engages in a variety of diagnostic singularities such as Beriberi if muscular pain is the main symptom, the neurological Wernicke encephalopathy, and the so-called psychiatric alcoholic Korsakoff syndrome. Fabulation, imaginary overexpression, social impeachment, or memory discriminative affections are in the scene to be different symptoms of a monadic

classification when characterised as a syndrome of its own. However, first, when the scene is evidenced through different properties of distinguished cluster diagnoses before the proper syndromic diagnosis is ascribed to the patient, it is actually observed by a plausible multiple draft strategy of comorbid states in a pre-clinical diagnosis: this is, the monadic-dichotomic problem is yet a blurring scenario (Kessels et al 2008). One reason for singularising this approach is that treatment in all these previous statements works with B1 vitamin plus different polymorphic therapies: prognosis, treatment/prevention and catabasis for the different multifarious states of what is understood as the Wernicke-Korsakoff Syndrome are maintained as a singularised entity because clinical practice appears to be transversal to them. Instrumental reasoning has ruled the case at hand, nonetheless the multiple drafts strategy is an equally plausible solution for opening accurate prognosis and beginning intervention, involving transdiagnostic approaches and vulnerability factors without requiring a monadic or singularised classification.

Another argument about multimorbid origination and classificatory clustering runs the fact that many disorders share, especially those of neuropsychiatric import, their behavioural and sensorial neural bases in specific functions and morphology (Gaebel & Zielasek 2011): plenty neuropsychiatric diseases and disorders manifest through different locations or regionalised ambiances in the nervous system, affecting as clinical entities many of the functions proper to different neural systems, which sometimes are intrinsically homotopic (that share specific neural connectomes or attitudinal networks). In so doing, when a disease of importance affects some neurological aspects of a system, manifested in a shared regionalised ambiance with other systems affected by other disease (for example a secondary disorder), it comes accompanied with the worsening

or improvement of the latter, involving with it the functions and/or neural integrity of another condition, thus, introducing a comorbid state. A clear case could be non-cognitive starting dementias (eg, Parkinson or Huntington diseases) that co-occur in the long run with further cognitive symptomatology proper to full-fledged cognitive dementias. One reason underlying the diagnostic transformation of such diseases, and their comorbid identification, is due to the neurodegenerative processes that end up destroying the neural underlays of cognitive functions like movement attitudes, memory consolidation or generation, and emotional characteriology. In this sense, a proper neurological disturbance, by the plain course of time, reshapes from neurological into neuropsychiatric (affective, cognitive, behavioural-interpersonal) maleficence, and it is clinically portrayable as a comorbid characteristic of its further development (this classification then surmounts the prognostic value over the categorial instrument of organisation).

In summary, taxonomies must be careful, interpretable, flexible and shapable in the form of the patient: emotional, ethnic, economical, epochal, social, psychological, territorial and further considerations inform better about the causal linkages these kinds can produce in classification schemata (Mumford & Anjum 2011; Anjum et al 2015).

## II — *Revaluating Prognosis & Multifactorial Assessment: Introducing Epiagnostics*

Clinical practices involving comorbid and multimorbid states conform a complex ambience affected by many obstacles. Some of the main problems discussed above include divergence in common definitions (usually approached by means of fuzzy pragmatic accounts), uncertainty about the grounds of etiological classifications and nosographies, non-singularisable pathological characterisa-

tions, or unitary diagnostic approaches that face heterogeneous presentations of symptoms, in scenarios where multifarious diagnosability comes to trouble a proper clinical intervention, thus, promoting undecidability. These meet other frequent difficulties: significant examples are psychiatric comorbid complications, including emotional, behavioural and psychosocial traits, and pain-associated comorbidities, being the latter the one exposing most clearly the feature of multifarious symptomatology with/without etiological bond. Additionally, further methodical issues tend to obscure clinical interpretations (Cf. QIII, §2), incorporating problems with contrasting information, un-reproducing experiments, avoiding a clear validation for, and application of, new statistical, epidemiological and ethno-demographical data, or making use of singular, unitary field explanatory strategies (Shamliyan, Kane & Jansen 2010; Iqbal et al 2016; Darden 2006; Cowan & Kandel 2001; Martin 2002). These and other problems justify the so-called ‘comorbidity puzzle’, and it suffices to interpret such clinical scenario as an ‘overflowing object’, in Helmreich’s (2016) terms, of medical theorising.

The diagnosis of complex syndromes, in cluster, spectrum, or scattered polythetic form, need to rethink the validity and utility of systematic relationships, statistical and demographic bondings, and category-suited etiological schemata for the overflowing diagnoses at hand. Beyond-scope unitary diagnoses provoke unsatisfactory responses because comorbid states involve and require a multifactorial perspective. Accordingly, some authors have equally envisaged a re-definitional outlook for psychiatric comorbidity problems, to which efforts at caring about such scenario «will probably bring with itself new scientific paradigms and perspectives with new diagnostic phenotypes; this process will naturally lead to a re-definition of the old diagnostic phenotypes.» Jakovljević & Crnčević (2012).

These authors followed on their argument with an important conclusion, pointing out how the future research in comorbidity and multimorbidity «should deconstruct existing mental and somatic disorder/disease/illness categories and start with bottom-up measures of key mental, neural and body systems», a regenerative attitude that implicates rethinking classificatory requirements, biopsychosocial organisers, pathological taggers, etiological attachers, and the different structural informers that give shape to medical ontologies in order to fulfill diagnostic criteria, and to be able to identify pathological abstractions from patients's instantiating particular symptomatology.

Different works have recently proposed some alternatives for generating medical ontologies, divergently organising the grounding factors that are believed to underpin current classifications. These have been offering also mereological solutions through Artificial Intelligence, text analysis and statistical cross-comparison technologies, most of which have been applicable to more efficient distributions of pathological taxa, the intelligent contrasting of diseases, or in redefining epidemiological boundaries (Grenon, Smith & Goldberg 2004; Johansson et al 2005; Hoehndorf, Kelso & Heré 2009; Schulz, Brochhausen & Hoehndorf 2011; Kozaki et al 2012; Masuya & Mizoguchi 2012; Yamagata et al 2013). Such problems and solutions affect many biomedical sciences, from genetics, to functional and biodynamic anatomies, to comparative disease models, to cultural and ethnographic distribution, characterisation and prevalence of health conditions, etc.

In the aim of giving form to plausible proposals for denoting comorbidity and multimorbidity-driven clinical practices, the present text suggests a perspective stressing two characteristics of such a renewal: an attitudinal shift towards (1) prognostic detection, prevention and more accurate intervention, and (2) multifactorial assessment of the multiple dimensions

of stressors affecting a patient's health status. These include both, the clinical preconditions to assure a wary and cautious treatment; empowering therapeutically the patients's multidimensional functionality, clinical autonomy, decidability and self-evaluation and reasoning on their clinical burden; and the prevention or forecast (clinical prediction) of further pathologies associated with, or correlated to, a previously detected disease (that may serve as an index disease or not in a multiple draft strategy).

Such a depiction would justify the introduction of 'epidiagnostic practices' for characterising these specific diagnostics, examinations about the over-(*epi*)-flowing scenario that brings together a multifactorial panorama of complexity and heterogeneity with a strategy of hypothesisable multiple drafts directed to systematically identify different coexisting pathological instantiations. Completing these plural diagnostic practices and theorising strategies oriented to attain a clinical assessment of comorbid and multimorbid states, the epidiagnostic attitude works stressing the two previously addressed characteristics: understanding dappled, multidirectional mosaic prognosis, and multifactorial, personalised assessment.

#### . *Closure*

In the spirit of this attitudinal shift, some conclusions can be given for defining, structuring or conceptualising multifarious coexistent pathological presentations in clinical theory making through epidiagnostic practices:

— '*Comorbidity is a presentation circumstance*'

A contributive scenario of symptoms presentation engaged by a particular patient, disposed to clinical depiction, recognition, comparison and relational inference, enriched by multifactorial conditions.

- *‘Pain-associated & psychiatric-associated comorbidities reshape both, patients & classifications’*

Pain reinforcement performance and psychiatric-associated comorbidities are the most significant and common features of current complex diagnostic practices, presenting the case of a clinical identification that affects both, patients’s experiential tenure of distress in their daily life, and the very clinical procedure which characterises pathological instances performing in multiple grounds, from physiological, emotional to interpersonal. QIII, §6 analyses neuropsychiatric comorbidities associated with pain.

- *‘Comorbidities & multimorbidities work as tendencies’*

Comorbidities and multimorbidities present as a tendency to increase the probability of suffering reciprocally related pathologies in comorbid circumstances, and the tendency to increase the probability of suffering from co-existing although not necessarily correlated pathologies in multimorbid circumstances. As tendencies offer a directionality, a future beyond the current presentation, the epidiagnostic attitude seems fairly adequate as a definition of co- and multimorbidity trend seeking.

- *‘Diagnosability performs in accordance with diagnostic multiplicity’*

In examining the diagnostic characterisation of a patient’s health conditions and his or her relation to comorbid and multimorbid states, many factors weight for identifying index and peripheral (comorbid/multimorbid) instances: some factors focus this multiplicity by considering the nature of the relationship among clinical entities, like temporal priority, severity, possible further emancipation, exclusion, causal

independence, consequent adherence, relational adherence (ie, non-consequent adherence), antithetical dispositions among clinical entities, etc.; other factors work by focusing the origin of the multiple scenario, informing about multi-systemic origin, iatrogenic origin, behavioural/consumption/ingestion/addiction/lifestyle origin, genetic origin, age origin, gender origin, family dependence, etc.

- *‘Overflow puts on value Epidiagnostic Practices’*

The overflowing effect introduced by complexity and heterogeneity affecting diagnosability puts in value the characterisation of epidiagnostic research and practices. The overflowing characterisation suffices to suggest an attitudinal shift to epidiagnostics as defined in the present text, and to consider the value that new technologies present in assisting clinical decision making with new emergent ontologies and mereologies (particularly in Artificial Intelligence assisted diagnosis), probabilistic and frequentist.

- *‘Direction of Epidiagnostics’*

Epidiagnostics are oriented towards overflowing scenarios involving complexity and heterogeneity in symptomatic presentations’ — Epidiagnostic practices are fundamentally directed to determine collateral and correlational factors to better decide the detection of plausible comorbid instantiations of pathologies in a patient’s clinical picture, and primarily aligned to finding the appropriate treatment interventions, informing about prevention and prognosis of further comorbid possible scenarios, given any index diseases under study.

- *‘Epidiagnostics involve Pathological Traits, Pathological Architectures & people instantiating them’*

These practices shall understand the definition of comorbidities not just from the point of view of their being a peripheral category within a particular system of diseases attached to an index clinical entity, but as an instantiation of a multiple mereology of ‘pathological traits’ (instantiated by a particular patient’s symptomatology) corresponding to compositional ‘pathological architectures’ (actualised by a particular patient’s disease or health status).

— *‘Epidiagnostics are pluralised working hypothesis, multiple plausible drafts’*

Comorbidities present a personal scenario that affects both, the validation of clinical classifications (if contrasted with methodological classifications using abductive logic) and the consequential epistemic accommodation of new approaches and proposals of interrelation. This empowers the validity of plural diagnostics, requiring of different ‘interfield strategies’ (Darden 2006; Cf. QII, §1, and QIII, §1-3) to frame and approach multiple pluralistic interpretations, opening the diagnostic practice of depiction, recognition, comparison and relational inference to a reconsideration in terms of probabilistic multiple-decision making. Comorbidity circumstances, in manifesting overflowing diagnoses, actualise different sorts of explanatory and descriptive strategies, assessable through interfield standpoints, valuing communal, cooperative, multi-modal hypothesis making.

To conclude, the value of epidiagnostics as a discipline lies in how it focuses multifarious, heterogeneous, complex, multimorbid, comorbid circumstances employing all efforts to suggest differential diagnoses for depicting anti-thetic processes, using probabilistic inference for organising plausible hypothesis, practicing multiple drafts theory making, and orienting the circumstantial nature of a patient’s symptomatology with a clinically significant prog-

nostic account (including concurrent or future comorbid/multimorbid peripheral distress), and a more contrasted treatment than few-dimensional, univocal, systematic diagnostics.







## QIII, Chapter §6

### Neuropsychiatric Dysfunctions Associated with Pain Reinforcement Comorbidities.

(In Niche B — Framing Psychiatric-Epidemiological Characterisations)

☛ 335 — 345

—

#### Parts

. *Introduction*

#### I — Executive Attitudinal Dysfunctions

- . *Depression*
- . *Developmental Depressive Traits During Growth*
- . *Major Depressive Disorder*
- . *Suicidality: Self-Injury & Lethal Intention*

#### II — Impotence, Worry & Habits Dysfunctions

- . *Anxiety Disorders & Fear-Anxious Pictures*
- . *Substance Abuse & Dependence: Addictive Traits*
- . *Post Traumatic Stress Disorder*
- . *Sleep Disorders*
- . *Fibromyalgia*

#### III — Affection, Mood, Character & Personality Dysfunctions

- . *Stress-Associated Disorders*
- . *Anger Traits in Mood & Character*
- . *Sadness Traits in Mood & Character*
- . *Bipolar Disorder: De-Consolidation (Personality Reshaping)*

#### IV — Dysfunctions Related with Central Neurodegenerative Disorders

- . *Alzheimer Cognitive Dementia Complications*
- . *Parkinson Prodementia Complications*
- . *Huntington Prodementia Complications*
  
- . *Closure & Chart of Dysfunctionality Clusters (I—IV)*

## . Introduction

Many difficulties arrive to the diagnostic practice when patients feel incorporated to their general health status pain reinforcement processes. The previous chapter has dealt with some of the overflowing methodological problems coming to the neuropsychiatric ambience through reinforced pain experiences, along with the pragmatic accounts that physicians tend to use when referring to the terms created since the 70's for addressing comorbidity, multimorbidity, and their classificatory requirements. According to that base, the present chapter will approach the specific neuropsychiatric pathological architectures that most often present with, or develop into, chained dysfunctional pictures. The text composes a neuropsychiatric framework to observe comorbid states and overflowing conditions that worsen reciprocally with reinforced pain processes, leading to a clinical overview of plausible epidemiological characterisations.

Patients suffering from reinforced pain processes usually acquire personal and interpersonal dysfunctions, coming down with several emotional re-attunements to their living phase, a change of attitude, of mind frame and, finally, agency and actions that, using PL Goldie's terminology on emotion, character and personality theory (Cf. Goldie 2000; 2002a; 2002b; 2003; 2004), 're-shape' the activity of their nervous system and express through personality. Of especial psychiatric attention are mood de-consolidation (mood and character traits tend to change in pain-bearing people, affecting humour and the direct responses involved in the social, familiar, working or scholar roles they play), emotional-perceptive complications (pain thresholds tend to turn more sensitive), affective and evaluative difficulties (how they proceed to assess their experiences, life quality and social, friendship, familiar, laboral and learning ambients) and self-judgement prob-

lems (eg, how pain-bearers produce self-beliefs: beliefs about themselves and their experiences attached to their clinical conditions and the collateral, implicated circumstances). When tracing a diagnostic path for neuropsychiatric comorbidities affecting index diseases overflowed by pain reinforcing processes, factors are classifiable in multiple manners: there is no major taxonomic orientation to follow for organising comorbid gains, and many times sheer epidemiological or statistical prevalence accounts do not fit for particular diagnoses. Researchers show and discuss (*infra*) how, for each study, precise symptomatic classifications, and contextualised scales of comorbid factors and stressors (leading to clinical worsening and its diagnostic detection) have been created. General diseases that aggravate with pain reinforcement processes gather dementias; both mechanical prodementias like Parkinson or Huntington, and cognitive dementias like Alzheimer; and depressive, anxious, stress disorders undergoing with fear. Neuropathic pain accompanying mental disorders tends to worsen both, pain sensitivity and affective, cognitive processing. Psychoses and psychotic traces are inevitably aggravated if the patient bears ostensive physical pain, chronified or slightly sustained (however prevalence is low and experimental studies insufficient), affecting thematic fabrication or reshaping personality and their interpersonal projections, fear, care-avoidance and distrust. Episodic migraine and chronified pain affecting attention and mood, or related diseases as fibromyalgia, post traumatic stress disorder, or addiction and substance abuse, are also implicitly linked with pain reinforcement. Attitudinal and habits kindred conditions like obesity, dietetic unbalance, fatigue, sedentarism, sexual disorders, smoking, alcoholism or attitudinal alcoholic traits, sleep disorders or parasomnias, and anger, sadness and somatisation disorders

inform about many symptom clusters that present dispositional diagnostic details suggesting comorbidities of bearing reinforced pains. It is important to recall that not just the ostensive sense of pain is elicited by these patients (ie, an immediate physical pain), but also life quality, future-linked, concern, mental weight senses of pain, that drag pain-bearing patients to feel a highly dysfunctional, severe, unhealthy impotence, furrowing many aspects of their life and day-to-day actions and experiences.

The neuropsychiatric frame introduced by the present text can help in identifying such multifarious comorbid contributors, overviewing the following diseases sorted by four epidiagnostic clusters. These have their epistemological fundament in QIII, §5, and are mainly driven by relational, multifactorial and prognostic values. It is worth to note that this is not an organisation of diseases, but of clinical complications within pathological architectures that contribute to reinforce the patient's context of pain. The clusters include: I 'executive attitudinal dysfunctions' (Depression, Developmental Depressive Traits During Growth, Major Depressive Disorder, Suicidality), II 'impotence, worry and habits dysfunctions' (Anxiety Disorders and Fear-Anxious Clinical Pictures, Sleep Disorders, Substance Abuse, Dependence or Addictive Traits, involving compulsiveness, Post Traumatic Stress Disorder, Fibromyalgia), III 'affection, mood, character and personality dysfunctions' (Stress-Associated Disorders, Anger Traits, Sadness Traits, Bipolar Disorder: De-Consolidation or Personality Reshaping), and IV 'dysfunctions related with central neurodegenerative disorders' (Complications in Alzheimer Cognitive Dementia, Parkinson Prodementia, Huntington Prodementia).

#### I — *Executive Attitudinal Dysfunctions*

Reinforced pain, whereas added, emphasised or enlarged (Cf. QIII, §5), comorbid to the family of dismal symptomatology in psychiatric

conditions, can develop in lingering barriers, both personal and interpersonal dysfunctions, key in a healthy execution of self-oriented actions, delivered, planned and believed through attitudes that oneself is projecting, to him or herself and to others. Depressive and Terminal dysfunctions (when presenting suicidal attempts) are a main constraint in pain-bearing populations.

#### . *Depression*

Depression and depressive traits have determinant biochemical, anatomical factors that reshape patients's executive attitudes (Marchetti et al 2012). A ratio of 2 out of 10 patients suffering from a chronified pain circumstance appears to be diagnosed with comorbid depression (Breivik et al 2006; Chou 2007). Almost a 70% of the general depressed population is a pain-bearing population, and in pain reinforcing scenarios, the majority of pain-bearers present depressive traits, in character, personality and affection, being pain reinforcement a very prevalent psychiatric comorbidity to depression, and vice versa (Cf. a well known review in Bair et al 2003; and more recently Elman, Zubieta & Borsook 2011; Nekovarova et al 2014; Nicholl et al 2014; Torta, Ieraci & Zizzi 2017). It also affects prognostically, in accordance with studies on neuropathic pain comorbid with fear-anxious pictures (Radat, Margot-Duclot & Attal 2013). Clinically, it has been observed that depression is misdiagnosed in the general population, and many pain-bearing patients are addressed with improper diagnostic accounts and, coherently, not well treated (Katon & Sullivan 1990, Biar et al 2003): almost 8 out of 10 depressed pain-bearers inform about their distress in terms of their being suffering depression, sometimes hiding cluster symptomatology or hindering clinical recognition of further important copathologies (Kroenke, Jackson & Chamberlin 1997; Nolen-Hoeksema 2000). In addition, pain

involved in depression has a prognostic value for many neurological and multisystemic diseases (Brochet et al 2009; Wen et al 2012). Attentional attitudes and self-judgement are also executively dysfunctional in pain-bearers, and may head them toward a depressive disposition (Nolen-Hoeksema 2000; Lemogne et al 2012). Emotional dysfunctions provoked as by-product of pain reinforcement are also important factors that mediate coping strategies (Rokyta, Haklova & Yamamotova 2009): eg, in reports of a Canadian population (Patten 2001), by default, 6 out of 10 depressed patients stating physical distress elaborated their complaints exposing how pain and coping with it affects their life quality.

Physiologically, depressive traits have a great impact on pain sensitivity (Torta, Ieraci & Zizzi 2017; Torta and Munari 2010; Bondy et al 2003), as sustained inflammatory gain is usually a company of pain reinforcement, both emphasised (Walker et al 2014; Chapman et al 2008) and enlarged (Farmer et al 2012). Depression reinforcing pain is a good example of how 'master nuclei' (specific neural regions that appear to help to coordinate whole-viewed systems in a connectomic standpoint) can be affected by copathologies instead of index diseases, thus, interfering with diagnostic recognition, identification and differentiation, which is a typical trait of comorbid instances (Starfield 2006).

Physiological and anatomical changes have been pointed out to lead to mnesoceptive (ie, experiencing by remembering) learning through reshaping cognitive, attentional, affective neural ambiances (Monleón et al 2008): these are plasticity-related changes collateral to a neural over-exposition to sustained distress, and stressors affect distinct neural systems which, in turn, provoke mnesoceptive learning processes via activation or de-activation of modulatory cooperating systems. Interconnected systemic crises are the neuropsychiatric basis to argue about how distant cells's faulty communication fosters

the common involvement of mental disorders associated with patients suffering from pain reinforcement (Fishbain 2007; Schuh-Hofer et al 2013; Tegethoff et al 2015). Up-projecting and interconnected cortical regions (especially prefrontal and somatosensory regions) jointed to hippocampal and anterior cingular structures and the amygdala, have been pointed out to be dysfunctional in depressive patients, affecting the activity of down-modulating processes, and the coordination between intentions and affectivity about self-promoted actions, leading to clear and continued changes in mood and memory consolidation (Marsden 2013; Murren et al 2011; Lee et al 2012).

#### *. Developmental Depressive Traits During Growth*

Patients living their early and medial growing life phases showing depressive traits are associated with psychiatric and neurodevelopmental issues collateral to bearing and coping with pain (Murray et al 2012). Stress, panic and generalised anxiety disorders are very familiar to children and youngsters exhibiting pain features (Asmundson & Katz 2009): the stressful feeling of being exposed to significant interpersonal situations, which increases if involving bodily contact, is a generally observed dysfunction that appears comorbid in multifactorial diagnoses of depression, and usually too in diagnoses contextualised to adolescents growing with an enlarged pain-bearing process (Murberg & Bru 2004; Zis et al 2017). For young depressive patients, it has been reported (Holley et al 2013) that 95% of them presented pain symptomatology —of high prevalence headache, limb and back pain.

Yet, anxiety is sometimes installed in a deeper clinical relationship with pain than depression is (McWilliams et al 2004). When depressive traits are accompanied with anxious pictures and develop into fear in young

pain-bearers, the connexion can produce very disrupting effects on this group: fear to awaken pain when playing or participating in sports, collectively with other friends or schoolmates, is a fear of being exposed to more damage, however, this involves multiple risks if maintained, including social dysfunctions, scholar impairment, distrust (about oneself and others), a blurred definition of the sense and virtues of common care, interpersonal introjection, abandonment and personal resignation, etc., realities that reshape the proper development of a personality in a context of pain through the patient's coping strategies (Bullis et al 2014; Palermo et al 2009; Logan et al 2009; Forgeron et al 2010; Gauntlett-Gilbert et al 2007; Kashikar-Zuck et al 2012).

#### *. Major Depressive Disorder*

Common characterisations of general maintained sadness (depressivoid mood disorders), episodic depressive traits, major depressive disorder, and its chronification (dysthymia) are emotional pessimism, sadness, generalised dismal, irritability and social projection dysfunctionality. Inferred from some therapeutic approaches (Beck's interpretation of self-worthlessness is common; present as well within different diagnostic-therapeutic scales, like Montgomery Åsberg's rating, Cf. Svanborg & Åsberg 2001), the personal characteriology of asperity towards one's actions, guiltiness, and resentment in self-judgement are also symptomatic charges included to criteria.

Major depressive disorder presenting with a serious pain burden is very common (Bair et al 2013; Elman, Zubieta & Borsook 2011), and usually instantiates a somatoid reshaping (neuroanatomical, but also behavioural rearrangements derived from dysfunctional affectivity), disturbing key factors of interpersonal resolution and personality (dysfunction, loss, or softening of executive and evaluative control

on attitudes, intentions and decisions). Episodic (more than, or at least, 2 weeks) and cyclical presentations of such symptomatology can be helpful to determine diagnostic validity for major depressive disorder or its chronification (2 years for adults, 1 year for children and youngsters) into dysthymia (Cf. new classification in DSM-5). Pain and severe depressive mood provokes worsening of reinforcement processes (Lin et al 2003), which tend to be self-perpetuators (Fishbain 2007; Koike, Unutzer & Wells 2002). Affective disexecutiveness contributes to chronification, besides, the self-perpetuating effect prevents these neurotypical patients from therapy intervention or medication (Rokyta, Haklova & Yamamotova 2009).

Major depressive disorder has been subjected to neuroanatomical, morpho-functional studies in search of the neural trends that help to explain how the nervous system substantiates behavioural symptomatology: generally, patients instate significant serotonin and tryptophan lacks in master nuclei coordinating a proper cell connectivity and functionality, regarding anxiety and motivational factors; dopamine and norepinephrine transmission shows irregularities, regarding cognitive, imagination, future-ideation, attitudinal and mnesic function (Goldenberg 2010; Frodl et al 2006). Here, maintained multi-systemic brain dysfunctions (cognitive, affective, attentional, etc...) give sense to the so-called neuroanatomical 'depressive scar' (Monleón et al 2008), which also reflects the neurotype (or diagnostic phenotype) for a clear classifiable disease, modelling how depressive traits get reinforced or sustained avoiding therapeutical intervention by overloaded mnesic work (hippocampal ambiances have been observed deficient in volume in these patients, provoking asymmetric remembrances between memory and emotional weight, Cf. Frodl et al 2006), or actualising anon a traumatic event occurred previously in the life of patients diagnosed with major depressive disorder, whose decay sprints if pain-bearing and cop-

ing comorbidities emerge (Goldenberg 2010). Inflammatory processes (Chapman et al 2008; Miaskowski et al 2012; Walker et al 2014; Torta, Ieraci & Zizzi 2017) are being currently studied as a key for determining the development and integrity of many neuropsychiatric problems; especially addressing depression and dementias; because immunological primary reactions evoking an extension of the inflammatory biochemical ambiances through the brain can be selective diagnostic alerts of a central (specific and overlapped brain systems) accommodation to a depressive trend, thus, being such 'scar' interpreted as a process of neural acceptance of the disease. As inflammatory biochemical ambiances tend to extend and perpetuate over pain reinforcement, pain associated comorbidities attached to major depressive disorder can be a paramount scenario for future research on this topic.

#### . *Suicidality: Self-Injury & Lethal Intention*

Suicidality, including both, self-injury (derived from a suicide attempt), and lethal intentionality (of a self-induced death), has been defined in multiple ways, but of special attention for psychiatric and primary care medicine are concerns about behaviour and beliefs associated with pain (Nock 2009; Takahashi 2001; Ilgen et al 2010): suicidality is a potential (futurible) prognosis, an actualisation of a self-desired belief or an amendment of a personal biography (for depressive traits incorporated to suicide symptomatic clusters) with non-fatal resolution, in which the intimate intention or interpersonal threat to terminate with oneself's life appears the major trait provoking secondary damage (injuries derived from the episode), and even the unintentional mutilation of oneself's body, a component that conforms a form of theatricality in suicide (involving threatening of bodily destruction without fatal result, an 'emotion-towards' something or someone in Goldie's framework: Cf. Goldie 2000; 2002), without it

being a fake or fictitious attempt (modern open definitions of suicide involve repent in the very process too).

Pain and depressive traits can settle the map for suicide prognostic factors. Among them are hormonal, attentional, cognitive, affective and neuroplastic stressors that vary from person to person, and which are able to gather different, further, concomitant pathologies (Law & Liu 2008; Price, Verne & Schwartz 2006; Nock et al 2013; Lumley et al 2011), likewise for early life stages (Eaton et al 2008). Common possible causes inform about biological, social, genetic or neuroanatomical deficiencies: for example, in compensation nuclei, basic dopaminergic and serotonergic biopaths, reward and anti-reward ambiances mediating in motivation and intentionality, etc., manifest dysfunctions (Blum et al 2008). More open causes can value the impulse for avoiding a worsening scenario (anti-reward motivation, most cases introducing pain reinforcement, and in severely ill or aged patients who hold an intimate desire of ending their suffering circumstance), or fear of developing stronger overflowing pathologies, or tragic life quality changes (delusions and fabrications, grief, sexual orientation, social acceptance, family or friendship losses, economic problems, etc., Cf. Russell & Joyner 2001), along with accidental overdoses, substance abuse or further unintentional causes of self-harm (as well a contemporary definition valid for suicide), that could be present as collateral effects of heterogeneous comorbid and multimorbid conditions to a prior index disease (Roose et al 1983; Linehan 2008; van Orden et al 2010; Cheatle 2011; Russell & Joyner 2001; de Peuter et al 2011; Takahashi 2011). Epi-diagnostic practices (Cf. QIII, §3-5) put special attention to prognostic and multifactorial analysis: the development of a contrasting epi-diagnosis would help the clinical recognition of prognosticable futurible contexts, carried by comorbidities present in the patient. Suicide ideation and attempt are clear examples of its significance.

## II — *Impotence, Worry* ↳ *Habits Dysfunctions*

Symptom clusters that can verify pain reinforcement processes usually include personal frailty, inability to handle one's emotional brunts and episodic, however critic, onslaughts in neuropsychiatric patients undergoing comorbid pain. Fear and panic attacks can call some attention if repeated. Regarding fear, however indeed it constitutes an epidiagnostic comorbid trait, cyclical prevalence is not very common alone, and context-based circumstances explain better how general fear arrests can result to be: expectations and desires can contradict how fit a person is (under pain with a comorbid or multimorbid neuropsychiatric picture) for facing a circumstance that has the potential to ensue him or her. Thus, not invoking an original factor of comorbid dysfunctionality per se, fear happens to emerge as a consequence of a prior clinical picture: anxiety. Fear and anxiety have been spotted as co-reinforcers by historical discussions on the matter (Cf. a well known landscape in Bourke 2003). Studies on fear and anxiety have revealed (*infra*) a quite relevant clinical factor, that fear onset appears to be generally preceded by an extended anxiety overflow with severe biographical impact. Impotence and worry are characteristic of many of these symptomatic clusters, and provoke, or are able to attach, further pathologies, including somatoid dysfunctions due to worry (like lack of Sleep hygiene, or permanent structural and biochemical changes in the brain, forcing cognitive, attentional, mnesic and affective behavioural disorders through Stress, Post Traumatic Stress Disorder, and sustained Anxiety Disorders), and habit-based dysfunctions due to impotence (generally a coping strategy and consequence of both, pain reinforcement and scattered symptomatology peripheral to pain, or to other neurological prior diseases, like psychiatric dysfunctions comorbid to Fibromyal-

gia), habits that can also work as dispositional coping strategies, and which can be evoked from genetic, physiological niches, and mainly emerging through severe anxiety (in adverse cases, Substance Abuse and Addictive Traits).

### . *Anxiety Disorders* ↳ *Fear-Anxious Pictures*

Anxiety, has been defined, in the light of clinical ensuing anxiety pictures, as an anticipation process that provokes significant oppression and is related with further angst-kindred emotions, like panic, fright and fear: stressor niches (the multiple dimensions of diagnosis) in the symptomatology for anxiety have been observed to emerge and spread in pain-bearing patients (Burke, Mathias & Denson 2015), including social or interpersonal anxiety (Cox, Fleet & Stein 2004; Gadermann et al 2012), and fear disorders (Cf. relations in DSM-5: 'Anxiety Disorders', 'Separation', 'Selective Mutism', 'Specific Phobia', 'Social Phobia, Social Fear', 'Panic Disorders and Attacks' and, especially, 'Anxiety Disorders Due to Another Medical Condition'). Anxious pictures are commonplace for pain-bearing populations (Wise & Taylor 1990), and present as comorbid traits to further diseases, very often amplifying pain reinforcement processes, both enlarged or emphasised (Aloisi et al 2016; Flaten et al 2011; Radat, Margot-Duclot & Attal 2013; Breivik et al 2006; Ploghaus et al 2001; Wiech et al 2014; Finnerup et al 2015).

In this sense, for pain and anxiety scenarios, the expectation of a plausible threat, damage or even warning as external stressors (that might be imagined by the subject settled within a continuum of worry), are conductive factors partly accountable for fear-and-anxiety responses. Controllability of external (not self-decided) actions is thus an important feature of predisposition to feeling pain (Moseley et al 2003). These responses are mediated by ex-



pectations and by the recognition of a possible future, plausible or not (anticipatory behaviour and prediction, associated with brainstem, hippocampal, anterior cingulate activity): studies have been showing how pain thresholds turn more sensitive as fear-expectation, attention, and anxiety-driven beliefs rise too (Phloghaus et al 2001; Fairhurst et al 2007), incorporating depressive traits in many cases (Torta, Ieraci & Zizzi 2017; Torta and Munari 2010), and retracing memory consolidation (MacDonald et al 2011). The contrary process, anxiolytic, non-expectance, or low-expectance of pain is associated with opioidergic and placebo physiology (Cf. experiments in Tracey et al 2002): the rostral anterior cingulate cortex and the periaqueductal grey matter show metabolic activity enacting down-regulation, thus, modulating (coadjuvating to inhibition) spino-reticular cord-to-brain activity that further on would have been experienced and contextualised by integration as pain. The down-regulating system (Duan et al 2014) extends fibres through the periaqueductal grey and nucleus magnus Raphé, which, in posterior position, sends mesencephalic-spinal fibres to the medulla, ending in Rexed laminae I and II, helping to inhibit A-delta and C fibres through enkephalinergic and dynorphinergic neurons (Cf. QIII, §2-4). The modulatory system resembles ventrolateral cortex activity too, and minor hippocampal function is pointed out to help desensitisation (Moseley et al 2003; Valet et al 2004; Flaten et al 2011; Shurman, Koob & Gustein 2010).

*. Substance Abuse & Dependence:  
Addictive Traits*

Pain-bearing patients presenting further symptomatology of neuropsychiatric tenor, usually instate as well substance abuse disorders, probably developing dependence, and sharing polythetic addictive traits with clear-cut addiction disorders (Fishbain et al 2009; Clark

2007). Substance abuse may not fit a neurotypical standard, but it is generally recognised as a comorbid complication of pain-bearing when other coping strategies offer not much help: opioids, common analgesics, hypnotics, antihistamine medications (for alleviating sleep disorders), barbiturates and familiar drugs, including unintentional iatrogenic over-dose, are, in many cases, objects of abuse or misuse (Boscarino et al 2010; Martin et al 2007; George & Koob 2010), both in young adults and people advanced in age with sustained contact with anxiety-evoking stressors (Shurman, Koob & Guststein 2010). Similar data has been provided for smoking addictive habits, sometimes acquired as by-product of pain comorbid states, searching for relief or analgesic effects (Krebs et al 2010). Addiction (consistent, obsessive, unmissable contact or ingestion with something or someone, mainly drugs and cataphoric experiences) and dependence (the physiological accommodation to a deficit of a very specific biochemical and functional activity that the body cannot produce in sufficient amounts, leading to incorporating it through external aid) can be a by-product of pain reinforcement (for example, by looking for relief to an emphasised or added pain) or of a prior neurological or neuropsychiatric disease (onset of over-medication, street-drug consumption, alcoholic traits, etc., collateral to anxious, sleep, depressive disorders, personality and affective dysfunctions), and many times both involve anti-reward characteristics (avoiding futurible damage or worsening of an actual circumstance) in a general neurological basis (Jamison et al 2010; Elman et al 2002).

Addictive traits bring in neuroanatomical and physiological changes (Scott et al 2006): for instance, spiralling effects (substance-abuse related to habits that may reinforce pain), which are collateral to opioids intake, can cause anti-relief dysfunctions and even help to worsen the bioevaluative cortical and limbic ambiances

in direct contact with pain self-assessment (Fishbain et al 2009). Dopaminergic fibres in severe pain circumstances appear to contribute to reshaping behavioural emotional dispositions, involving craving effects, for being exposed to a continuous opioid over-dose is predictive of mesolimbic dopaminergic unbalance, provoking hyperalgesia (hypersensitivity to pain) and, less commonly, allodynia (pain evoked by stressors that should not instate to pain) in pain-vulnerable patients (Leite-Almeida et al 2009; Berridge & Robinson 2003). Affective deterioration also runs this neural system, making addictive and abuse-like behaviour to perpetuate along an adaptive negative-reinforcement that is able to bring with it deep personality and character changes (de Felice & Porreca 2009; Okada-Ogawa, Porreca & Meng 2009). Addictive traits related to food intake (informing recurrent edacity), obesity and sedentarism, and change in sexual habits (erotomania, philias) have been less studied (as they are more present in multimorbid instead comorbid dispositionalities), but can also weight as important day-to-day comorbid traces (Großschädl et al 2014) if implied as pain coping strategies to particular patients in a clinical sense —thus, these are also valuable diagnostic markers.

In many cases, addictive traits in symptom clusters of pain experiences, related to neuropsychiatric conditions that contribute to its reinforcement, are intentionally motivated coping strategies: ie, patients tend to facilitate themselves bona fide a continuous intake of substances as shortcut to remediate their distress, involving depressive traits that characterise impotence (eg, self-beliefs of inability to overcome pain problems otherwise). Lack of exercise, of social interpersonal stable bonds, of constructive play and spare time, of mental future-planning intentionality, of a healthy diet or of a proper therapeutical approach to the neuropsychiatric issues reinforcing pain, are epidemiological factors that may mediate addiction ha-

bituation, introducing easy or immediate relief with severe consequences. Therapies modifying these and other factors can improve pain alleviation through enhancing reciprocal processes between endorphin cycles, pain down-regulating systems, and neural and behavioural reshaping.

#### . *Post Traumatic Stress Disorder*

Post traumatic stress disorder is usually understood as a complication of anxiety conditions with depressive traits subsequent to a traumatic biographic threatening event. The clinical combination of pain and this psychiatric disorder can be mediated by depressive features, comorbid with mood, fear, anxiety and sleep disorders, both from diagnostic and neurophysiological standpoints (Fishbain, Burns & Disorbio 2010; Cox & McWilliams 2002; Engel et al 1993; Engel et al 2000). Post traumatic stress disorder can occur via self-beliefs (self-judgement through blaming oneself, or the opposite scenario, through victimisation), or beliefs surrounding others, objects or themes (oneiric, remembrances, imaginary lapses or false perceptions leading to possible pseudo fabulations are generally thematised and projected towards the traumatic event), however it is currently not absolutely clear how neurological traces build physiologically the mnemonic connections, reshaping and neuroplastic readjustments during 'shock' stages in the course of such events. Accordingly, a contextual hippocampal-limbic-cortical axis dysfunctionality is suggested to be emergent in these patients, and it can be a therapeutical niche for alleviating pain reinforcement and unaffordable coping strategies, as anxiety and pain therapies benefit in coping with post traumatic stress disorder effects (Elman, Zubieta & Borsook 2011). Dopaminergic ambiances are observed dysfunctional, specifically reward (Cf. an extended review in Borsook, Becerra & Carlezon 2007) and attitudinal systems, where espe-

cially aggressiveness and defence dispositions are evoked (Pavic et al 2003).

Pain interferes with post traumatic stress disorder, and the latter is observed to contribute in pain reinforcement (Breivik et al 2006; Sharp & Harvey 2002; Wagner et al 200; Otis, Keane & Kerns 2003), as fear and anxious pictures comorbid with pain, particularly when chronified, appear in the clinical recognition of similar symptom clusters (Burke, Mathias & Denson 2015). Pain-bearing patients's vulnerability (through pain reinforcement; Cf. QIII, §5) and hypersensitivity (through contextual anxiety and predictive, hypervigilance behaviour; *supra*) can rise as co-occurring affective comorbidities are introduced within daily activity, affecting general health status beyond specific symptomatology (Cf. Asmundson et al 2002 in Wurm 2018).

#### . *Sleep Disorders*

Sleep disorders (especially insomnia), including parasomnias (events difficulting correct sleep: prodromic walk, dyspnea, night terror, dream/sleep paralysis arrests or inability to wake up, etc.) and failure in maintaining a scheduled rest time, are somatic comorbid complications involving neural dysfunctions related to impotence (generally worsening sleep attempts) and worry (generally preventing onset of sleep). Pain-bearing patients hold a common relation with insomnia, due to episodic or sustained distress during night, inflammatory reactions linked to day-end fatigue, and anxious and depressive traits presenting sleep avoidance via intentional or unintentional over-problematisation, worry and catastrophising coping strategies (Finan, Gooding & Smith 2013).

The general incapacity to attain a proper quality of sleep (problems initiating or maintaining it) increases both, evidences of pain reinforcement (Schuh-Hofer et al 2013; Roehrs et al 2006), and of pain reinforcing insomnia

(O'Brien 2010): treatment must be direct, with multimorbidity and comorbidity oriented therapeutical approaches (focusing several clinical pictures, the neurological, painful and the psychiatric ones). Nonetheless, as many analgesics do not work as efficiently as they might work over these patients, and opiate family medications like morphine appear to decrease REM sleep and provoke several parasomnias, pharmacotherapeutical access is difficult to practice (Block & Wu 2001). Hypnotic antihistaminics can be a good alternative. Onset of pain can trigger onset of sleep disorders (Smith et al 2000). Severe lack of sleep can modulate mood and attention, or evoke irritability, reshaping patients's character traits (Busch et al 2012; Nicholson & Verma 2004; Sivertsen et al 2015): some of these physiological changes affect stability in certain liminal mental diseases, generating further psychiatric symptomatology (Monti & Monti 2007) and, if integrated within a cycling tension, can maintain a pain-bearing circumstance which, remaining without treatment, is studied to provoke personality, functioning and employment disabilities in the long run (Lallukka et al 2014).

#### . *Fibromyalgia*

Fibromyalgia is predictive of pain-reinforcement comorbid dysfunctionalities related to impotence (affective interpersonal weakness oriented to social, familiar, sexual or friendship maintenance, involving too sustained frustration and diminishment of the personal 'affective reserve/strength'), worry (uncertainty of proper care or medication, over-vigilance, fear-expectation, sleep disorders) and habits acquisition (lack of movement, sport, diet, constructive play, probable narcotic, opiates, analgesics, alcohol, food abuse, plus plausible iatrogenic pain reinforcement through overmedication in multimorbid scenarios). Fibromyalgia is a central chronic pain syndrome informing about a neurological scenario characterised by anomalous

pain evaluation, with possible anatomophysiological niches in down-modulating (Raphé-spinal descending biopaths) and limbocortical projections of the Central Nervous System (Julien et al 2005), dopaminergic unbalance (Holman & Myers 2005), and irregular cortical excitatory cell activity (Napadow et al 2010; Cook et al 2004; Gracely et al 2002), hypothesising GABA-ergic excitability in ventral tegmentum, associated with victimisation and penalising-reward dynamics (Cohen et al 2012; Nair-Roberts et al 2012). Neural dysfunctions in endogenous pain inhibition can also explain the troublesome effect of opiates in these patients (Hauser, Thieme & Turk 2010).

Chronification and intensification is a standard, inviting patients suffering from fibromyalgia to approach to many psychiatric problems comorbid with pain reinforcement: for example, fibromyalgia patients can acquire depressive traits, shifting mood and character and, thus, worsening pain reinforcement processes (Lin et al 2003), especially enlarging and emphasising pain events evaluation, as depression and pain tend to perpetuate each other (Fishbain 2007; Koike, Unutzer & Wells 2002). Diagnosis identifies clinical pictures through symptoms like hyperalgesia, allodynia, and multisite cyclical deep or immobilising pain (migraines, aureate or not, upper and lower limbs dystonia and muscular distress, inflammatory pain, loud and mild sound hypersensitivity, distinctively voices and continual noise, ocular pain from bright lights, or eye movement and fixation; eg, when reading or watching bright screens; etc.). This scene makes fibromyalgia a neuropsychiatric condition with plausible comorbid prognosis via over-sensitisation (Okifuji, Turk & Marcus 1999): for instance, pain thresholds turn more sensitive as fear-expectation, attention, and anxiety-driven beliefs rise too (Phloghaus et al 2001); sleep disorders emerge very frequently (which can be treated through antihistamines, anxiolytics, antidepressants and myorelaxants:

Cf. Hamilton et al 2012; Staud, Robinson & Price 2005). Opiates abuse with addictive traits can present, generally due to untreated anxiety comorbid disorders (Shurman, Koob & Guststein 2010; Boscarino et al 2010), for this, and because of enkephalinergic unbalance in the down-regulation Raphé-spinal projections, opioids are not advised for alleviating pain in fibromyalgia (Hauser, Thieme & Turk 2010).

### III — *Affection, Mood, Character* & *Personality Dysfunctions*

Many symptomatic clusters instantiated by a patient may be affected by multifactorial, blurry and heterogeneous pathological traits that can facilitate diagnostic practices (when clearly pertaining to well defined clinical entities) or block them (when polythetic diagnosis complicates relational thinking of scattered pathological traits pertaining or not to different but shared pathological architectures). Affection (emotional experiences directed towards people, objects or themes, including oneself, events and circumstances, family, economic burden, etc.), mood (humoural alterations) and personality dysfunctions (severe reshaping of character traits or, if sustained, personality traits, plus the personal behaviour within the frame of public, intimate actions and decisions) are some of the clinical factors that tend to alter diagnosability, as they can occur in many ways, in many diseases, with many other comorbid features, and even being comorbid themselves to any index disease. Of special attention to the neuropsychiatric assessment of comorbid instances running with pain reinforcement processes are Stress-Associated Disorders; that can lead or be led to severe anxiety pictures if conditions sustain; mood alteration; of which significant focuses are Anger and Sadness Character Traits Shifts; and the De-Consolidation (character's collapse, emotional 'reshaping' in Goldie's terms) of personality in pain-vulnerable patients suffering

from Bipolar Disorder (cycles of mania-hypomania psychotic traces, subsequent or prior to depressive traits), and blurred diagnostics with Borderline Personality Disorder (in previous classifications sharing similar symptomatic clusters with manic depressive disorder) —two clinical dispositions that have been very little studied in association with pain reinforcement until the 2nd half of the 20th Century.

#### . *Stress-Associated Disorders*

Sustained pain-bearing processes, along with collateral coping strategies, maintain a tight connection with stress and stress-related copathologies, understood in both senses, biologically and behaviourally (Murberg & Bru 2004; Fiore & Austin 2016): pain thresholds sensitise as stress accompany personal mood instability in circumstantial, episodic and event-driven beliefs, where hyper-vigilance, fear-expectation, attention, and anxiety dynamics are reported to rise pain experience intensity (Phloghaus et al 2001; Fairhurst et al 2007). Stress is a biological marker presenting the clinical value of a patient's hostile or belligerent context, where attentional, alert, and preserving dispositions are dysfunctional due to their increase, more or less (depending on the degree and sustainment of stressful temper) incompatible with biological routines, metabolic requirements, sleep restoration, interpersonal connectivity, or mental agility, with severe implications in brain reorganisation, plasticity neuronal reshaping, and physiological interneuronal function (Sandi 2011; Fiore & Austin 2016; Torta, Ieraci & Zizzi 2017). Stress, and anxiety derived from stress overflow, are associated with depressive traits (Torta, Ieraci & Zizzi 2017; Torta and Munari 2010), memory consolidation (MacDonald et al 2011), and with heterogeneous cluster symptomatology, generally related to depression and dismayed mood that can be hindering a proper clinical recognition of contributing neuropsychiatric

copathologies (Kroenke, Jackson & Chamberlin 1997; Nolen-Hoeksema 2000).

Stress involves prognosis and/or diagnostic comorbidity of sleep disorders, that in the presence of pain can coadjuvate to promote mutual reinforcement and acquisition of further psychiatric pathological traits: depressive dispositions are salient (Monti & Monti 2007; Hamilton et al 2015). Sustained stress has been observed to provoke rising levels of specific steroid hormones with disruptive repercussions for memory, with dendritic synaptic dysfunctional connectivity in hippocampus and upward bondings through limbocortical impairments, amygdala, and anterior cingular regions (Carballedo et al 2011; Popoli et al 2011; Hölscher 1999; Love, Stohler & Zubieta 2009; Silva et al 2008). Projective and interconnecting cortical regions (particularly prefrontal and somatosensory regions) jointed to hippocampal and anterior cingular structures and the amygdala have been pointed out to be dysfunctional in depressive patients (Marsden 2013; Murrrough et al 2011; Lee et al 2012). The fact that the neural scenario of stress shares neuropathological features with depressive traits helps to explain how medication for the latter alleviates or prevents from harm due to the neurodeveloped effects of the former.

#### . *Anger Traits in Mood & Character*

Anger traits are usually observed in pain-bearing population because of immediate mood impairments collateral to the burden of an enlarged and/or emphasised pain reinforcement (Janssen 2002). Anger traits are perceivable expressed strategies for coping with pain, nonetheless, the sustained behavioural instantiation of anger, annoyance, rage or indignation can provoke more than character and temper shifts, involving a neurological reshaping of personality. Anger mood shifts involve fear and anxiety prior pictures, attentional and dispositional over-re-

actions, and opioidergic reactions —especially in periaqueductal grey matter participating in down-modulation—, as prefrontal, insular and rostral anterior cingulate regions, projecting to mesencephalopontine ambiances, show diffuse metabolic activity provoking pain regulation dysfunctions in anger-disposed patients, whose pain thresholds appear sensitised as expectation, attention and anxiety attitudes shift too (Peyron et al 2000; Torta, Ieraci & Zizzi 2017; Phloghaus et al 2001; Fairhurst et al 2007).

Affection (with the significant component of being directional emotions, oriented to someone or something) experiments reshaping process too in people suffering from comorbid angry temper: rostral cingulate cortex, along with orbitofrontal cortical regions, appear intermediary regulators of some neuropsychiatric dysfunctions (Graybiel & Rauch 2000; Macoveanu et al 2014; Bruehl et al 2006; Bruehl et al 2008), including affectional mood shifting to anger, obsessive ideation (*idée fixe*) and compulsive reactivity (behavioural repetitiveness).

These markers show coping strategies (pain-kindred anger shifts) that instantiate in patients through both, distress introjection strategies (usually addressed as ‘anger-in strategies’, leading to depressive traits and sadness mood shifts, *infra*) and distress projection strategies (commonly put as ‘anger-out strategies’, leading to outbursts, explosive indignation, exasperation, fits of rage). These are physiological symptomatic accounts of a neuropsychiatric comorbidity picture, typical to pain reinforcement: early treatment affects pain alleviation and prevents from personality shifts (beyond mood and character traits shifts), and from further neuroplastic reshaping.

#### . *Sadness Traits in Mood & Character*

Sadness traits presenting prior mood shifting in pain vulnerable patients are a capital risk factor. Epidemiologically, sadness traits reshaping

ing mood and character, and if sustained, personality, are a paramount marker to detect in diagnostic evaluation by focusing prognostic, multidimensional, multifactorial analysis in the aim of preventing further neuropsychiatric comorbidities, pain reinforcement processes, and self-perpetuating pathological chains.

Sadness enters pain-bearing patients’s life through multiple accesses: inability to attain a personal satisfaction for escaping from pain is not the only factor, but also a deteriorated interpersonal situation, lack of confidence in one’s decisions, treatment failure, cognitive collapse/decay due to medication (iatrogenic faults), exposition to traumatic events, advanced age, solitude and loneliness, etc., can contribute to mood shifting (Baudino et al 2012; Bullis et al 2014; Forgeron et al 2010; Palermo et al 2009; Kamping et al 2013), all in accordance with pain-bearing comorbid instances and pain reinforcement processes (Logan et al 2009; O’Brien et al 2008). Sadness mood shifting can introduce depressive traits through common neuroplastic stressors, for example low production or functionality of serotonin, tryptophan and reward systems related to pain and opioid down-modulating dysfunctions provoking pain reinforcement (Price et al 2006; Jokinen et al 2009; Law & Liu 2008; Wei et al 2010; Russell & Joyner 2001).

Hippocampal activity has been shown to appear dysfunctional too via noradrenaline unbalance (key to access upwards connectivity through limbic-cortical structures to further cortical regions), provoking mnemonic and affective changes due to inner brain organisation during exposition to sadness-related stressors (Booij et al 2003). In order to prevent fixture of depressive disorders, reshaping sadness character traits and mood shifting shall be approached therapeutically in pain-bearing populations as a proper copathology presenting a severe risk of poor developing prognosis if remaining mis- or untreated.

. *Bipolar Disorder:*  
*De-Consolidation (Personality Reshaping)*

Bipolar disorders, type I and II, show a characteristic clinical unbalance in mood that is provoked by personality astasia (behaviour and beliefs instability), usually swivelling and polarised in two phases (within ~2 days to whole weeks), from depressive, anhedonic, unenthusiastic, to hyperactive, hypercreative, hypervigilant. In comparison, type I is generally exacerbated in mood shifts and contrasts, causing work and familiar problems, evoking interpersonal disabilities, and requiring treatment (possibly straightforward if episodes sustain). Pain reinforcement comorbid to bipolar disorder can alter such statuses, make them faster and/or peaked. Following Fishbain, Goldberg & Meagher (1986), the relational salience and prevalence of bipolar disorder ongoing with a pain reinforcement process is marginalised. In more recent years, numerous reports have been indicating that bipolar patients (some of them underrecognised for borderline personality disorder and vice versa in the clinical practice, Cf. Zimmerman et al 2010) suffering from chronic pain, also suffer from comorbid implications of its reinforcement, affecting emphasis (intensity thresholds) and enlargement (larger time span) of painful experiences (Cf. Nicholl et al 2014; Cerimele et al 2014). Impulsivity, hasty conduct and abrupt acting have been neurobehavioural markers associated with addictive traits and bipolar disorder (Love, Stohler & Zubieta 2009), and proposed as clinical values. Manic phases informing pain coping strategies can be related to impulsive reactivity and addictive traits (anti-reward dynamics, *supra*) with unfavourable results (Gunderson 2006) and, particularly, comorbidities with specific, regional and acute but sustained pain (eg, trigeminal neuropathy) are associated with psychotic brunts, tactile-pain fabulative behaviour, and unquiet, anxious pictures (Remick et al 1983).

Pain stressors appear to be more prevalent for bipolar than psychotic disorders, however there are currently insufficient studies.

The possibility of shifting not just character traits by mood and temper fluctuations (in this case impinged by pain reinforcement processes), but personality traits as such attributed to a person from a clinical perspective (3rd person standpoint attribution of personality dysfunctions), expresses the importance of therapeutic intervention for preventing personality de-consolidation (collapse, affected by underpinning neuroplastic central reorganisation and behavioural reshaping), that can lead to sleep disorders and parasomnias, depressive traits, paranoia, stressed mania, psychotic traits in attitude, and further psychiatric comorbidities associated with pain and lack of treatment.

A critical note can apply to the contemporary existence of Bipolar Disorders, type I and II: current treatment (generally in type II) is approached to the disorder as an entity which, in its epistemological sense, nonetheless, requires a historical recension, rethinking the requirements that a manic-at-times-&-depressive-at-times patient is installed in. Bipolarity requires of a more complex and heterogeneous strategy for intervening at the precise time of those poles, using a more precise and inflational pathological account, deciding a broader nosography on these specific symptomatic instantiations, instead of covering the entire picture with a nosological generalisation that happens to come as invalid as reductionism. A more descriptive epidemiological characterisation would inform of bipolar structures not as the proper pathology but recognised as its mode of presentation.

IV — *Dysfunctions Related with  
Central Neurodegenerative Disorders*

Neurodegeneration, primarily affecting central ambiances (cortical areas, basal nuclei, and midbrain-spinal regions), affects structur-

ally (cell architecture: neurons, glial bodies, adjacent tissue, superficial coverage, implied fagocitation agents, etc.) and functionally (synapse activity, inter and inner transmission of chemicals, metabolisation, cellular energy supply, etc.) to cognitive, motivational, attentional, mnemonic, affective and self-regulation (homeostatic-allostatic balance) requirements. In cases where pain reinforcement dynamics approach neurodegenerative patients, some biological complications can emerge, affecting diagnosis, prognosis, treatment and basic healthcare. This final section reviews affectional and cognitive dysfunctions due to pain reinforcement processes complicating three common dementias, Alzheimer (cognitive), Parkinson and Huntington (motor and procognitive, in severe and advanced phases).

#### *. Alzheimer Cognitive Dementia Complications*

Symptom clusters, implied in the recognition of the neurotypical diagnosis of Alzheimer (detection and intervention of neurological markers instantiated by a neurotype, clear classifiable disease, or diagnostic phenotype) usually involve psychiatric traits in neurodegenerative patients and vulnerable population (Selbæk et al 2014), multifactorial because of genetic charge, traumatic biographic events, age, etc. (Selbæk & Engel 2012 in Habiger et al 2016). Many dementias course with psychiatric symptomatology, moreover, the case of pain reinforcing scenarios comorbid to Alzheimer are observed to contribute to the general manifestation of affective dysfunctions: panic and anxiety-related symptoms, presenting pain or physical complain, loose irritability, agitation, mood shifting processes, psychoses and pseudo-fabulations, or negative affections directed to specific targets show to be common (Wong et al 2015; Cheng, Kwok & Lam 2012; O'Brien et al 2008). Transdiagnostic vulnerability factors (Cf. Wurm 2018) for emotional comorbidities im-

plying pain reinforcement problems and functional neurodestruction are also burden-related comorbidities (specifically those affecting hippocampal and limbocortical structures, informing about mnemonic, cognitive, declarative, evaluative dysfunctions, usually thematised upon biographic events, thus, possibly provoking episodic burden-related symptoms of dementia, appearing in depressive, psychotic, neuro-executive comorbidities: Cf. Gibson et al 2001; Cole 2001; Monroe et al 2012; Greicius et al 2003; Pickering et al 2000; Dickerson et al 2001) worrying the psychiatric picture for these patients. These can be stressors that reinforce and self-perpetuate throughout different copathologies: sleep disorders, concomitant paroxysmal (reinforcing) psychoses, addictive traits, unintentional substance abuse, attention-driven dyskinesia, and other alterations denoting uncertainty in treatment, or its lack (Busch et al 2012; Schaefer et al 2010).

Pain thresholds are observed to rise in sensitivity for Alzheimer (Cole et al 2006; Pickering et al 2000), maybe mediated by dysfunctional limbocortical interconnectivity and abnormal effects on down-modulating projections from opioidergic mesencephalic nuclei to spinal areas. Accordingly, from studies of Monroe et al (2012), losses in the Central Nervous System hold a bond with cognitive dysfunctions regionalised in amygdala, insular and rostral anterior cingulate cortices, periaqueductal grey matter (along with the general reticular formation and enkephalinergic down-modulation systems inhibiting C and A-delta fibres). All these hotspots usually develop fibre tangles or neuritic plaques, the latter affecting insular regions resulting in apathy, the former affecting specific cortical ambiances resulting in kinetic functioning (Cf. Tekin et al 2001 in Monroe et al 2012).

Comorbid states related with Alzheimer's neurodegeneration and also derived from pain reinforcement processes may affect the func-



tionality of biosystems via evaluative, comparative-discriminatory, and narratives-making decay. As these patients tend to acquire some sort and degree of disexecutivity (Moriarty et al 2010), or interpersonal dysfunctionality via cognitive impairments (of mnemonic, imaginative, speech and events-recognition abilities), diagnoses can complicate in detection and intervention, mainly due to a common state of neurovulnerability towards other comorbidities that affects too diagnostic variability and, especially, prognosis (Boly et al 2007; Krulewicz et al 2000). Treatment for pain must be accessed prior to the onset of reinforcement dynamics. Regarding possible hallucinatory or fabulatory behaviour in dementias related to the hypothesised dopaminergic unbalance, opioids have been shown to affect very little the cholinergic reinforcing process, thus, compensatory use of opioids can be of benefit in these patients (Cf. Habiger et al 2016).

#### . *Parkinson Prodementia Complications*

The neurotype for Parkinson's clinical scenario presents a neurodegenerative, chronified, disexecutive procognitive motor condition. It is suggested to emerge through yet unclear but focused genetic factors (Shimura et al 2000). Parkinson presents with an identifiable symptomatic cluster that furrows clumsy walk, stumbling at starting march, tremor at rest (all of which have been included within the cluster of 'motor blocks': Cf. Giladi et al 1992), general stiffness, probable shivering convulsion (micro-myoclonias), slow movement (bradykinesia), and affective, intentional, attitudinal disorders as the disease progresses to a phase of proper dementia. In this sense, Parkinson's evolution to a neuropsychiatric picture usually emerges through affective dysfunctionalities and mood and character traits shifting to depressive traits (Fishbain 2007; Tandberg 1996). Physical distress, and further more specific pain-kindred processes

comorbid to neurodegeneration, are very prevalent in Parkinson patients (~60%), even more present in populations instantiating dystonic symptoms (Ford 2010; Beiske et al 2009).

Pain reinforcement processes aggravate the patient's own bioevaluation of distress (emphasis or hypersensitisation, plus a perception of increased time span suffering regional pains), and are, thus, plausible makers for prognosis of neuropsychiatric comorbidities associated with it, which potentially can have severe effects in the Parkinson neurotype: fabrications and pseudo-fabrications, irritability, mood shifts, anxiety, fear and panic episodes have been reported, and within the frame of sadness-kindred affection (from character to personality reshaping), patients in advanced age face a clear prevalence (~70%) for developing depression disorders (Lohle et al 2009), which along a chronified pain (hypersensitisation) and central dysfunction (like in opioid down-modulating dysfunctionalities), are prone to introduce pain reinforcement processes (Fishbain 2007; Heberlein et al 1998; Wei et al 2010; Mayeux et al 1981; Price et al 2006), along with physiological dysfunctions in central regions involved in reward and anti-reward systems, inclined to develop habit dysfunctionalities too (Cf. Borsook et al 2007; Shurman, Koob & Guststein 2010; Zubietta et al 2001; Boscarino et al 2010). Some basic medication for parkinsonism and Parkinson neurotypical symptoms, specifically L-Dopa, can affect down-modulation and internal regulation of pain, informing higher intensity in pain comorbid to Parkinson populations than the general (Perrotta et al 2010). This presents another example of epidemiological evaluation in multifactorial determination of treatment and prognosis, when accessing comorbid, complex diagnoses. Emergent psychiatric symptomatology (eg, change in personality traits through a chronified character and mood shifting) is usually given because of pain reinforcement: the role of what previously was hypothesised as a

premorbid Parkinsonian personality (Paulson & Dadmehr 1991; Todes & Lees 1985) in relation to faulty interconnectivity between affected basal ganglia and limbocortical projections can be of diagnostic import (once more, character shifts can have a prognostic value via multifactorial and multidimensional analyses: epidiagnostically valuable).

#### . *Huntington Prodementia Complications*

Sensorimotor integration is altered in Huntington disease, however its degenerative nature develops fast to cognitive and affective impairments (Ro et al 2007). As a motor procognitive dementia like Parkinson, Huntington is a neurodegenerative disorder: its neurotype informs about a biopredispositional genetic condition, autosomal dominant, usually unleashed between the 30-50 years in the patients's life (Ross & Tabrizi 2011), manifesting neuro-atrophic and biochemical dysfunctional values in striatum (Baake et al 2017), with dopaminergic unbalance in neurotransmission (Mattel & Meck 2004), and basal ganglia, especially over-expressed GABA-ergic dynamics in caudate and putamen (Nasrullah 2018), associated with choreiform, involuntary micro-myoclonic dyskinesias (affecting face and limbs), and limbocortical projections (expressing intellectual, affective, intentional, attitudinal disorders as the disease progresses to a phase of proper dementia).

Pain, chronified and emphasised by neurodeterioration, is a common however understudied comorbidity in these patients. Pain bioevaluation may correlate dysfunctionalities with Huntington's degeneration, poor interconnectivity and volume loss in caudate and rostral anterior cingular regions, as central integration for attaining a whole-viewed experience of pain is observed to be oriented by such nuclei (Koyama et al 2000). Pain-related comorbid reinforcement of the disease can involve psychiatric features, starting by depressive traits,

anhedonia, irritability, anger and sadness mood shifts in character, and anxiety, or emotional dysregulation and maladaptation to traumatic biographic events (Reading et al 2004), and continuing by aggravating neurodegenerative effects with neuropsychiatric disorders, weakening intellectual dispositions, mnesic procedures, mental integration of new concepts with old concepts, and pathological traits, including fabulation and delusional perception (Folstein et al 1985; Morris 1991).

Huntington patients face a very early onset of cognitive decline, which declares usually as a symptom included in the cluster for diagnosis (therefore, it is present before diagnostic access), and evolves fast (Raymond et al 2011). Huntington is, thus, ascribable to a neuropsychiatric clinical picture with cognitive and emotional weight (Neylan 2003; Paulsen 2011), and in combination with sustained pain-bearing, coping strategies, and pain reinforcement processes, comorbidity-centered diagnosis can be of much benefit to extract preventive prognostic markers.

#### . *Closure & Chart of Dysfunctionality Clusters (I—IV)*

Plenty evidences have been exposed throughout the past and the present centuries showing how emergent neuropsychiatric symptomatology appears along with pain reinforcement processes. The opposite direction, pain symptomatology followed by neuropsychiatric index diseases, or pain reinforcing such diseases, presents as well.

Treatment for comorbid instantiations must be efficient, cautious, and straightforward in the aim of preventing further chained clinical pictures, plus deterioration of the present health status. Neuroplasticity, brain intersystemic distant connectivity, and reshaping processes affecting a proper neuroanatomical and physiological work have been introduced as

crucial markers for identifying comorbid and reinforcement dynamics, and for approaching to plausible explanations. Prognosis and multifactorial analysis are two major focuses of attention for developing a strategically oriented diagnostic practice to comorbidity and heterogeneous, complex, uncertain presentations (ie, epidiagnosis, Cf. introduction, definitions and concluding implications in QIII, §5).

A contextualised scale of implied comorbid criteria, and of viable stressors that lead to clinical worsening, must be generated in diagnostic person-centered evaluation, especially if pain presents, understanding the patient as a whole, and his or her central nervous integration, affection, memory, thinking and coping strategies as an organic, unsteady, plural course of actions (Cf. clinical practice and assessment rethinking in QIII, §7). Changes in personality traits, focusing sadness and anger-in/out strategies, acquired as a result of lingering character and mood shifting processes are usually due to pain reinforcement, sustained untreated distress, pathological dispositions never accessed by therapy, or congested emotional and affective comorbid states, which, in turn, can contribute to triggering permanent complications if not clinically reversed.

In order to assist diagnostic detection, this chapter has introduced a neuropsychiatric framework for interrelating such multifarious comorbid contributors, overviewing some of the most common diseases affected by, or being affecting pain reinforcement processes and emotional functionality. Four epidiagnostic factors have been applied, mainly driven by relational and prognostic values, which may help in finding neurotypical features during the diagnostic search and evaluation of the patient as key signals. Vulnerability factors for emotional comorbidities implying pain reinforcement and functional neurodestruction are also implicit values. The framework (summarised below) consists in the following four dysfunctionality

clusters: I 'executive attitudinal dysfunctions', II 'impotence, worry and habits dysfunctions', III 'affection, mood, character and personality dysfunctions', and IV 'dysfunctions related with central neurodegenerative disorders':



■ **Summary Chart — ‘Dysfunctionality Clusterings & Plausible Comorbidities’**

<i>Dysfunctionality Clusters (I–IV)</i>	<i>Prognostic Complications Comorbid to Pain</i>
I <i>Executive Attitudinal Dysfunctions</i>	Depression (Sustained or ‘Sad Personality’) Developmental Depressive Traits During Growth Major Depressive Disorder Long Termed Depression (Dysthymia) Pienirrexia (low intention, volition, interest) Laboural, School, Familiar Dismay Lack of Sexual Appetite Severe Fatigue (leading to attitudinal inappetence) Suicidality (including Self-Harm: Intentional Injury)
II <i>Impotence, Worry &amp; Habits Dysfunctions</i>	Anxiety Disorders Fear-Anxious Clinical Pictures Sexual-Anxious Clinical Pictures Panic (Phobias) Disorders Severe Agitation Sleep Disorders (including Parasomnias) Substance Abuse Dependence (with iatrogenic factors) Addictive Traits (attention to opioids) Post Traumatic Stress Disorder (with prior event) Fibromyalgia Complications (reinforced via impotence) Obesity and Food Hyperconsumption Manias Compulsive Hyperreactivity (reward/anti-reward systems) Smoking Somatisation & Somatic Traits (due to worry)
III <i>Affection, Mood, Character &amp; Personality Dysfunctions</i>	Stress-Associated Disorders Mood Detrimental Coping Strategies Anger-In Traits (Outrage, Repression) Anger-Out (Explosive Episodes) Mood Hypersensibility (Irritation, Indignation) Sadness Traits (‘depressivoid mood’, depressivity risk) Bipolar Disorder (Personality De-Consolidation) Cyclothymia Borderline Personality Disorder Psychoses (low prevalence, but reinforcement is present) Psychotic Traits (fabulation, tactile pseudo-fabulation) Conversion ( <i>ante</i> Hysteric) Disorders (Paresis)
IV <i>Dysfunctions Related with Central Neurodegenerative Disorders</i>	Alzheimer Cognitive Dementia Complications Parkinson Prodementia Complications Huntington Prodementia Complications Motor Pro-Cognitive Dementia (Ataxias)



## QIII, Chapter §7

### Epidiagnostic Assessment as Clinical Practice. Navigating Person-Centered Diagnosis in Neuropsychiatry.

(In Niche C — Framing Clinical Characterisations )

☛ 346 — 352

—

#### Parts

. *Introduction*

#### I — Plural Attention for Personal Care

- . *Some Methodological Traits*
- . *Situation Dependence*
- . *Patient Proximity*
- . *Classificatory Requirements*

#### II — Social Studies

- . *Considering Pluralism*
- . *Sounding the Features of Scientific Practices*

#### III — Framing the Epidiagnostic Practice

- . *(1) Medical Language and its Validity*
- . *(2) Pragmatic Accounts*
- . *(3) Assertions on Pathological Traits*
- . *(4) Pathological Architectures*
- . *(5) Convention on Clinical Criteria*
- . *(6) Instrumental Experimentation*
- . *(7) Wild and Right Clinical Guesses (Athwart Theory - Error Making)*
- . *(8) Case Behaving (Case Reporting)*
- . *(9) Nosographic Inflation through Trust Knowledge Nosological Debate*
- . *(10) Assisted Diagnostics (Artificial Intelligence)*
- . *Further Features: A Practice of Clinical Care*
  
- . *Closure*

## . Introduction

The modern neuropsychiatric practice is seeing significant changes since the 1990's decade, mostly shifting the technoscientific systems oriented to evaluate the diagnostic state of health (Christodoulou 1987; Engel 1997; Milles et al 2008; Klinkman & van Wheel 2011).

Such changes primarily affect the manner in which physicians approach to their patient as to a person wholly (Person-Centered Medicine) vs. as to a case of symptomatic recount without broader social, familiar, political, economical or religious dimensions. Understanding better human conditions of pain and sorrow, it has been accepted as policies that Health Institutions (welfare plans and social organisms, beyond the sole action of medical personnel) shall concern and care about the ill collectively trying to undertake the most accurate proceedings (Engel 1988; Kitwood 1995; Bensing 2000; Martin et al 2004; Cloninger 2006; PCPC 2006), searching for an optimisation of the practice (Medicine of Care; Qualitative Medicine).

In regard to such movements towards pluralistic attention, some major factors of diagnosis are required to be revisited, taking into consideration its relevance as a communal practice. Facing a descriptive approach, this writing assesses how some newer epistemic architectures sounding the notion of 'scientific practice'—mostly from situated perspectives on Natural Pluralism (1960's–2000's and beyond), and especially using P Kitcher's framework— can be applied to identify and describe the so-called 'diagnostic practice'. In such context, the main goal of this work is to serve as a revision of our nowadays pluralistic clinical behaviour.

In three parts, the text exposes first (I) an outline of how the person-centered perspective implied in healthcare plural processes influences diagnostic practices, accounting for three of its main aspects: 'situation dependence', 'patient proximity', and 'classificatory requirements'. It

then (II) revises the notion of 'scientific practice' as portrayed by modern epistemologies to be applied to diagnosis, and concludes (III) proposing a framework for helping in defining modern clinical performances.

### I — *Plural Attention for Personal Care*

The development of a personalised primary care in Global Healthcare Systems has been of major significance for current world-wide policies. Recent work has shown a progressive tendency towards improving health status in large-growing populations, attaining sustainable healthcare systems (economically for governments, and financially for individuals and families), and re-centering clinical practices to the person suffering from a disease, instead of the disease acknowledged in case (PAHO 2007; WHO 2009).

'Care' as a term in use has been de-trivialised in medical speech, re-framed, re-empowered, and implemented in a responsible manner for healthcare systems. In it, attention, disposition and personal approach gather up as something accountable for the medical duty (Rittenhouse, Shortell & Fisher 2009). In this sense, the AAFP considers that such care shall be coordinated across all elements of the patient's community, which includes hospitals constituting the Healthcare System, but as well home health agencies, peripheral consultants, friends and family members, nursing homes, information registers, interpersonal information technology exchange, and so forth (AAFP 2009).

Person-centeredness has been established a fundamental requirement for methodology in clinical practice too (Mead & Bower 2000). When approaching diagnostics, discussions are re-oriented from 'what-strategies' to 'how-questioning': eg, how a specific person would undertake most optimally his or her disease iden-

tification and treatment (Stange & Ferrer 2009), how national systems's guidelines should incorporate caring training into practitioners's codes (BDP 2008), how the patient's or the family preferences ('cultural blood lines', 'values') could vary diagnosis, therapy or recovery phases (Lichtenstein & Slovic 2006; Pongsupap 2007; Thagard 2012; Nejad 2013), how should be physicians's values considered in the decision making process and exposed to the patient (Hunik et al 2001; Woodbridge & Fulford 2004), as for dysexecutive patients, mostly touching the psychiatric field (Young et al 2008), or how shall decision making processes be assessed in the debate of shared decidability, shared rationality and shared responsibility in bioethics medicine (Buchanan & Brock 1990; Elwyn et al 2011; Chewning et al 2012).

In the discussion about clinical performance of practitioners who consider their actions and behaviour important features of their practice, there is also a call to their pragmatic responsibilities in communicating with patients: the sense of 'performing' grasps here an ethical background to the way clinical practices get actually practiced. Performing clinically, thus, also means translating clinical terminology into personalised health information, summarising medical difficulties into manageable instructions, and relativising medical inputs for motivating patients's attitudes towards better therapy and recovery, in the aim of increasing medical results (Bartholomew et al 2006).

#### *. Some Methodological Traits*

Person-centered care presents a practice of Qualitative Medicine that furrows private and public domains: a medicine addressed to the private individual subject that makes possible the proper actions to be engaged, but in balance, performed in the face of public and communal benefits (Mercer 2008; IHI 2009). Considering its effectiveness, pluralistic person-centered

practices performed through empowering patients and communities, informing them, and making them a part of clinical discussions about their own organic and mental concern, have been evidenced to lead to healthier social outcomes, socio-pharmaceutical activism, reinforced self-consideration and self-esteem, higher interest in social and political matters, higher development rates in diversity-based contexts, and fewer hospital expenditures per person (Cf. Rapport 1987; Rogers et al 1997; WHO 2006; Datamonitor 2007; Lindenmayer et al 2007; Melnyk & Feinstein 2009; Macleod & Frank 2010; Bertakis & Azari 2011; Stewart, Ryan & Bodea 2011; van Dulmen 2011).

Certainly in this sense, the person-centered perspective is not reinforcing a realm of methodological knowledge limited by individual case-to-case causal implications —for an integrative perspective of evidence-based and person-centered medicine, Cf. Bolt & Huisman (2015)—. Instead, it is pushing forward the whole process of empirically-focused matters (societal distributive approaches, standardisation programmes, statistical analyses, etc.) once they are present to be reconsidered into particular ambiances, performing clinically with what is accepted generally for a situation in particular.

Nonetheless, serious concerns on the validity of applying large sample statistics to individual patient cases has been alarmed in the clinical space (Cf. Miller & Miller 2011; Hickey & Roberts 2011), an application usually confined to the validity of large numbers's laws and the not so reliable economically-driven social studies about massive populations (Heckman 1979; Hawkins 2004; Taleb 2007; Bland 2009; Raman 2011; Walsh & Gillet 2011). Such a probabilistic frequentism is challenged, faced to the complexities of patients's situation dependence, which are closer to a propensity theory of causation (ie, observing the correspondence between singular patients's propensities and pathologies). Unawareness of cross cultural and cross na-



tional failure of treatment rates, of experimental error rates, and of sample sizes's implications; as the overwhelming presence of un-reproducible and un-reproduced studies through meta-analyses; and the detected deficit in clinicians interpreting data, are all factors recently stressed by researchers betokening how standardisation instead of personalisation often favours bias and neglects difficulties (Shamliyan, Kane & Jansen 2010; Johnston et al 2016; Iqbal et al 2016).

Such panorama is forcing research to relocate the epistemic position of its methodological conditions in a redefined openness, as seen in the everyday aid of statistical measurements for diagnostic medicine when translating results from big cohorts to singular case situations, and moreover for psychiatric fields, where treatment (not just medicalisation but care itself) responds to even narrower samples.

As Hickey, Hickey & Noriega (2012, 76) expose, the primary utility of this kind of methodology shall be limited to providing background data for organisations and governments, as an indication about diseases incidence in large scales, but peripheral to the central issues of the clinical practice in individual case situations.

The very sense of 'performing for a situation' is openly implied in the concept of practice, but not so in the concept of methodology. A direct way of conceiving of such application of the generally valuable to the specifically valued is by shifting the idea of 'clinical methodologies' to that of 'clinical practices'. This moves the speech forward to the very clinical process: to clinical practitioners, to their actions and decisions, and to how they communicate with communities of practice and communities of patients.

Part III of the present text will consider the epistemological intricacies in the notion of 'scientific practice' and its adequacy to welcome the needs of nowadays person-centered clinical practice, proposing a framework for describing its utmost features towards Epiagnosis (Cf. QII, §I; QIII, §5-6; conclusions in QIV, §1-2).

Prior to that, 3 main aspects of the clinical performance and its needs will be outlined: 'situation dependence', 'patient proximity', and 'classificatory requirements'.

#### *. Situation Dependence*

We can see with the example of admissions how situated to the conditions of a person clinical processes could be. Clinical processes usually start by entering the healthcare system through therapeutic admission (a request of care followed by an intent of caring). Nonetheless, admission procedures shall not be thought of as given facts, but rather as situational composites.

If we think of entering the system from a person-centered approach, familiarity with diversity is a matter of importance: admissions are constrained by particular criteria that shape the very clinical process from its outside. They furthermore work independently if compared across countries, sometimes in function of personal ambits (illness severity, urgency, age, injury localisation, personal access to public/private services...), sometimes in function of wider intricacies (bureaucracy, existence of a required hospital, disposable personnel, availability of material and extra-medical resources, like family care, sufficiency...) though always modelling and pre-defining clinical actions thereby.

Ethnicity, language, gender and risk prioritisation play an important role in considering straightforward validation for care (Smith et al 2010; Galdas & Cheater 2010; Ong et al 2012; Asghar, Phung & Niroshan 2016), thus, rescaling the significance of situationalism in clinical practice before application. As any other clinical appreciation, therapeutic admission presents a subject-based ecology of actions, those of which are situated around the person, actions that define healthcare as a punctual instead of a general practice that is elicited for a particular subject, and not given prior to such event. Clinical actions are observed to depend upon

the patient's situation in most cases. Treatment and professional attention certainly depend too upon the amount of problems that can or cannot be appointed by each session within a few minutes, like family medicine studies manifest (Beasley et al 2004; Flocke et al 2001). Again, impacts on care grow considering introspective requirements for deepening into pain-experience outcomes (Rosenblatt & Attkinsson 1993) or transcendental experiences (Bernard, Dayringer & Cassel 1995) in psychiatric disorders.

#### . *Patient Proximity*

Many studies report the importance of understanding that the content of consultation is sensitive to the degree of familiarity with the patient (Zangrilli et al 2014; Fassaert et al 2008; Fotopoulou et al 2008). This is not only limited by attitudes from person-to-person contact, but also by time-to-time evaluation, and by its extension to family, friends, working ambiances and other core circles of patients's affect. Breaking such proximity, or under-caring its importance in diagnosis, medicalisation or therapy, by using a plain medical approach can lead to malpractice in patient's detriment (Levinson et al 1997; Kappen & Dulmen 2008).

Inside the idea of patient proximity we must include the 'building of empathy and trust' — both for approaching to patients's needs, and for consolidating reliability into therapy (Cf. an epistemological analysis is QIII, §9-10)—, and the 'mastering of empathetic techniques for generating qualitative physician-patient and patient-physician relationships' (Safran et al 2000; Benedetti 2002; Hoffman 2002; Kim et al 2004; Fiscella et al 2004).

Overcoming paternalistic models, and studying the shifts in the communication between patients and professionals is a task of the present (Thomasma 1983; Bensing et al 2006). In this regard, some integrative approaches have been developed for psychiatric interests, ex-

tracting strategies from the ambiance of the person-and-personality to be applied in diagnosis and treatment, beyond bodily and mental dichotomies (van Staden 2006; Matthews 2007), and integrating in the model the physician as a person too (Cox 2010), with skills and agencies to be trained. With that specific interest, personalised medicine comes actually re-defining itself to interpersonal medicine. An example is Frankel & Stein's (2001) proposal of the 'Four Habits Model', a skills programme for physician-patient communication working through empathetic exploration, including from its very beginning patients's standpoints (Cf. too Krupt et al 2006).

#### . *Classificatory Requirements*

Diagnostic psychiatry is also concerned with classificatory practices for assessing the reliability of the practice compared throughout separate periods of time (Cf. modern appreciations in the 'International Guidelines for Diagnostic Assessment of Mental Health': IGDA 2003).

Classifying diseases and symptoms is a creative practice mediated by social, psychological and cultural consensus that is not only affected by what is or is not a priori classifiable —not an obvious remark: limits of scientific observation change from period to period—, but also by how licitly things come to be grouped or associated, accepted or compared with other things, inside and outside the field —which incorporates ethical, methodological, ontological and deontological discussions— (Haraway 1976; Dupré 1981; Thagard 1999; Hacking 2002; 1998; Darden 2006): a reason why situationalism is a key factor for diagnosis is because labelling what is sufferable is also a manner of knowing what one is suffering, and because such label will automatically imply a burden to the patient (Cf. 'stigmatisation', Goffman 1968; Schwenk 1999).

Regards on classificatory kinds (and to this extent 'human kinds', Cf. Hacking 1995) connect

'suffered experiences' with the 'clinical practices of identification of pain', and in so doing, classificatory kinds communicate, through common naming, patients and clinicians. Either natural, social, analytical kinds; either pathological, clinical, definitional kinds; diagnostic practices are rendered by performing certain classifications, decisions of tagging and grouping that are both directed to patients and to symptoms (Ballerini 1997; Hacking 1986), and which borrow their theoretical depth from a tradition of studies in biology, genealogy, botany and zoology, that lead to historically designed structures managed for correlating organic levels of complexity with ecological emergent features (MacMahon 1978; Betchel & Richardson 1993; Lilienfeld & Marino 1999; Heylighen 2000).

Among classificatory problems are the technical means for classification, their risks and discussed rigour: medical tests (eg, BOLD techniques, MRI, fMRI, PET, CTA...), diagnostic observations, and clinical manipulations, by which perturbations upon the patient's self appear necessary in order to compare expressed symptomatic pictures, or to assess unclear polysymptomatologies through differential diagnostics. To this account, causal inferences during diagnosis, correlating such classificatory kinds with the expressions of diseases in the very patient, may get affected by comorbidities, severe heterogeneity, medical singularities, maleficeny polypharmacy, false positives, unmanifested genetic predispositions, or hidden psychosocial conditions or habits. This can promote diagnostic decisions to be taken beyond scope, thus, referring clinical identifications to idiopathic developments (Deary 2005).

In this regard, medically unexplained symptoms present a liminal example of the epistemic boundaries of diagnostic processes (for instance, the existence of meta-diagnostics), requiring a shift from the rigid, categorical paradigm to an opener, dimensional one (Musalek & Scheibenbogen 2008), focusing epidemio-

logical and aetiological orientations away from a mono-causal model of classification. A further step from dimensionalism are descriptive multifactorial pathological accounts, provided through assisted diagnostics (eg, Artificial Intelligence Assisted Nosographers), where paper printing fixed-point categorical nosographies are substituted by a new trust on agreeing a description of the 'pathological traits' (symptoms) of a specific patient in his or her interaction with a shifting milieu, that will finally provide a multifactorial rich presentation circumstance (symptomatology) adapted and contrasted with background data for identifying 'pathological architectures' —plurally and consistently assisted by smart comparison aided by contemporary software—. This can bring the patient to decide, or at least to participate in the decision making process, along with the rest of stakeholders within the problem (clinicians, family, friends, institutions and associations) in a more flexible paradigm of diagnosis what is he or she actually suffering, which in a clear form, de-stigmatises the effect of categories as it involves pathologies as diffuse stressors affecting the person but contextualised to him or her.

Moreover, mental diseases's classifications are being required of an even more subtle evaluation, more integrative between ill and healthy states (Cloninger 2004), and more conscious of subjective needs (Gask, Klinkman & Dowrick 2008). Mental diseases's classifications require their organisational taxonomies to flow among the various manifestations of symptoms, gathering expected and unexpected expositions of pathological traits, which must be synthesised and compared with standard clinical bases with a more flexible and personalised inclination (Philip, Klinkman & Green 2007).

Such taxonomies must be careful: they do not actually account clinical accumulations of pathological traits, but clinical manifestations of events suffered by patients, which complete analyses with far more complexities than just

anatomico-pathological topics (Eriksen et al 2013): emotional, ethnic, economical, epochal, social, psychological, territorial and further considerations inform better the causal linkages these kinds can produce (Anjum et al 2015).

In summary, a variety of person-centered actions highlights the complexity of clinical performance. They show how its situational and plural facet modulates diagnostics, and classificatory possibilities, as the process is put to work mediated by patient-professional, professional-patient relationships, in communal coupling.

## II — *Social Studies*

In the last half of the 20th Century, a developmental turn to the social implications of scientific decisions, methods, policies, and goals has arisen. Considering the renewal efforts in ethnography, anthropology, history and sociology, some modern epistemologies sprang as a new approach to identify the movements and boundaries science is facing. What was first programmed as a social epistemology towards general fields (Merton 1973; Goldman 1987; 1999; Fuller 1988), regenerated as a more detailed vision, marked by feminist studies, activism, and the era of biological technology (Haraway 1991; Keller 2002; 2005; Weed & Rooney 2010). This newer scope is eager to seek how scientists are occupied with producing, deciding, experimenting and thinking, in a populated context with economical, contextual, political and cultural factors, contributing to their reasoning, goals, results, and theory-making (Cf. van Fraassen 1976; 1980; Harding 1991; Galison 1996; 2004; Perdomo 2003; 2011; Cf. QII, §1).

### . *Considering Pluralism*

To great extent, such interest emerged in biology and primatology studies, from their growing criticism to a de-personalised, ingenuous,

awkwardly false, or inoperative form of contributing to science (Rossiter 1982; Southwick & Smith 1986; Fedigan & Fedigan 1989; Holmes & Hitchcock 1992), a methodological paradigm that, as shown in Part I in respect to medicine, did not respond to modern scientific needs.

In these terms, some scholars introduced the cohesive proposal of a fundamental plurality in scientific advancement (eg, Minnesota Pluralism, Perspectivism, Social Empiricism, Contextual Empiricism...), processed by epistemic subjects (to medicine physicians, but also nurses, patients, family, friends, laboratories, governments, pharmaceutical companies...) contextualised in diverse communities of knowledge, 'epistemic communities' (Longino 1990; 2001), and immersed within a wide range of methodological possibilities for dealing with scientific interests (Cartwright 1993; 1999; Solomon 2001); where each of the different and simultaneous perspectives offered, when characterised by the validity of its own explanations and results (Kitcher 1984; Kitcher & Salmon 1989; Giere 1999; 2006a; Mitchell 2002), is conceived of as by-product of the different fashions of actualising science as it is: a multiplicity of practices performed in plentiful manners and abroad a singular method. To that extent, such approaches aimed at observing an equilibrium between the positive sciences, and the studies of such sciences put in practice as plural, social composites, drawing a framework for a 'naturalisation' (to neutralise at the same level and context) of the efforts of both, epistemological and scientific makings (Stump 1992; Kitcher 1992; Giere 2006b).

In the present case, it came at forming a naturalised pluralism presented as a socially relevant philosophy of science (Fehr & Plaisance 2010, 302), or, as what has been addressed in QI, §1, a clinical form of contextualism.

The concept of 'scientific practice' is thus clearly rooted in such garden of probing sounding and criticism of the very actions taken by communities, a concept that has kin relations to

contemporary ethnographic, political studies of scientific making too (Mody 2005; Olson 2010)

*. Sounding the Features  
of Scientific Practices*

A clear organic structure of scientific practices's main features is proposed by Philip Kitcher's 1993 work. Let us then explore the concept: «Take a scientist's practice to be a multidimensional entity whose components are the following: 1, the language that the scientist uses in his professional work; 2, the questions that he identifies as the significant problems of the field; 3, the statements (pictures, diagrams) he accepts about the subject matter of the field.» (Kitcher, 1993, 74).

It can be argued that those first three features (1, the linguistic validity or acceptance; 2, the pragmatics applied to the use of such language for inquiring problems; and 3, the assertions and statements, both universal and specific) depend upon preferences of communities of scientists (and not scientists: eg, people affected by those classifications) immersed in cultural scenarios which modulate inferential proceedings before methodological processes elicited: such movements are what generates the very methodologies.

As Kitcher runs his argument: «Just as certain kinds of perceptual beliefs may be precluded for those with particular theoretical commitments, so too a scientist's acceptance of the propositions, goals, and procedures associated with a particular doctrine may make her unable to engage in certain feats of memory, or to be motivated by certain goals or to perform certain kinds of inference.» Kitcher (1993, 68). This is a logical construction connected with propositional logic, in which, scientists as epistemic subjects are put to be 'subjects of belief', and the content of their thoughts, 'contents of beliefs'.

This argument personalises scientific practices: by re-framing the naive paradigm of utmost-rationalistic, impersonal scientific devel-

opment, this newer conception actualises the real conditions and circumstances in which science is practiced, it de-trivialises the process, and integrates social epistemic values to it.

Kitcher continues the description of the practice: «4, the set of patterns (or schemata) that underlie those texts that the scientist would count as explanatory; 5, the standard examples of credible informants plus the criteria of credibility that the scientist uses in appraising the contributions of potential sources of information relevant to the subject matter of the field; 6, the paradigms of experimentation and observation, together with the instruments and tools which the scientist takes to be reliable, as well as his criteria for experimentation, observation, and reliability of instruments; and 7, exemplars of good and faulty scientific reasoning, coupled with the criteria for assessing proposed statements (the scientist's "methodology").» Kitcher (1993, 74).

Here, the term 'schemata' (in the 4th point) rises considerations upon how scientific progress gets actualised by practices, and how they are key to advance. Once scientific contents are produced, they gather up in formal structures of thought, resting to be re-engaged in future analyses by the scientific community. Those systems, inferences, schemata, are believed until then, but they rest not in vacuum, they are socially contextualised to subjects of belief, as «faced with explanation-seeking questions, the scientist is disposed to produce texts instantiating particular patterns [texts can be translated as theoretical volumes, treatises, compilations of methodological process and in this case, reports of diagnosis as well, from doctors or theoreticians]. These patterns, or schemata, although they are not likely to be formulated by scientists themselves [...], are implicit in scientific practice, and I would expect that practitioners could recognize them as underlying their own explanations.» (Kitcher 1993, 82). One shall understand those patterns, rules, laws or explanatory

strategies applied to the practice, as socially-oriented methodological mannerisms, comprised for inferring things in particular situations by using them as automatic dispositions.

This is also a reason why the text observed that «in each of the last three components [5, 6 and 7], there are two different levels to the scientist's practice —a commitment to cases (typically reflected in behavior) and an embryonic theory about why the behavior is correct.» (Kitcher 1993; 74). In this sense, such schemata, with time, can evolve and be contrasted, procuring a progressively better understanding.

In relation to such a progressive consensus, Longino's (2000) critique highlighted the need of plurality in the construction of a successful identity in science. As she poses, science luckily or not is cast out of community values, decided well or bad, not growing as a singular monolithic fad, but multidirectionally instead. In this sense, although Kitcher ascribed to her idea in further texts, in 1993 he composes a quite prudent way of community-like optimalism where scientific practices are the core point:

[symbolism eliminated] «There are two types of inquiry that are worth pursuing: first, we want to know what, given the range of possibilities, is the best approach to the problem situation in which we are interested; second, we should scrutinize which of the available combinations of individual decision procedures and sets of social relations would move the community closer to or further away from the optimal approach.» (Kitcher 1993, 304).

And this is to say that not methodologies but practices, through 'individual actions' and their conditions of 'social accepted modes of acting', invoke culturally values that do transform the suggestions communities trace towards optimal moves, thus breeding a coral common practice in every situation.

In this sense, social implications agree with Kitcher's (1993, 304) conclusion.

Discussed the main features of the concept, the present writing proposes to translate and amplify this structure to the clinical diagnostic practice.

### III — *Framing the Epi diagnostic Practice*

In regard to the points of discussion of Parts I and II, an application to epi diagnosis as a scientific practice can frame the following features, composing a descriptive proposal for better understanding the underpinning epistemic elements of its configuration as a clinical practice:

#### . (1) *Medical Language & Its Validity*

Clinical Practices (CPs) especially focusing epi diagnostics as the key reference, depend on language, its national and cross-cultural uses, and descriptive and explanatory metaphors in biophysical scenarios. They must be critical with the allegorical treatment of diseases, that might not be historically connected but that get to a social impact through the name they receive, or the tropic figures used in medical causal discourse affecting by stigma a 'labelled' trait.

#### . (2) *Pragmatic Accounts*

CPs need deep introspection in the meaning and sense of scientific evaluation in diagnosis, required of a historisable biography (anamnesis), a plausible future behaviour (prognosis) mediated by a treatment that must be started at some point (following a principle of catabasis identifying the treatment works and starts a therapeutical process of recovery or paliative or symptomatic alleviation), and started thanks to the recognition of the previous dimensions: by itself, the diagnosis. It involves too the ethical circumstances of care that promote empathy and comprehension in decision-making routines, which apply to specific patients as it does to the rest of stakeholders, including patients's environment, clinicians and institutions.

. (3) *Assertions on Pathological Traits*

CPs employ schemata for observing and discerning the causal, frequentist or, in a more modern framework through propensity theory, probabilistic links and implications among what the patient presents (presentation circumstance; Cf. QIII, §5-6) and what the clinical knowledge informs and describes as background standards for pathological identification and characterisation.

. (4) *Pathological Architectures*

CPs include descriptive and pro-explanatory arguments of cross-social, cultural, historical, economical, and statistical data of pathologies being manifested in specific forms: while pathological traits inform of medical identifications of symptoms proper to a specific patient, which may be highly heterogeneous, pathological architectures would work as the standardised, demographic and epidemiological clusterings of such traits, composed by them and actualised in a general and constant form through new incoming data. In this sense, contemporary pathological architectures conform and are called to re-shape nosographies in an adaptive way through convention (Cf. QII, §1). At diagnostic application, this shall be re-elaborated when put in practice in particular circumstances, confronting it with multifactorial presentation and prognostic values for fixing differential diagnosis and comorbid instantiations (Cf. QIII, §5-6).

. (5) *Convention on Clinical Criteria*

CPs follow the need of a 'pathological principle': criteria are decided by multiple conditioners, socialised, and localised to the extent of what a historically traceable subject of belief can reach to assess and validate, integrated to each of the individual members composing the common trust on pathological accounts (nosography).

Criteria, then, need to focus on perspectival trust protocols of convention decision making (QII, §1), of 'democratic' (well informed and cross-culturally transigent) debate refuting or accepting proposals about what is a value knowledge and what are its applications and validity for making it a standard against which results and experiments can be contrasted.

. (6) *Instrumental Experimentation*

CPs could identify every diagnosis as an experiment, in theory making or in clinical practices: providing clinical methodologies to perform superficial or ultra-deep observatory and medical examination, including interpersonal and qualitative measurement strategies too, many traits of such practices are referable as technical and procedural. Their success in differential tests and confirmatory processes shall be treated as dependent too upon the practitioners's reliability on the commonly accepted paradigms of experimentation and observation, which are too a byproduct of convention.

. (7) *Wild and Right Clinical Guesses*  
(*Athwart Theory - Error Making*)

CPs, by hitting the possible answers to an individual's pathology, or being deceived by such decision, show as processes of interpretation, hypothesising and trying out contradictory attempts. This is applicable to guessing the most probable answer (diagnostics use abductive logic), but also in treatment, follow up and control, rehabilitation, and aid in self-growth.

. (8) *Case Behaving (Case Reporting)*

CPs are also conduits for case reports, exposing to the community some events in the course of the patient care, for being analysed, compared, criticised and incorporated into wider pathological pictures. Case behaving shows

personal habits, particular organic responses, specific coincidences, but as well, de-centralised cohorts of patients that can be associated in further researches.

. (9) *Nosographic Inflation through Trust Knowledge Nosological Debate*

CPs are and will be facing from the second to the fourth decades of the 21st-century (20's to the 40's) an inflationary effect in the amount of pathological accounts claimable for a specific patient. This inflation grows too the need of handling the information flow, recognising it as a value knowledge, and expands the requirement of the scientific practice to adapt for person-centered perspectives into more technological, however socially and politically decided, ways of understanding nosographies. The turn to new trust protocols in nosology that will help to rethink and discuss final nosographies will empower the practice with assistance for dealing with inflation, not as a problem nor a risk, but, contrarily, as a multifactorial, prognostic and contextualising tool applicable to specific patients in diagnostic dispositions. This decision making process in deciding nosologically what is sufferable through descriptive aim will also translate into a more descriptive recognition of pathological traits and architectures, swifting from fixed categories to multiple drafts making and heterogeneous characterisational claims.

. (10) *Assisted Diagnostics (Artificial Intelligence)*

CPs are in a transition process, because of such inflationary effects and needs, to provide care in diagnostic practices through assisted diagnostics (eg, Artificial Intelligence Assisted Nosographers; Cf. QIII, appendices in §9-10; QIV, §1-2), fixed nosographies are substituted by a new trust protocol engaging a new agree-

ment of description about the clinical 'pathological traits' (suffered symptoms) of a specific patient in his or her interaction with a shifting milieu —further on providing a multifactorial rich presentation (suffered symptomatology) of plural clinical circumstances: 'pathological architectures'—. Assistance adapted and contrasted with background data for identifying 'pathological architectures', plurally and consistently assisted by smart comparison aided by contemporary software, can bring the patient to decide, or at least to participate in the decision making process of characterising what he or she is suffering from, along with the rest of stakeholders within the problem (clinicians, family, friends, institutions and associations) in a more flexible paradigm of diagnosis. This makes the process centre in the diagnostic efforts in the patients and his or her instantiations of pathological traits, that might be heterogeneous and complex. This, in being more descriptive, multifactorial and contextualised within-the-patient's-context-of-instantiation, in a clear form, de-stigmatises the effect of categories as it involves pathologies as diffuse stressors affecting the person but contextualised to him or her.

. *Further Features: A Practice of Clinical Care*

As appointed by Cloninger, we need a new model for practicing diagnostics that incorporates domains of health for healthy and ill statuses; including 1, clinical disorders, 2, disabilities (regarding self-maintenance, occupational, working, familiar, social functioning...), 3, narrative approaches to the experiences of patients and their circles, the topics and definitions of their sufferings, values, preferences and their cultural vision of sickness, 4, risk factors, heredity, habits, stressors and contributors to ill health; but as well 5, a following observation of their remission, health restoration and growth, 6, their functioning recovery, 7, and their narrative approaches to their experience of quality of



life, 8, caring about their incorporation by seeing cultural and social tensors of identity and psychological integrations, and finally 9, the protective factors that promote positive health, resilience and social support (Cloninger 2004).

This is the story of the prosecution of a frame of diagnosis as a form of caring, of understanding, that has been psychiatrically — mainly from existentialism (Sonnemann 1954; May, Angel & Allenberger 1958; Laing 1960; 1961; 1967; Callieri, Castellani & Vincentis 1972)—, philosophically (mainly interpersonal theory: Sullivan 1953), and clinically demanded since the mid-century (Arieti 1966; McKeown & Lowe 1967; Spitzer, Uehlein & Oepen 1988; Dörr-Zegers 1995; Valdés-Stauber 2002).

In this need, it is proper to see evidence-based medicine in diagnosis as a social conflate of cultural, personal, situational dispositions too (Cf. Mumford & Anjum 2001 for a medically oriented ontology of causal dispositionalism). We shall draw such medicine as a 'practice of evidencing', not produced by evidences, but by performing detections, indications, and denoting symptomatologies that are subsumed within specific contexts of rationality, instead of appearing as naive expositions of organic damage.

In these lines, Anjum et al re-reported how clinical judgement and experience «must be given high epistemic value, since it is only in clinical situations that different types of evidence can be evaluated as a whole.» Anjum et al (2015; 430). In summary, personal experience needs to be located at the centre of any medical model, a model which shall be conscious the practice lacks adequate tools for handling the complexity of individuals, illnesses and evidences, and that shall avoid reductionism to a single method because of this.

#### . *Closure*

Running forward to a pluralistic interpretation of the diagnostic performance, the main features of the practice have been defined as a

response to the contemporary conditions that modern medicine is establishing: (1) favouring personalisation by relocating patients's situation at the centre of clinical care, (2) accounting for patient proximity and interpersonal care as two pragmatic keys towards a more empathetic physician-patient relationship, and (3) assessing the intricacies of clinical classifications as situated confluences of kinds, socially elicited and decided, affecting patients, symptoms, diseases and healthcare systems.

The proposed framework of features outlines a practice comprised by: (1) the medical usage of language and its validity, (2) the empathy-based pragmatic accounts of such terminology in anamnesis, diagnosis, prognosis and catabasis, (3) the assertions on pathological traits clinicians infer, as (4) the pathological architectures (comparative, statistical, aetiological and epidemiological) that serve for classifying illnesses, symptoms and patients, (5) the common criteria, socially, culturally, and chronologically situated among communities of practitioners, associations and patients, (6) the instrumental experimentation through which clinical tests are applied along with the observational criteria decided for it, (7) the wild and right clinical guesses required to actualise clinical hypothesis and, finally, (8) the commitment to a tailored diagnostic case behaving.

It has been explored how efforts at de-trivialising rigid, mono-causal and categorical diagnostic methods can lead to a more flexible concept of epidiagnostic practices, more profitable to neuropsychiatric needs. By rethinking its multimodal requirements to respond to multifactorial symptomatologies and prognosis, and by adopting pluralistic, contextualised epistemic values to it, the practice's movements towards its optimalism can be more easily assessed, observing community-based decisions, and re-designing previous schemata through error-learning.



# QIII, Chapter §8

## Measurement Strategies: Assessing Pain Self-Judgements & Self-Belief

(In Niche C — Framing Clinical Characterisations )

☛ 353 — 360

—

### Parts

. *Introduction*

#### I — Wide-Range Assessment of Pain Beliefs

- . *Assessment of Beliefs & Attitudes Towards Pain*
- . *Multidimensional Pain Assessment*
- . *The Brief Pain Inventory*
- . *The McGill Pain Questionnaire*
- . *The Nottingham Health Profile*
- . *Assessing through Visual Analog Scales*

#### II — Assessment of Pain-Bearing & Outgrowths

- . *Assessment of Fear & Avoidance*
- . *Assessment of Coping Strategies*
- . *Assessment of Pain Acceptance & Self-Compassion*
- . *Assessing Self-Efficacy or Pain-Induced Degree of Disability & Dysfunctions*
- . *The Pain Disability Index*

#### III — Comorbidities-Oriented Assessment of Pain

- . *Assessment of Anxiety*
- . *Assessment of Depression*
- . *Assessment of Sleep*
- . *Assessment of Mood & Emotions: Multidimensional & Discrete Approaches*
  
- . *Implications*
- . *Broad rather Than Resolution Feeds*
- . *Demanding a Reflective Attitude*
- . *Assessing Self-Beliefs through Contextualised Decision Making*

## *. Introduction*

Clinical diagnostics of pain experiences and outgrowths, reinforced pain, pain-bearing processes, and their consequences for further comorbid scenarios, are subjected in great extent for neuropsychiatric practices to the diagnoser's performing the interpretation of pathological traits (specific symptomatology contextualised to the patient at case) and pathological architectures (socially and scientifically accepted diseases, health complexities, conditions, disorders, etc., instantiated by patients). Such guesses are guided by his or her experience and savvy, estimated through comparison among many similar cases, and involved in case-to-case decision making patterns. In other circumstances, interoperative diagnoses are required, when patients's personal, qualitative introjection and projection are introduced in such guesses and interpretations: normative (measurable) clinical diagnoses are informed by the patients's performance on several tests, analyses, scales and interviews, which are scored, ranked, situated (to nationalities, gender, age, further diseases, etc...), and that shall be validated and accepted by scientific communities in order to function as valuable clinical criteria for diagnostic and prognostic use.

Interpretations extracted from these data, emerged through patients's self-beliefs, self-judgements, and self-narratives about themselves suffering specific symptomatology, must be sharp enough to avoid simplistic readings, which, underestimating intimate self-identification of the patients's experience, can lead to assessment errors, inefficient prognosis, and wrong treatment or the lack of it (Chou & Shekelle 2010), ignoring deeper dysfunctions, dimensional niches accommodating further pathological traits, or comorbid complications not well evidenced. This said, interoperative normative diagnostic processes involving patients's decisions show numerous leading major aspects to future enhanced diagnostic

practices (Cf. QIV for results and conclusions of this thesis), including trust, interpersonal behaviour, standardisation and contrast plus case-to-case decision making protocols, personalised attentive care, and prognostic tracking over multifactorial niches of stressors increasing morbidity, both co- and multimorbidity risks (Cf. QIII, §5-7).

Social, interpersonal, economic, environmental, dietetic factors are getting progressively significant for searching, identifying and tracking pathologies in these co- and multimorbidity settings, where heterogeneous and complex assessment may need to follow patients's life performance and day-to-day habits, impotence, worry and their narrative discourse on their pain experiences and implications. Multifactorial assessment is in great advantage to this regard. Modern approaches to multifactorialisation of diagnostic practices take this issue back to metadiagnostic values (Kens & Turk 1983), key values that must be extracted through patient exploration, analysed, and contrasted with epicritic information, stored as epidemiological and statistical standard values that could offer a hint for an acute assessment to be made. Such clinical actions that serve for obtaining relevant subjective information about the patient from the patient; for examining multiple plausible factors in search of stressor niches and dimensional characterisers of pathological traits; and for inferring a probable prognostic and initiating treatment, or starting caring medicine protocols if needed, involve all 'measurement strategies': activities that deal with being informed by trustworthy knowledge through a tool measuring patients's beliefs, inclinations and feelings upon their own life in pain, being able to analyse data and to extract compared key values to contrast them with standardised, socialised, contextualised epidemiological values, and being able to make decisions about the clinical status of a patient given such comprehensible information.

The present chapter navigates the main diagnostic tools for assessing beliefs and judgements on pain experiences, outgrowths, pain-bearing processes and plausible comorbid complications. Three main clusters have been developed for accounting pathological trait specifications, a 3-fold cluster frame that gathers a total of 15 topics facing measurement strategies challenges. Topics by no means exhaust any list of measurement tools, however can be presented as a guide to generally reviewed, in-use, major utilities in the field. The clusters proposed are I, 'Wide-Range Assessment of Pain Beliefs'; II, 'Assessment of Pain Bearing & Outgrowths'; and III, 'Comorbidities-Oriented Assessment of Pain'. Clusters can be understood as three steps in a multifactorial characterisation. The following lines summarise them: Part I approaches the main tools for measuring neuropsychiatric pain-specific traits in different clinical circumstances (topics are: Beliefs & Attitudes Towards Pain, Multidimensional Pain Assessment, Brief Pain Inventory, McGill Pain Questionnaire, Nottingham Health Profile, Visual Analog Scales). Part II exposes some of the main tools in use for measuring pain display, consequences, coping processes and dysfunctionality values (topics are: Pain Acceptance, Coping Strategies, Fear & Avoidance, Self-Efficacy/Pain-Induced Degree of Disability & Dysfunctions, Pain Disability Index). Part III faces challenges in comorbidity scenarios, and describes some of the main diagnostic tools that may be used for accessing the prognostic neuropsychiatric factors epidemiologically associated with dysfunctions derived or co-causing pathologies (topics are: Anxiety, Depression, Sleep, Multidimensional Mood & Discrete Emotions).

It is a pragmatic utility hoped by the present chapter that this cluster frame could help physicians in reviewing and practicing a 3-fold strategy for measuring pain complex diagnostics: 1st, by identifying the pains that are self-believed by the patient to be bearing, their

qualities, body topic regionalities, acuteness, etc.; 2nd, by inspecting the dysfunctionalities that pain-bearing processes introduce in patients quality of life; and 3rd, by searching for probable further pathological traits gathered around main signature diseases, enabling thus a multifactorial prognosis. The theoretical and methodological background for such cluster frame can be found in QII, §1 and QIII, §5-6 of this thesis (the epidiagnostic proposal). Conclusions report a stimulating view on the contemporary challenges that measurement strategies introduce into the scene, regarding current inefficacies of interoperative, normative diagnostic tools, mainly problems affecting efficiency, interaction, performance and progress accommodating 21st-century technology. Three ideas are presented to face such challenges from a Cognitive Ergonomics perspective in the hope that future lines of research would get involved in the prosecution of a better understanding of patients's experiences and difficulties, and the clinical practice and work that enhances such comprehension.

#### I — *Wide-Range Assessment of Pain Beliefs*

The first cluster concerns the challenges that diagnosers face regarding pain-focused quality traits, their extraction from the patient's context of belief and self-judgement, comparison, contrast to standards, and implementation into diagnostic account as valid criteria to inform about plausible decisions, which interact (interoperate) with the patient in several domains, from clear identification of symptoms, ascription of trusted categorical and dimensional niches of stressors in the patient's ambiance, attribution of certain diseases from socially and scientifically accepted pathological classifications (Cf. QIII, §5-6), initiation of treatment, therapy or care assistance, and to the prosecution of prognostic values for tracking further pathologies. After performing such work, the

whole process would constitute a fair epidemiological characterisation.

Cluster one informs about the major tools approaching a 1st step in such characterisation: pathological exploration.

*. Assessment of Beliefs & Attitudes Towards Pain*

Beliefs and self-judgements upon a felt pain surf the main characterisations about preliminary quality traits on pain: these scenarios define and get implied by patients's arriving to their own suffering by informing about how they understand and conceive of their own experiences. Pain beliefs focus on such experiences and narrate them, exhibiting them and their believed causes through attitudes towards pain events, disabilities, and individual, familiar, scholar, laboural, economic consequences of having themselves bearing such pains. Pain beliefs do not solely apply to personal (felt) and interpersonal (consequently suffered by others) barriers developed in pain-bearing circumstances (Ward et al 1993), but also to pain acceptance and chronographic details, information which is believed by patients and displayed towards actions that can or cannot be undertaken due to feeling acute pain, a pain reinforcing process, or a comorbidity reflecting behavioural impotence (Thompson & McCracken 2011; Strong, Ashton & Chant 1992; Edwards 1957).

In order to facilitate attitudinal-and-beliefs-based measurement, some tools have been designed to explore emotional influence on pain and its clinical signature. The Survey of Pain Attitudes (Jensen et al 1994; 2003; 2007) is one of the major instruments in use indicated for such an endeavour: it helps patients and physicians to extract information on pain qualitative traits, medication intake, attentional, caring and help barriers, along interpersonal and disability focuses summarising dysfunctionalities and stressor niches. The Survey of Pain Attitudes

proposes 5 degrees of truth (from 0, 'completely false'; to 4, 'completely true'). In its brief scale (Tait & Chibnail 1997) pain beliefs are arranged through 7 common domains: 'solicitude' (interpersonal help and need, involving family members, friends, etc.); 'emotion' (affecting the pain in intensity or reinforcing other pathological traits related to mood and affection); 'medical assistance' (the degree of validity attached to healthcare instruments and therapeutical aid); 'control' (ability, disposition and willingness to cope with pain); 'physical harm' (avoidance, fear and introjection, especially in exercising); 'disability' (functional inability); and 'medication' (substance use/abuse and the degree of help they provide). The survey attunes to each patient and offers a general schema for characterising basic, straightforward, immediate clinical data, that may be useful for further analyses.

*. Multidimensional Pain Assessment*

One feature recognised by many modern theorising trends in the field is the given significance to multidimensional approaches. This line of thought flourished in the 70's with the emergence of metadiagnostic values and niche-oriented diagnosis. Diagnostic dimensions —to the epistemological extent of this thesis as reviewed in QII, §1— are considered niches, ecologically implied areas of development and growth of stressors, material, pathological, psychological and social agents that aggravate the suffering circumstance of an organism. In the 80's, a well known tool was designed to review and detail the multidimensional facets pain manifest in patients, the West Haven-Yale Multidimensional Pain Inventory (Kerns, Turk & Rudy 1985), later the Multidimensional Pain Inventory (Rudy 1989), considering the implications that the Control Gate Theory was introducing to the understanding of pain experiences (Melzack & Casey 1968): pain was theorised to refer at least to three exhibitions: sensory-discriminative,

affective-motivational and cognitive-evaluative features. The overall social, interpersonal, laboural, friendship, familiar perception of the patient in a pain-bearing/reinforced situation is a priority to measure, information which is also considered in the eyes of important persons to the patient's living environment: this content explores relational bonds, mood, negative emotional habits and character, care-taking, distractive and attentional coping strategies, along with physical dysfunctions. For such reason, this scale is considered a predictor of interference in chronic pain outcomes (Dworkin et al 2005). With a similar aim, an alternative instrument, the Oswestry Scale (Turk & Rudy 1986; Turk et al 1998), also considers patient-relatives interoperability.

The West Haven–Yale Multidimensional Pain Inventory informs about several traits of patients's pain-based emotions, experiential, developmental qualities, including the proper pain-bearing process and the interpersonal actions and decisions enabled as coping strategies to face with it. In this sense, the scale shares a biopsychosocial perspective (Turk & Monarch 2002). In order to assess projectional and caring circumstances, the inventory introduces the concept of a 'significant other', a person to whom the patient relates as feeling the closest relationship in his or her emotional ambiance (such person being a housemate/roommate, partner, spouse, parent, son/child, other relative, neighbour or friend). The analysis is answered through 7 possible degrees of severity in relation to each question (from 0 to 6), consisting of 3 sets (A, with 20 items; B, with 14; and C, with 18), reporting A, the degree and quality in which pain affects the life of the patient, how it changes during time and how worried due to his or her pain-bearing context the patient feels; B, reporting how this 'significant other' treats, responds and cares about the patient and his or her pain-bearing circumstance, involving emotional attitudes projected towards the context

of the patient, help at home/work/other duties, activities for alleviating pain, distraction, entertainment, etc.; and C, listing day-to-day activities and requirements that show how self-efficient the patient considers him or herself due to felt pain, exposing possible disabilities and dysfunctions.

Some limitations and challenges have been presented to the West Haven–Yale Multidimensional Pain Inventory (Broderic, Junhaenel & Turk 2004), especially informing about the spontaneity and arbitrariousness of patients's responses. This critique has been exposed frequently too for many scales and inventories, and is mainly agreed by the present article due to the consideration that actual interoperability is not clearly respected by such analyses: as patients are not offered an open space to discuss, re-think, resolve, mediate and decide on past self-narrative possibilities through reflection, but in its stead are offered minimalistic impressions regarding their immediate memorabilia, answers involve a generous probability to be resolved accidentally, spontaneously and biased by short-lapse requirements.

#### . *The Brief Pain Inventory*

The Brief Pain Inventory has been proposed as a core measurement of pain interference: a tool for measuring the severity and extension that pain-bearing and pain reinforcing processes introduce to the patients's life and day-to-day actions, mainly applied to cancer pain assessment (Anderson et al 1995; 2001; Atkinson et al 2011). Both, 'affectivity' (emotional, sentimental projection) and 'activity' (daily agency requirements), focusing developments and performance, conform the general traits to measure. Two key values that are assessed by the scale are 'severity values' (qualitative degree of pain feeling) and 'functionality values' (informing about physical, interpersonal, further pathological dysfunctions, etc.). Regionalisation of pain

long-term effects, placement of pain irradiation body spots, medication and relief (lasting between one day to one week) are also accomplished rates.

The questionnaire includes 9 common sections, first discerning between episodic pain, generally circumstantial, or major/chronified pain (which can be due to enlarged pain reinforcement processes). It offers a visual analog of the human body to be used as a target doll for specifying pain locations. It approaches intensity (highest and lowest scenarios in separated rating scales), assiduity-continuity, medications used/misused, their effects in relief (in percentages), and a final section informing about pain interfering with the following values: 'general activity', 'mood', 'walk', 'laboural and housework issues', 'interpersonal relationships', 'sleep' and 'life quality/enjoyment' (Cleeland & Ryan 1994). The arithmetic mean of the chosen items is to be used as a trusted measurement of pain interference in patients's life. The Brief Pain Inventory is usually applied for extracting and contrasting pain behavioural patterns (patient behaviour measurement strategies) and clinical impedance (activity struggle) in self-assistance, movement and routine work execution (Wu et al 2010). Additional niches, like 'manual/cooking/laundry abilities', 'housekeeping', 'self-maintenance/care', 'social intercourses', 'sexual interference', 'food intake', etc., have been also implemented in extended scales based on this inventory (Jensen et al 2002).

#### . *The McGill Pain Questionnaire*

The McGill Questionnaire is one of the most applied pain-quality-centered scales used in general medicine, in-hospital pain units, psychiatric diagnosis and cancer medicine. Developed by Melzack and colleagues at McGill University (Melzack & Torgerson 1971; Melzack 1975; Melzack 1987; a review in Waldman 2009) focusing the theoretical framework

introduced by the Gate Control Theory in its multidimensional contour (Cf. QIII, §2 of this thesis; Wall 1960; Melzack 1961; Melzack & Wall 1962; 1965; Melzack & Casey 1968), it has been mainly put in practice for understanding pain self-judgement through patients's responding to pain qualitative traits, in contrast to mono-dimensional scales —as for example visual analog scales or numerical ratings (Cf. Huskisson 1983).

Through 4 general areas ('qualitative intensity', 'severity', 'location-periodicity', and 'collateral symptomatology along plausible comorbidities'), the McGill Questionnaire informs researchers about how pain is being felt and feared, adjectivised and verbalised, beared and coped with, and spotted throughout different multisite regions of the body. Multiple research and diagnostic requirements get answered by this scale as its flexibility presents a well suited person-centered groups of topics that can be addressed through several standpoints, rethought and recognised with time. The full-length version of this scale overviews an introductory area of semantic analysis with 7 modules divided in 20 sets of adjectives defining pain qualitative traits (1, 'sensory components of pain', through adjectives in sets 1-10; 2, 'affective-emotional components of pain', through adjectives in sets 11-15; 3, 'evaluative terms', through adjectives in set 16; 4, 'miscellaneous sensory terms', through adjectives in sets 17-19; 5, 'miscellaneous affective-evaluative terms', through adjectives in set 20; 5, 'total of miscellaneous terms', through adjectives in sets 17-20; and 6, the total score, through adjectives in sets 1-20). These modules conform the first area: 'present pain intensity'. A second area informs about severity through 6 possible options (from 0, 'no pain'; to 5, 'excruciating pain'): this section is also targeted as the 'pain rating index'. A third area locates the regions of the body felt in pain with a body-figure visual aid, an analog that helps to include specifications, like chronicity-enlargement traits

(‘constant’, ‘periodic’, or ‘brief’). The final fourth area informs about comorbid implications through accompanying symptomatology, including psychosomatic collateral effects, sleep, activity and food intake dimensions. Analgesic intake, dose and intentional usages are also met, and spaces for commentaries are present in most of the questions. The McGill Questionnaire can be performed in 15-20 minutes, it is a personalised, contextualised measurement, and has been validated as one of the most efficient instruments for exploring pain diagnostic and evaluative multidimensionalities in pain medicine (as far as it is directed to executive, communicative patients).

#### . *The Nottingham Health Profile*

The Nottingham Health Profile (Hunt, McKenna & McEwan 1980; Hunt, McEwan & McKenna 1985; Erdman 1993; Essink-Bot et al 1997) is a simplified, multidimensional, patient-oriented scale of much use in Europe. It ranges answers and commentary replies through patients’s beliefs on the severity of their pain, pain-bearing/reinforcement processes, and how those affect to their overall life quality. Some studies maintain this profile appears a sensitive tool for understanding treatment performance (Klevsgård et al 2002) and its validity has reaffirmed competent in comparison to other alternative short form profiling strategies (Prieto et al 1997; Meyer-Rosberg et al 2001). The scale ranks a percentile short numerical answer to topic-closed questions (from 0, ‘no problem’; to 100, ‘absolutely not optimal’), addressing each item included in the profile, which is divided in two major parts (Jans et al 1999). The first part introduces 38 items clustered in 6 domains (these are ‘physical mobility’, ‘ostensive pain’, ‘sleep quality and problems’, ‘activeness/energy’, ‘social inclusion/isolation’, and ‘sentimental/emotional reactivity’). The second part, additional, includes supplementary items

that develop a multidimensional extension of the analysis, consisting of 7 life aspects (including ‘employment’, ‘housekeeping’, ‘socialisation’, ‘personal relationships’, ‘sexual life’, ‘interests’, and ‘use of holidays’): for each of these topics patients are required to report the degree of impedance or effect introduced by their pain-related conditions.

#### . *Assessing through Visual Analog Scales*

Visual Analog Scales are simple, easy reproducible, responsive instruments used for helping in the assessment of pain-emergent mood, and in pain-location identification when the human body is the object of the analogy. Visual analog scales are commonly applied to children, elderly people, and dysexecutive, untalkative or incommunicative patients (Miró et al 2005; Price et al 1983; Li, Puntillo & Miaskowski 2008). One of the most acknowledged instruments is the Face-Line Visual Analog Scale, which presents a card split in two parts: the top one is printed with two faces along the extremes of a 10 cm line, the left end shows a smiling face above the expression ‘no pain’, the right end shows a bitter-sad face along the expression ‘worst pain ever’. The other part is only printed below with another 10 cm line in a score from 0 to 10 in parallel position to the previous line, folded up in order not to show numerical marks to the patient. When the patient marks the face-containing line in a certain extent of its length, the second part can be unfolded and cross-compared with the first one by the analyst, extracting a simple quantitative score. As an alternative presentation to the folding option, it can also be double-printed. This scale admitted some criticism (Loomes, Jones-Lee & Robinson 1994; Robinson, Loomes & Jones-Lee 2001), as it is said to lack a core theoretical foundation (Johannesson, Jonsson & Karlsson 1996), and does not present multiple choice, unable to trace strength of decision (Brazier et al 1999). With it there also exists



a problem of uncertainty in dysexecutive patients, for whom self-assessment of pain may be disabled due to interference in major limbocortical processes, relating emotional arousal with mnemonic and attitudinal behaviour. Other uses are surgical: patients can point out the scale by gaze. The Wong-Baker Faces Scale is a derivation of the Face-Line Visual Analog Scale, generally applied in paediatric pain assessment (Hockenberry & Wilson 2009). It substitutes the line by 6 faces in transformation along 6 expressions informing of pain and pain-bearing related contents in the following order: 1, 'no hurt' (happy face); 2, 'hurts a little bit' (smiling face); 3, 'hurts little more' (hieratic face); 4, 'hurts even more' (sad-unpleasant face); 5, 'hurts a whole lot' (rueful-dismayed face); and 6, 'hurts worst' (constricted-crying face). Below the faces is common to appear a 0-10 dotted scale with numerical assistance for the option or double options of the patient.

The Facial Affective Scale (McGrath et al 1996) is another alternative to the Wong-Baker Scale, making use of 9 different faces arranged to include risk/fear/avoidance parameters among a 'happy face' and an 'utterly crying face'. The Coloured Analogue Scale (McGrath et al 2001) is another different visual analog measurement for paediatric, surgical and geriatric use, in which patients are asked to point out with their finger the level of pain being suffered in a reddish-coloured rectangular plaque. The left extreme is shortened, presenting a white blurry fade out, growing strong to a darker-burgundy colour in the right end, slightly wider in form. This alternative is especially appropriate for psychiatric dysexecutive and incommunicative patients.

## II — *Assessment of Pain-Bearing & Outgrowths*

The second cluster concerns the challenges that diagnosers face regarding the characteri-

sation of their patients's pain-bearing processes, coping strategies, fear-avoidance schemata, lived pain and life-in pain acceptance, and the outgrowth of this whole picture, dysfunctionality values. The extraction of key values is usually enabled by drawing a contour of patients's self-judgement, interoperating with them by helping patients and their proximal context (family, friends, co-workers, etc.) to explore the implications of their lived pain, how they mediate and modulate it, how committed they are to live a life with a reinforced pain, and how such decisions make them able/unable to undertake other activities, social roles, being interpersonally relevant and efficient. Cluster two informs about the major tools approaching a 2nd step in a multifactorial characterisation: exploration of life implications.

### *. Assessment of Fear & Avoidance*

Fear is a central key factor in the development of pain reinforcement life-damaging experiences. Fear of pain events, of pain-believed causes, of situations that generally associate with painful stress is generally reported by populations who suffer clinical pain-bearing (Lundberg, Styf & Carlsson 2004). Avoidance is a defensive characteristic in the patients's behavioural-decision agency: to avoid circumstances that probably will produce harmful sensations, or that will compromise a roughly maintained health balance, can be a constant anxious state of judgment over future neglectable situations that may limit in great extent the activities and social interactions of pain-bearers. Fear-avoidance beliefs, thus, are in need of a trustful measurement strategy. Two of the most spread tools are the Tampa Scale of Kinesiophobia (Miller et al 1991) and the Fear-Avoidance Beliefs Questionnaire (Waddell et al 1993), the latter being specific to back pain, however the methodological protocol can be substituted easily to generate other wide/specific neuropsychiatric

life quality evaluative measurement strategies. Some works have validated a short form of the Tampa Scale of Kinesiophobia (11 item) with 2 major markers (Cf. Roelofs et al 2007, international; Bunketorp et al 2005, Swedish version): 1, 'somatic focus' (ostensive physical pain); and 2, 'avoidance of activities' (behavioural, decision making, and pain control markers). The goal of this instrument is to serve as a general reading of patient's functionality. The Tampa scale measures fear and avoidance values through 4 degrees of agreement with 17 statements (from 1, 'strongly disagree; to 4, 'strongly agree'). Patients resolve their attitudes towards avoiding pain-provoking situations by reflecting on the significance of their pain reinforcement processes. Of special attention are those activities that appear common to general non-pain-bearing population, and that help to reinforce chronic pain, or that involve further pathologies if anxiety-driven strategies are maintained. The Tampa questionnaire uses inverted thinking to contrast scores: eg, 'beliefs of being exposed to plausible self-injuries if exercising' are contrasted by informing further inverted scores, like questions about 'overcoming pain by doing exercise and participating in sports'.

#### *. Assessment of Coping Strategies*

Coping strategies engaged by patients for facing a life towards pain experiences, acute or sustained, chronic or spontaneous, are in need of trustful measurement strategies. There has been exposed a conflicting problem in framing how coping strategies can be standardised, socialised, contextualised or case-to-case abstracted, as their clinical transformation and adaptation to clinical criteria for individual cases will be in difficult situation compensating non-transferrable qualities from person to person, thus, schemata on this sort of attempts have been noticed to be worrisome (Benyon et al 2010). There are different tools to measure how

patients react and adapt their own lived pain and their life-in pain. The Coping Strategies Questionnaire (Robinson et al 1997; Rosenstiel and Keefe 1983; Monticone et al 2014) assesses in major tenor patients's cognitive strategies; the Vanderbilt Pain Management Inventory (Brown and Nicassio 1987) measures active and passive pain-coping strategies (decided and undecided strategies of pain-bearing populations to face pain experiences); the Chronic Pain Coping Inventory (Jensen et al 1995; Jensen, Turner & Romano 2001; Jensen et al 2003) focuses behavioral strategies, including postural and physical comfort willingness (sleep, sports, calisthenics, interpersonal value exchange, etc.). Another tool, Daily Diaries (Lefebvre and Keefe 2002) can be helpful in social experimentation for extended research to enable patients an actual comprehensive reflection on their day-to-day interpretations of coping with pain.

As an usual instrument, the Coping Strategies Questionnaire has been influential in its theorisation of 4 factors that inform about dimensional axes building coping strategies for chronic pain in particular, and sustained life-breaking pain in general (Harland & Georgieff 2003). This has the potential to extend the patients's feed, informing about lateral pathologies and comorbidities, especially those of psychiatric and interpersonal colour. These factors gather 1, 'catastrophising attitudes' (involving also depressive traits, sadness and mood shifts due to pain reinforcement processes); 2, 'diverting attention' (involving attentional distraction and intentional diverted attention for alleviating or reconducting pain, from onset to decay of intensity); 3, 'reinterpreting sensation' (attitudinal shifts introducing distance towards pain, imagining different contexts, re-associating pain with other sensations and ignoring pain); and 4, 'cognitive decisions and assertions' (involving verbalisation of helpful statements, self-judgment orienting personal capability, situation control, and ignoring strategies). A note on the

limitations of this tool comes with clear psychiatric estimations (given values of depression, fear and anxiety, etc.) that may be reported using it, however are not recommended to be used as key values: multifactorial analyses present in wider/specific psychiatric scales would be used preferentially to measure the incidence of such features in a much proper manner (Wilson et al 2001).

*. Assessment of Pain Acceptance  
& Self-Compassion*

The psychiatric instruments regarding patients's pain acceptance, along with the therapeutically-oriented value extractions, cover numerous facets for measuring pain-bearing processes, coping strategies, beliefs and self-judgement efficiency in pain reinforced populations (McCracken 1998; McCracken & Samuel 2007). Measuring the acceptance of an experience affecting as deep as a sustained pain can affect life quality, is also a measurement of self-trust, self-implication, and self-evaluation of personal and interpersonal decisions on different events, events that require the patients to attitudinally face life, or events that rather force them to avoid living (McCracken & Vowles 2008). In this sense, lived pain and life-in pain acceptance strategies can be taken to offer clinical value in understanding patients's behaviour, adaptation, and decision making protocols within a reinforced pain circumstance (McCracken & Eccleston 2003; McCracken, Vowles & Eccleston 2004; Viane et al 2003). Therapeutically, acceptance requires to some extent a disposition to bear pain (a moral implication and commitment that suffering pain and living along with it introduces more value than the other way around). Psychological flexibility is also a generally referred term (Vowles et al 2009; Veehof et al 2011) informing about the necessity to ignore fear of probable pain events, which are seen in return as self-beliefs over-sensitising

biological pain assessment, mediating through stress, victimism, overcompensation and anxiety the very experience of pain felt (McCracken & Yang 2006).

Acceptance measurement strategies generally incorporate instruments with two components (McCracken & Vowles 2008; McCracken, Vowles & Eccleston 2004): 1, 'pursuit of life', being able to participate in habitual activities regardless being in pain; and 2, a trusted recognition that pain avoidance strategies and control intentions do not facilitate any therapeutical gain. The Pain Acceptance Questionnaire (McCracken 1998) was first introduced for assessing chronified pain (enlarged reinforced pain): the body of statements is evaluated by 7 degrees of truth (from 0, 'never true'; to 6, 'always true'). The scale associates 20 items that involve two major domains, 'engagement in activities', and 'pain willingness' (the latter introducing reversed items). Statements value from 'life quality despite the pain', 'controlling dispositions', 'interference in undertaking responsibilities', to 'attention' and 'worrysome attitudes'. In the same area of interest, measurement of pain willingness and patients's engagement in personal and interpersonal, familiar, laboural, recreational, etc., activities are another two critical values to involve in clinical criteria for understanding pain experience qualitative traits impairing patients (Vowles et al 2008).

Exploring the topic of acceptance, not over pain as such but over the whole person suffering the pain-reinforcing circumstance, self-judgement theory has afforded the concept of self-compassion. P Gilbert's model of social mentality (Gilbert 2006; Gilbert & Procter 2006) exposes how the potential for compassion evolves the care-giving feature engaged in behavioural and neural systems of interpersonal attachment, which require enaction of different cognitive and metacognitive processes, involving motivation, reward, future-planning, expectations (Cf. neurological comorbid im-

plications of fear and avoidance attitudinal and attentional schemata, QIII, §6). In a more interoperative perspective, K Neff (2003a; 2003b) observes self-compassion as integrating 3 major tensions: 1, self-kindness—self-judgment (tendency of believing oneself with care or harshly); 2, common humanity— isolation (the idea that imperfection is not to be necessarily reproachable, that failure occurs, that guilty and shame do not help in facilitating acceptance of one's self); and 3, mindfulness—over-identification (awareness of the positive, constructive, balancing aspects of the present circumstance instead of destructive or uncomfortable features of the circumstance).

*. Assessing Self-Efficacy or Pain-Induced Degree of Disability & Dysfunctions*

Self-efficacy is a clinical notion: the concept gathers those patients's self-beliefs on daily task resolution, acceptance of challenging events, interpersonal endeavours and general ability to perform day-to-day given duties and exercises regardless lived pain (Bandura 1977; 1989; Nicholas 2007; Asghari & Nicholas 2009). The usual tool is the Self-Efficacy Questionnaire, with a common time of administration of 10 minutes (Miles et al 2011). The scale's general versions inform the clinical feed through 7 degrees of confidence (from 0, 'not at all confident'; to 6, 'completely confident'). The scale measures the following 10 items, in relation to 'enjoyment regardless lived pain', 'housekeeping', 'social and interpersonal intercourses', 'coping attitudes and strategies', 'work and laboural requirements and performance', 'hobbies', 'medication' (use/misuse/abuse), 'goals in life', 'decided/undecided lifestyle', and 'general activity' (exercises, recreation). An interesting key value association is that coping strategies corresponding to dysfunctions/inabilities reported through self-efficacy factors can be used to predict vulnerability to comorbidities (Benyon et al 2010). Mediation

between disability and sustained pain has also been explored through self-efficacy concepts (Arnstein 2000).

*. The Pain Disability Index*

The Pain Disability Index (Tait et al 1987; Chibnall & Tait 1994) is used as a tool for understanding the extent of interference in patients's life (wide spectrum: family, work, sexual life, studies, economy, etc.) due to pain-bearing/reinforcing processes. The index provides analysts with standards from which to begin contrast strategies with patient case data, especially in chronified (enlarged reinforcement) pain circumstances (Pollard 1984), where prognosis protocols and continuous revisions usually extend for several years.

The scale measures how pain-bearing and coping strategies (generally negative strategies, fear/avoidance for example) prevent patients from undertaking daily activities, required duties, resolving familiar, laboural, personal responsibilities, and achieving important life goals. Interoperationally, patients's feed inform about the overall perceived impact that pain deploys onto their life quality, scoring 11 degrees of disability (from 0, 'no disability'; to 10, 'worst disability'). In order to assess perceived disabilities 7 items are designed: 'family and home responsibilities', 'recreation' (including hobbies and sports), 'social activity' (friends, co-workers, etc.), 'laboural activity' (work, housework or volunteering are too included), 'sexual life and behaviour' (quality and frequency), 'self-care' (personal maintenance and independence; general self-efficacy), and 'life support activity' (basic biological behaviours: nutrition, sleep, etc.). The minimal index will rate 0, maximal 70. Related to such index number, the scale addresses three general classes of disability (mild, moderate, severe), characterising the patient's degree of behavioural dysfunctionality due to pain-bearing/reinforcement processes. These

items inform about interference in executive living possibilities, thus conceiving of disability as an incidence factor (Tait, Chibnall & Krause 1990; Chibnall & Tait 1994).

Other two major measurement strategies for approaching life quality boundaries due to pain-bearing processes are the Oswestry Disability Questionnaire (Fairbank et al 1980), and the Waddell Disability Index (Waddell & Main 1984), which include assessment of functional restrictions (eg, walking, sitting, standing, lifting, etc.), and interferences within the social role the patient performs (interpersonally-oriented scale: social roles, familiar roles, sexual roles, laboural roles, etc.).

### III — *Comorbidities-Oriented Assessment of Pain*

The third cluster gathers strategies for facing major clinical challenges in characterising key values for the identification of comorbidity scenarios. This part will describe the major diagnostic tools that may be used for accessing the prognostic neuropsychiatric factors epidemiologically associated with dysfunctions derived, or helping to cause, further problems within the pathological ambiance of a patient due to pain-bearing/reinforcement processes. The extraction of such values generally departs from the patients's self-judgement on their performance and attitudes towards 1st, 2nd and 3rd order activities (1st order activities would gather agency towards the very person and the felt pain; 2nd order activities would be directed to interpersonal situations, responsibilities, ability to communicate and enjoy social intercourses, etc.; and 3rd order activities would recall future, expected, desired decisions, options and wanted goals in life that may not be fulfilled due to their lived pain or their life-in pain). Interoperation is crucial to assessing self-judgement on fear-anxious schemata, depressive traits, sleep/rest problems and mood shifting. Cluster three

informs about the major tools approaching a 3rd step in a multifactorial characterisation: exploration of comorbid pathological traits.

#### *. Assessment of Anxiety*

The State-Trait Anxiety Inventory (Spielberger et al 1983) was designed to incorporate cross-cultural variables, social and personal values, and emotional projection styles into the diagnostic process, and holds a wide literature and experimental research background (Spielberg 1989; Spielberg, Gorsuch & Lushene 1970; 1982; Spielberg & Díaz Reguero 1976; 1983; 1986; Spielberg, Díaz Reguero & Strelau 1990). This inventory has been broadly used in the clinical and research-oriented understanding of patients's anxious traits and psychiatric anxiety pictures accompanying reinforced pain, especially designed for intervening in differential diagnosis for dismay symptomatology (sad traits in mood and character, depressivoid dispositions, stress-melancholic attitudes, etc.). The scale is configured by 40 items for trait and state anxiety characterisations, involving positive and negative narratives, built up in 2 sets of statements: Form Y-1 and Form Y-2. Form Y-1 presents statements 1 to 20, selected as standard beliefs generally occurring in people suffering anxious/depressive-driven situations. Some of these statements are: 'I feel calm', 'I feel strained', 'I feel upset', 'I feel satisfied', 'I feel nervous', 'I feel indecisive', etc. Questions are answered as how the patient feels in the moment of application. Form Y-2 introduces statements 21 to 40, which are answered as how the patient feels in a usual basis. Some of these statements are: 'I feel nervous and relentless', 'I feel rested', 'I feel secure', 'I am content', 'I worry too much over something that really does not matter', 'I am a steady person', etc. Each item is assessed by the patient through 4 possible answers: in Form Y-1 the rank goes from 1, 'not at all', to 4, 'very much so'. In Form Y-2, the rank goes from 1, 'al-

most never', to 4, 'almost always'. Methodically, the clinical assessment is inverted, associating ranged weights to the previous patient's marked answers. Weights associated in Form Y-1 range from weight 4 for answer 'not at all', to 'very much so' with weight 1. In Form Y-2, the range goes from 'almost never' weighted 4, to 'almost always' weighted 1. Although some authors have proposed this scale as a multifactorial predictive tool for assessing caregivers's distress (in correlation to the anxiety levels exhibited by the patient, also positing difficulties to the support chains enabled for individual pain-bearing populations by healthcare institutions, Cf. Elliott, Shewchuk & Richards 2001), some criticisms on the amount of factors taken into account have been exposed (Suzuki, Tsukamoto & Abe 2000; Hishinuma et al 2000).

Another anxiety-oriented scale for helping diagnostic feasibility is the Beck's Anxiety Inventory (Beck et al 1988), a 21 item self-reported measure of anxiety, similar to the revised Hamilton Anxiety Rating Scale. Items are comprehensible adjectives defining activities, intentions and beliefs, or statements with an extending explanatory aim. These are answered by the patient through a 4 ranked scale of severity (from 0, 'not at all'; to 3, 'severely'/'it bothered me a lot'). The feed focuses on the patients's experiences during their past month, with common symptoms of anxiety. Some of the items included are as follows: 'unsteady', 'nervous', 'wobbliness in legs', 'hands trembling', 'scared', 'faint', 'difficulty in breathing', etc.

The Pain Anxiety Symptoms Scale (McCracken et al 1992) forms a 40 item measuring strategy oriented to inform about pain-related fear-avoidance behaviours, psychosomatic changes, attitudes and beliefs on felt pain and self pain control. There is a newer short form developed with 20 items (McCracken & Dhingra 2002). Some of the items express the following statement structures: 'I cannot think straight when in pain', 'I find it hard to concen-

trate when I feel pain', 'as soon as pain comes on I take medication to reduce it', 'I try to avoid activities that cause pain', 'I find it difficult to calm my body down after periods of pain', etc.

#### . *Assessment of Depression*

Along with anxiety, depression is one of the most concurrent pathological architectures and character traits shifting protagonists of diagnoses addressed to pain-bearing population (Asmundson & Katz 2009; McWilliams, Goodwin & Cox 2004). There exists a diverse variety of instruments to identify, characterise, differentiate and track depressive scenarios. The Beck's Depression Inventory (Beck et al 1961; Beck, Steer & Brown 1996), the Emotional Distress-Depression Item Bank (de Gagné, Mikail & D'Eon 1995), the Major Depression Inventory (Beck et al 2001), the Centre for Epidemiologic Studies-Depression Scale (Radloff 1977), the Zung Self-Rating Depression Scale (Zung 1965), and a slightly oriented to comorbidity-based diagnosis form of scale in the Burn's Depression Checklist (Burn 2002) configure the usual options, which are also available from originals for children (Helsel & Matson 1984) and adolescent populations (Hodges & Craighead 1990).

Although the Beck's Depression Inventory is withal subject of commonly evidenced methodological problems present in self-reported inventories —mainly, the danger of exaggeration or minimisation by the responding patient (Bowling, 2005)—, it is still the most common instrument. It composes a multiple-choice self-reported scale with 21 items, to which patients are asked to indicate their degree of identification using 4 given neurotypical statements (in sum from 0 to 3). The 21 features are the following: 'sadness', 'discourage', 'failure', 'satisfaction out of things the patient usually does', 'guiltiness', 'feeling of being punished', 'self-addressed disappointment', 'self-judgement of

blame, 'self-injury or desires to terminate one's life', 'frequency of cry', 'irritation', 'interpersonal interest', 'personal image decay/ugliness', 'laboural performance', 'sleep/rest', 'tiredness', 'appetite changes', 'weight loss', 'state of worry', and 'sexual life'. Results flow through two extremes: when scores sum over 40 (from a total of  $21 \times 3 = 63$ ) assessment is to inform 'extreme depressive disorders', yet when scores sum around 10, the result is considered an 'ordinary non-depressive neurotype'.

The Burn's Depression Checklist (version of 1984) consisted of 15 questions: the upgraded version of 1996 nowadays has increased to 25 questions. The chronotypical context for approaching answers is past week to present day, scoring depressive bearing from 0 to 4 (ranging from 'not at all' to 'extremely'). The Hamilton Rating Scale for Depression (Hamilton 1980) is usually applied for assessing recovery through self-beliefs.

The Major Depression Inventory (MDI) was designed by the World Health Organisation to focus mood shifts through a self-reported questionnaire, and has been clinically validated to achieve, or help to assure, ICD/DSM diagnoses. The scale overviews severity of symptomatology (mild, moderate, severe, to major depression), thus, increasing the score would inform about increased severity of depression (Bech et al 2001; Olsen et al 2003). A similar measurement instrument is the Centre for Epidemiological Studies Depression Scale, a 20 item self-reported questionnaire designed to estimate the presence and severity of depressive traits (Fava 1983). Items are ranked in a 4 raked scale (from 0, 'rarely'; to 3, 'most of the time'), from which a total sum is extracted: the score ranges from 0 to 60, and like in the Major Depression Inventory, increase in score informs about increased severity of depressive traits (Radloff & Locke 1977).

Another important scale is the Montgomery-Åsberg Depression Rating Scale, generally used as extended appendix to the Hamilton

Rating Scale for Depression (Montgomery & Åsberg 1979). The questionnaire, scoring from 0 to 27, summarises a personalised symptomatic recount that encircles 'noticeable sadness', 'self-judged sadness', 'personal tension', 'lack of sleep/rest', 'lack of appetite', 'difficulties in concentrating', 'apathy', 'attitudinal lack for acknowledging experiences', 'pessimism in beliefs', and 'suicidal beliefs' (Svanborg & Åsberg 2001).

#### *. Assessment of Sleep*

Patients undergoing a process of pain reinforcement with plausible comorbid instantiations usually report disturbances in sleep time, frequency and quality of rest (Finan, Gooding & Smith 2013). Lack of sleep increases both, evidences for pain reinforcement (Schuh-Hofer et al 2013; Roehrs et al 2006), and of pain reinforcing insomnia (O'Brien 2010), which in sustained circumstances has been studied to prompt long-term personality (reshaping patients' character traits), functioning (mood, attention, irritability), and laboural disabilities (Lallukka et al 2014; Monti & Monti 2007; Busch et al 2012). It is very significant, for these reasons, to warrant an interoperative sleep/rest assessment within the frame of a 3rd step multifactorial or epidiagnostic characterisation.

Two instruments are commonly used in clinical ambiance: the Pittsburgh Sleep Quality Index (Buysse et al 1989; Cole et al 2006; Smith et al 2000), and Personalised Sleep Diaries (Haythornthwaite et al 1991). Both strategies focus comorbid dysfunctionalities reporting how pain interferes with sleep/rest, and how this circumstance aggravates pain and undertaking further activities, in a day-to-day basis (Stacey and Swift 2006). Short scales, like the Epworth Sleepiness Scale (Johns 1991), measuring different kinds of sleep disorders, have been developed and implemented in comorbid-oriented diagnostics as well, especially in relation to narcolepsy. Scale strategies

usually approach qualitative and multifactorial traits interoperationally, from the patients's self-beliefs on the topic.

For instance, the Pittsburgh Sleep Scale measures 7 constituents regarding poor-good sleep qualities in adult population. These include: 1, 'subjective quality of sleep'; 2, 'frequency of sleep time' (latency); 3, 'duration of sleep time'; 4, 'general efficiency of sleep time'; 5, 'disturbances during sleep time' (parasomnias); 6, 'need of medications for initiating/stopping/preventing sleep'; and 7, 'daytime sleep dysfunction' (during the last month). The scale is formed by 9 items answered by choosing among the given statements the appropriate report for the patient's experience of sleep, or in others by specifying a number or by writing the statement. The numbered option is required for items 5 to 8, measured by a 4 ranged scale of periodicity (from 0, 'not during the past month'; 1, 'less than one week'; 2, 'once or twice per week'; 3, 'three or more times per week'). In item 9 ('how would you rate your sleep quality overall?'), the score ranges from 0 ('very good'), to 3 ('very bad'). Some of the questions are as follows: 'when have you usually gone to bed?'; 'how long (in minutes) has it taken to you to fall asleep each night?'; 'how many hours of actual sleep did you get at night?'; or in questions from 5-8: 'during the past month how often have you had trouble sleeping because you... Have pain/ Cannot breathe comfortably/Wake up in the middle of the night or early morning/Have bad dreams?'; etc.

Sleep measurement instruments are useful clinical tools: successful treatment of pain-bearing scenarios can be reflected in sleep/rest improvements.

Specific biological and therapeutical treatment of comorbid insomnia, parasomnias and brain patterns associated with sleep dysfunctions may reduce pain medication, as it is observed to be scored through these same sleep scales (Tompkins et al 2011).

#### *. Assessment of Mood & Emotions: Multidimensional & Discrete Approaches*

Mood is a prominent shifting factor in pain-bearing population, requiring of immediate assessment in search of prognostic values that could help in determining whether the patient presents or not clinical probability for undertaking further pathological pictures or comorbid scenarios in his or her diagnosis. The Profile of Mood States (McNair et al 1971; 1992) informs about the mood that a person may manifest in the moment of application of the test, which scores through a 5 Likert scale (from 0, 'not at all describes me'; to 4 'absolutely describes me'). There are versions for adults (aged 18+) and adolescents (aged 13-18), both long and short versions (from 65 to 35 mood items), and a 40 item model (Grove & Prapa- vassis 1992). The contents of the scale range mood contrast, listed in the following lines for comparison: tense, angry, worn out, unhappy, proud, lively, confused, sad, active, on-edge, grouchy, ashamed, energetic, hopeless, uneasy, restless, unable to concentrate, fatigued, competent, annoyed, discouraged, resentful, nervous, miserable, confident, bitter, exhausted, anxious, helpless, weary, satisfied, bewildered, furious, full of pep, worthless, forgetful, vigorous, uncertain about things, bored, bushed, and embarrassed.

Other cross-questionnaires (evaluating mood, interference and pain-bearing performance and outgrowth) involve assessment for hospitalised patients, like the General Hospital Questionnaire (Cf. the original 60 item version, Goldberg et al 1976), or the Wisconsin Brief Pain Questionnaire (Daut, Cleeland & Flanery 1983), which is a modification of the Brief Pain Inventory contextualised for mood and task performance. Different scales have also been applied to regional niches: eg, the Norwegian Brief Pain Inventory Questionnaire (Klepstad, Håvard & Borchgrevink 2002), the Malay Brief



Pain Inventory Questionnaire (Aisyaturridha, Naing & Nizar 2006), the Greek Brief Pain Inventory (Mystakidou et al 2001), or the Multilingual South African Version of The Wisconsin Brief Pain Questionnaire (Mphahlele, Mitchell & Kameron 2008). The basis for the assessment of mood in any of the previous examples builds variations from a standard, that reports common psychiatric features of pain-bearing and pain reinforcement processes for contextualising experiences thereupon.

Other measurements of emotional self-judgement can be found in widely known psychological and psychiatric scales, including the Multiple Affect Adjective Checklist (Zuckerman, Lubin & Robins 1965), and its revised version, which are used for estimating about hostility vs. positive affectivity traits, anxiety pictures, depressive traits and overall pursue of experiences in life. The scale searches prognostic values in the aim of detecting mood shifting patterns in affection and emotional projectionality. Another mood traits contrasting scale is the Positive & Negative Affect Schedule (Cf. relationship with anger traits in Harmon-Jones & Harmon-Jones 2010).

Along with dimensional and multidimensional approaches—which try to accommodate emotionality in specific niches of diagnostic stressors: dimensions—, discrete approaches to emotions view the phenomenon as a pluralised multifaceted event, full of collateral implications that are also emotional traits linked, attached or arborised from state mood emotionality (well defined emotional phenomena). These discrete emotions, like jealousy, shame, gratitude, envy, compassion, embarrassment, tend to end uninformed in diagnostics, which for the most part focus state well defined emotions and mood measurements. There are some instruments that have been developed to examine these critical however ambiguous, collateral mood projections (McCullogh, Emmons & Tsang 2002; Shiota, Keltner & John 2006; Cohen et al 2011).

The Discrete Emotions Questionnaire (Harmon-Jones, Bastian & Harmon-Jones 2016) is a modern and revised proposal. Several studies composed this scale through social experience research, word listing expressions, and title-descriptive clustering: subjects in different experimental scenarios informed about the ‘emotional banners’ that best describe these collateral emotions perceived in an interview-presentational fashion.

The metacognitive value of this research is implied within the experimental strategy, requiring subjects to make themselves aware of their own feelings, how they would define them, verbalise them, and expose them in a social and interpersonal context, involving the reviewer, who is expected to be able to understand and assess the multiple hues different emotions manifest. Emotions are treated as affective events that can be explored in search of further emotional ‘drop-offs’, or released emotional attitudes accompanying those basic events (ie, clustered intended emotions). The Discrete Emotions Questionnaire makes use of story prompting strategies to evoke personalised events in relation to 7 ‘intended emotions’ (anger, disgust, fear, anxiety, sadness, desire, relaxation). Three studies were performed during the design of the questionnaire. Study 1, contextualising those 7 intended emotions within story themes that subjects wrote in response to the stories the analysers proposed them, identified a good variety of different topics, included as attitudinal characterisations (eg, for anger: ‘blaming other people’, ‘physical harm’, ‘loss’, ‘negative/positive anticipation’, etc.). Different stories were then written by the subjects, and examined, from which topic-contextualised words anchored to the 7 intended emotional themes were extracted and gathered as items for subsequent studies. Those items were listed to achieve other subjects to rate them (ranging 1 to 7) the extent to which they experienced such emotions. The final conclusions of the Discrete

Emotions Questionnaire studies communicate 5 factors that could be measured for extracting discrete, collateral emotionality from patients, that can also be applied to assess mood shifting clinical traits and detecting mood shifting patterns. These factors include 'positive emotion', 'fear/anxiety', 'anger', 'sadness', and 'disgust', with 8 sub-scaled reliabilities informing about 1, 'anger' (mad, bad mood, rage); 2, 'disgust' (revulsion, sickened, nausea); 3, 'fear' (terror, scared, panic); 4, 'anxiety' (worry, anxiety, dread); 5, 'sadness' (lonely, grief, empty); 6, 'desire' (wanting, craving, longing); 7, 'relaxation' (calm, relaxation, chilled out, easygoing); and 8, 'happiness' (enjoyment, satisfaction, liking).

#### *. Implications*

Measurement tools for assessing pain-experiences, their bearing, outgrowths and reinforcement processes, face contemporary challenges regarding the current state of patient-physician interoperability. Four basic inefficiencies of normative diagnostic tools that hamper interoperability and diagnostic feasibility can be pointed out, including 1, 'narrow efficiency' (a tool can be validated, however after some time running, newer technologies could work better for assessing deeper grounds that such tool's scope cannot actually focus); 2, 'low interaction rate' (patient-physician and patient-instrument interaction within the most of the scales, questionnaires and inventories is restricted to numbers, single-termed words, fast and ostensive evocations, or imagined, hypothetical, very general or vaguely-coloured scenes); 3, 'rudimentary performance' (generally, the platform for a feed is paper or written text in a digital format: deeper clinical key values, implied in most of the reviewed measuring tools, can be extracted from machines's sensors, involving virtual reality, or assuming other means for accepting the patients's feed, as computerised diagnostics are being developed for Parkinson's

assessment through digital patterns mapping, or computerised ocular fundus examination in search of psychiatric traits), and 4, 'slow progress accommodating 21st-century technology' (the majority of the most common instruments are developed using measurements strategies imagined by 1960-1980's research parameters: contemporary mathematical methods on narratives, Artificial Intelligence, text analysis and data flows can inform considerably much more straightforward and acutely than short paper forms, facing more efficiently problems in gathering constraining information for assessing pathological taxa, in differentiating among similar pathological architectures, or in comparing epidemiological standards: Cf. experiments in Grenon, Smith & Goldberg 2004; Johansson et al 2005; Kozaki et al 2012; Yamagata et al 2013).

Three ideas (1, 'broader resolution feeds'; 2, 'space for reflection'; and 3, 'inclusion of decision making protocols') are presented below to face such challenges from a Cognitive Ergonomics perspective in the hope that future lines of research would get involved in the prosecution of a better understanding of patients's experiences and environment's difficulties, as the clinical practice and work that enhances such comprehension.

#### *. Broad rather Thin Resolution Feeds*

However the general acceptance of some minimalistic scales among practitioners (probably due to the fact that they serve as shortcuts to decide whether implementing further scales, interviews and tests), simple scales introduce the opportunity to note a main critical observation: economy in time and effort, along with a minimalistic design, embed answers into highly rough guesses, superficial accounts that result in somewhat obvious, rustic, salient traits without actual major benefit for complex, heterogeneous nor differential diagnoses, resulting of little use for pain prognostic values extraction.

Introducing a Cognitive Ergonomic approach, this sort of scales fits an example of what can be called ‘thin resolution’ (in contrast with ‘broad resolution’), affecting interoperability in diagnosis: as the physician sits in a position which diagnostic feasibility requires trustworthy interoperability via interactions with the patient (collaboration from the patient’s side, informing about his or her experiences, reporting beliefs about what is suffered, and endorsing them into the diagnostic account), the thinner this information gets, the weaker the diagnostic feasibility through this information grows. Low feasibility presents a trust-knowledge imbalance, as the thinner this information gets, the more the diagnoser needs to guess, elaborating 3rd person perspective judgements in the lack of patients’s self-narratives, contextualised to situations or decision making processes. Put in other words, the less the instrument relies on the patient’s feeding the scale, the more the diagnoser (a 3rd party) is required to feed the answer with 3rd-party information, being it epidemiological typical data, general standards, or personal/experience-based guesses.

The contrary phenomenon, a broad information feed implemented in the resolution of measurable queries open to patients’s life experiences, would necessarily derive in more data (an increased amount of value to the patient), which is offered to be assessed, contrasted, and taken into account for an educated decision to be made, and thus analysed for being attributable or not as clinical criteria, contrasted with metadiagnostic epidemiological backgrounds and standards (this is, in a second movement, ‘contrast’, not in a first movement, ‘feeding’). For such a reason, what here is being called ‘thin resolution’ will probably present a lack of applicability to modern and future text analysis, Artificial Intelligence, Big Data analyses and value-oriented technologies (like blockchain protocols for a safer storage, querying, contrast and management of clinical data). In contrast,

‘broad resolution’ oriented feeds (Cf. an example in the cognitive ergonomic implications of the Discrete Emotions Questionnaire, *supra*) appear a line of progress to follow in nowadays protocols.

#### *. Demanding a Reflective Attitude*

The majority of scales do not force nor induce patients into effortful reflection, striving to recall and reshape their experiences. In other words, scales do not have an implicitly designed therapeutical role, but a performative extraction of information. A note can be then addressed to the ambiance of trust in which such extraction has been performed. When patients do not reflect effortfully on a given topic where just themselves are trustful agents (because the instruments work for understanding self-beliefs and self-judgements), more probabilities arise for arbitrary, shortcut-like answers to be developed, testimonially spontaneous (similar criticisms were directed to the West Haven-Yale Multidimensional Pain Inventory: Cf. Broderic, Junhaenel & Turk 2004).

Reflection, identification, rethinking of experiences, naming and renaming of emotions, peripheral tension evocation strategies, and personalised attentional baits would improve data gathering and contrast, which would also benefit of a more interactive (with the paper/software method of the instrument) and therapeutical (with the interviewer/analyst/diagnoser) approach.

#### *. Accessing Self-Beliefs through Contextualised Decision Making*

Inventories, scales, interviews or questionnaires seem to focus much more on topic-specific matters of experience rather than on the surrounding situation that provoked, and could provoke anew, pain-concerning events, personalised to the context of each specific patient.

Self-beliefs and judgements appear to be accessed via straightforward addresses to experiences, context-free, instead of via attentional, attitudinal, reflective contexts. From a situated epistemological point of view, this form of experimental measurement would suffer a lack of orientation (Cartwright 1999; Longino 1990; 2001; Kitcher 1993; Harding 1991; 1993; Giere 2006a; 2006b). Involving situation and orientation in measurement strategies would imply centering patients within pain-bearing/experiencing situations, circumstantial to their life and interpersonal case, attracting episodic, intentional memory and affection for an affective simulation to be engaged (Cf. the intentional rendering of the concept of 'feelings towards' in Goldie 2000; 2002a; and of emotional simulation through personality implication in Goldie 2002b). In a similar sense, when situation recalls actions, agency implies the person, his or her decisions, reasons to act and to feel, and this involvement entangles the patients into their feelings through inscribing themselves with perspectivity (Goldie 2003), a new 3rd person perspective enacted by memory and effortful reflection (Cf. QIII, §9). Focusing a vision inviting thinking on actions and attitudes, possibilities of thinking of specific situations where pain has been felt, managed, associated with other issues or overcome would rise. This enables trust knowledge to be obtained, generating a broader feed.

Situation-based measurement strategies would bring the patient the possibility of reviewing through texts, stories, intentional terms (especially verbs and adjectives), and so forth his or her decision making protocol, a behavioural determination and choice that goes beyond a number, a colour, a face or a word as an answer. Complex interactions would also inform better about the patients's resolution of problems through sensing the decision making patterns projected towards a given personalised situation. Additionally, performance could also

be opened to online digital formats, developed by patients or accompanied by caregivers and other health stakeholders, carefully, with time and consciousness of their feelings, from the commodity of their home, through an app directed to the hospital, pre-analysed through a smart instrument plus their physician, and finally uploaded into their own personal information health bank. Future lines will tell how measurement strategies evolve into these new possibilities.





## QIII, Chapter §9

### Barriers in Self-Assessment of Pain & Its Comorbidities: Indetermination in Self-Beliefs & Narrative Perspectives.

(In Niche D — Framing Interpersonal Characterisations)

☛ 361 — 363

—

#### Parts

. *Introduction*

I — Perspectives, Narratives, Beliefs

- . *On Peter Lawrence Goldie's General Perspective Theory*
- . *Effortful Memory Scenarios*
- . *Double Feelings: Feeling Twice Once*

II — Formalising Indetermination

- . *Formalisation of Self-Beliefs through Perspectives*
- . *Suggesting 1st Person Perspectives Self-Beliefs as Defining Experiences*
- . *Self-Beliefs Given a Circumstance of Indetermination*
- . *Closure*

—

*Add. I — Graphic Formal Summary*

*Add. II — On Expanding the Logical Materiality of Contents of Belief*

*Add. III — On Double Feelings. Examples from Neurogastronomy,  
Cognitive Neuroscience, Psychiatric Sexology & Therapeutics*

- . *Neurogastronomy*
- . *Cognitive Neuroscience*
- . *Psychiatric Sexology*
- . *Therapeutics*

QIII, §9 examines how a pain-bearing patient's inability to discern a proper definition of his own pain experiences, and further conditions comorbid to them, affects clinical self-assessment. Indetermination in the patient's reports acts by blurring the characterisations of pain and comorbid conditions that he may offer to physicians and evaluatory instruments when the patient is asked to explain and reflect about his own current emotions, given the case that he feels seemingly contradictory experiences. This problem presents especially when dealing with personalised diagnostics incorporating interoperational feeds (Cf. QIII, §7). These feeds are interoperational as they involve relations of the kind patient-physician, patient-instrument, patient's ambiance-physician, etc. Indeterministic assessment can occur in 1st, 2nd and 3rd phases of neuropsychiatric multifactorial evaluations (Cf. QIII, §6; QIII, §8), leading to general biases and to relatively weak practicality in dysfunctional and dysexecutive populations: sometimes patients, due to cognitive or dysexecutive dysfunctions comorbid to pain scenarios (Cf. QIII, §5; QIII, §6), can generate beliefs upon themselves (self-beliefs) containing contradictory, opposed, seemingly unmatching feelings, that are reported by means of different narrative points of view, multiple focuses that guide the patient's discourse exposing how he acts and feels, along with certain reasons for having acted and felt in a particular manner in other moment.

In regard to therapy theory, indetermination introduces this patient's inability to defend a specific continuous narrative, prompting his self-evaluation of pain and comorbid conditions, with a past, futurible or possible scenario of feelings valued with the same trust as actual ones. This provokes uttering pragmatic accounts (the way the patient uses utterances and propositions for justifying or responding

for the contents of such) where a singularised identification is unable to be reported: rather the principle of relevance is broken, or both characterisations are relevant to the patient for accounting for what he says he believes is experiencing. Such accounts would function via self-narratives that may not seem to be justified to the therapist as conveyed on account to both, present and non-present feelings, for the patient is incapable of 'characterising through' (to determine) a single mindset, consequently impeding a continuous identification of his experiences, emotions and feelings, and of the orientation of those feelings towards something, someone or certain situation.

In this work, indetermination is suggested to have an epistemological interpretation, formalised through propositional logics for self-beliefs. This presents the case for exploring 'indeterministic self-beliefs' in defining how the subject may hold such perspective narratives. Applying Peter Lawrence Goldie's general perspective theory, the question raises to investigate where and how the patient puts trust on when asked for reporting his experience. The aim of this chapter is to define an analytical description for explaining why and how this indeterministic circumstance comes to be propositionally possible, in order to clarify the process that allows a patient to report a 'conflicting double feeling' —two seemingly incompatible or asymmetric experiences (eg, to feel pain and to feel relief) felt at once— that blurs the production of a proper self-assessment.

Integrating Goldie's general perspective theory, the work presents that there are two main forms of reporting through self-narratives: (1) by using, establishing and accepting the meaning of a 1st person perspective for characterising such experiences, being the case that a narrative in 1st person will identify a current, actual, present mindset; and (2) by using a 3rd person

perspective in a self-belief, involving a memory scenario where the patient identifies with himself as in 3rd person in a past, future or possible scenario, in which certain reasons for acting and feeling in a particular manner appear, offering the conditions in which the subject of the narrative feels his experiences, emotions, actions and so forth justified as proper pragmatic accounts where he felt the way he might have felt (thus he is narrating in the present as if he was feeling now what he was feeling then, in the past, in future or possible imaginary memory scenarios).

Conclusions expose how indetermination affects these two circumstances as the first case is being currently actualised by the 1st person perspective, however, since reasons in the second case maintain justified his experience from the past in the present, which he is re-experiencing in the moment of report by reviving the memory scenario tracking such conditions, a new feeling comes to be actualised, shifting the 3rd person perspective narrative into a 1st person one: thus, a perspective shift is defended. Formalised as propositional beliefs, both beliefs will get to the point in which the subject may put trust on both at the same time: it occurs that the subject finds no manner by which to determine what he is actually feeling, emerging an indeterministic self-belief.

Composing the issue in this framework, the text introduces a propositional description of the perspective shift, which is suggested to be useful for formalising and explaining the problem of indetermination in self-assessment. The text is divided in two parts and three *addenda*. Part I reviews and comments Goldie's approach on perspectives and narratives, and exposes the ideas behind double feelings. Part II focuses on formalising propositionally the logics for indeterministic 1st person perspective self-beliefs, proposing what is hoped to be a fiat description of the process. Add. I includes a graphic summarising the process, Add. II contributes with

a logical note on the expansibility of contents of belief, and Add. III closes the chapter with examples of actual double feelings excerpted from the fields of neurogastronomy, cognitive neuroscience, psychiatric sexology and therapy theory.

### I — *Perspectives, Narratives, Beliefs*

Human experiences acting in everyday life was a main topic of Philip Lawrence Goldie's literature. He proposed a very well accepted plural and perspective outlook that contributed with a modern epistemological approach in scholarly philosophy of mind, feelings and cognition. Goldie refreshed many fields, especially focusing on how subjects act, believe and feel towards multiple schemes that provide a growing management of self and others's emotional supply. Experiences, and especially when remembering a past experience or ideating future or possible ones, involve as he exposes a form of storytelling: Goldie's works note how the way subjects participate, as feelers, in the creation of a scenario of believing requires them to be rooted into a perspective of action, their own perspective of actions, thoughts and beliefs. Being emotional creatures require of such intelligence for understanding, characterising and accounting for the emotions that may be felt, and is this last detail what makes Goldie's general perspective theory worth of study for assisting the complex issues that self-assessment faces in contemporary therapy theory and clinical diagnosis.

#### . *On Peter Lawrence Goldie's General Perspective Theory*

Goldie's conceptions of emotional activities are tremendously attuned to subject's activities, which change over time, get renewed by other actions, other feelings and have different consequences in how people in a social stance are



able to understand other subjects's experiences, attitudes and beliefs. Narratives, and especially of the kind that self-oriented narratives allow, make these phenomena affordable when approaching the meaning of one's and others's emotions through pragmatic accounts (utterances exposed by narratives and characterisations that the patient may feel able to justify, defend, or respond about; Cf. pragmatic responsibility and accountability in Witek 2014; Haugh 2013). Descriptions, identifications and attributions of different traits of feelings (character traits, variations on personality, and so forth) from subject to subject also create social contexts (Cf. 'empathetic contexts' in QIII, §10; Cf. Green 2017), patterns of emotional actions and, to a certain extent, assessment ascriptions that may serve for generating both, personal and interpersonal beliefs on such matters (Cf. notions on 'emotional communities' in Rosenwein 2006; and 'emotion as a form of practice action' in Sheer 2012). At the same time emotions can be seen as consuetudinary actions that arrange social paths to cultural-specific interpersonal dynamisms (Bourke 2003; 2014; Griffiths 2009), which lead to healthy and unhealthy relationships, responsibility and reason-&-excuse identifications —that rather create future stability or unbalance, again rearranging social landscapes (Cf. Reddy 2001; Gammerl 2012; Leys 2011).

Emotions perform a great link between the individual and the collective, pressed within the history of subjects's performances (an intimate, private biographical account): on 'Narrative and Perspective', Goldie (2003) proposes a reflection upon that kind of history, upon past and how believing in causal links of action (through previous chains of actions) is significantly relevant to understand how subjects actualise their own emotional and experiential beliefs, claiming that the needs of the subject are the realities of the subjective emotional and believing entanglement. This claim exposes a perspective, the subjective emotional perspective to the past that

everybody could assume as self-reflection. This can be entitled for the extent of this chapter's usage of the concept, a 'memory scenario', which involves not just past identifications, but future, possible or fabulatory creations based upon different imaginaria individually situated within the person's biographical account of experiences that make possible that new experiences get identified with past feelings. Narratives on past activity 'model out' (externalise from 'thinking of just a memory' to 'feeling an emotion'). The conception of a narrative for the subject's emotional being is introduced as a need for identification as it is understood in terms of self-evidences of the subject's actions (Cf. 'actions out of emotion' in Goldie 2000, 147).

This idea of being emotionally identified with some feeling of the past frames the analogy of subjects being identified within a contextual position on a map: subjects can manage when looking at a map and trying to find whereabouts they are on it, for a sense of context in such case is more or less equivalent to the sense of an emotional or empathetic context, summarised by some expression such as 'what happened at the stage where I was when x or y...' These 'x' or 'y' are conditions that help the subjects to relate themselves within the map through a context of buildings, parks, street numbers. These past conditions are brought into present emotions via having reasons for feeling in such a way: as when 'x' or 'y'. Emotions, Goldie always tried to point out, colour those contexts, thoughts and believing scenarios, informing about experiences modelled out from a narrative that puts the necessary perspective in order to arrive to the context in which such experiences make an actual sense (Cf. Goldie 2000, 148; Cf. 2003, 201).

Through the first pages, Goldie (2003) exposes how such multiple perspectives reflect how subjects look at things as justified or not providing for a narrative that allows them to fill the gaps they may observe: for revealing the accountability of the very experience, the sub-

ject might look for the narrative's perspective involved in justifying such experience, being it fictional, trustworthy, roughly certain or believable, concluding that determining whether such emotionally coloured narratives are trustworthy or not is a fact that may variate depending on the subject's perspectives modulating his ability to recall a proper determination or not (these ideas go along with propositional truth as a dependent feature of the context of the propositions that address to a given truth value: Cf. MacFarlane 2005; 2007; 2014; Kölbel 2002; 2008). His concern with truth and trust in the daily construction of stories and reason-giving explanations is central, for his conception tracks the idea that narration is always perspective, that it is underpinned by a narrator's focus guiding the exposition, a subject's view (Cf. Goldie 2003, 203).

To properly understand a theory on mind, when contrasting the two general 20th-century theories —the simulation theory (one characterises other's mindset by' simulating other's mindset) and the theory theory (one characterises others's mindset by having a theory of such mindset)—, he clarifies that no single unity would be able to resolve the emotional paradigm, which requires more integrative, dynamic and complex interpretations, and notes for grasping the whole problem: not just internal but also external perspectives are needed. In that way he bound both concepts, simultaneous 1st-3rd perspectives and narratives. Concerning a subject staging the other's mindset or trying to explain it, Goldie has been plain in different texts considering what he called 'emotional contagion' as a form of empathy and sympathy —which comes close to that of the 'emotional plague' offered by Reich (2010, 267) on account of affective pathology in psychiatry (for a deeper context, Cf. Goldie 2000, 189-192; Cf. Wikan 1990; 1992 for the also well accepted concept of empathetic 'non-verbal resonances'; Cf. Hatfield, Cacioppo & Rapson 1992; Hatfield, Rapson & Le 2009 for a different treatment of the concept).

His intention commenting co-cognition and situation-scheme orientation, and the so-called imaginative identification where propositional attitudes are involved, was to show the artificial division between internal and external perspectivism that some authors accept, stressing 1st perspectives versus 3rd's ones. Perspectives present an agent-observer divergence: for developing explanatory attempts (answering to why-questions), perspectives influence our understanding of why subjects did what they did and felt how they felt: a 1st person perspective generally requires to «appeal to how the situation struck us, whereas we tend to explain the actions of others by appeal to their fixed character traits [in a 3rd person perspective]» (Goldie 2003, 205). In his view, every ascription of a character trait to some other subject (as defined in previous texts: Cf. Goldie 2000, chapter VI, 151ff; 2002b, parts II and IV) is a sort of prediction upon an action (or set of actions) of such individual, made under the considerations of the ascriber about how the ascribed will respond to certain previously explored and experienced situations. Both perspectives are mixed subsidiarily through memory processes for identifying the focus of attention implied in any story.

Regarding not just this text of Goldie's, but the generality of them, this integrative concept of perspectivity in narratives can be suggested to handle a memory scenario. This scenario would seem to bear the conditions and reasons for having acted as the ascribed subject has been observed to have acted. Walking along these lines, and within his notion of an agent-observer divergence, 1st and 3rd person experiences get divided by personal-public relationships that elicit different epistemological divagations upon how subjects access to theirs and others's knowledge (experiences transference will be dealt in QIII, §10). The usage of Goldie's perspective theory to expose mixed 1st and 3rd person perspective self-beliefs, however, is not

treated in any of his texts. Let this section experiment with the results from a propositional point of view.

If in an utterance of a self-belief, the reference (subject) exhibits a logical link that suggests it changes over time (usually, by changing internal time in the narrative vs. external time in the utterance), propositionally the subject requires to be dealt as an indexical (a content of the proposition that varies and needs a context to engage a proper meaning: eg, 'today' has been true and will be for any day of the year, requiring a context to supply its meaning because the reference changes over time —the same is true for the word 'I' in 1st person perspectives). Once the subject gets access to those contents, his attitude towards them will change the way his 'I' in the present narrates what happened to him in the past. This will make for a 3rd person perspective self-belief, where 'I' always appear, but have another value: this 'I' is not addressing the present narrator, but himself in the past, the one version of him that is being narrated, involved in a scenario with reasons for having acted some way or another. Memory scenarios in self-beliefs of this kind are used for framing such reasons as conditions required to justify having acted or felt in this or that manner.

To the needs of self-assessment, perspective theory can help installing how the narrative gets shifted from 3rd to 1st person perspectives even though the subject is always talking about himself: in a 3rd person perspective self-belief the narrator perspective (in 3rd) identifies with 'another person' (a past instantiation of the reference for 'I') which is involved in a memory scenario with room for reasons to having acted in some manner. However, when studying the experience of being remembering something, with the emotions that this new feelings imply, this 3rd perspective appears to shift to a 1st person perspective narrative, to be applied to his own present conditions of experiencing the situation that led to self-identification, imagin-

ing a past 'I' positioning the narrator (in 1st) as actualising his own actions through a new feeling. In this sense, the interpretation of the present chapter on self-beliefs through perspectives will propose to treat 3rd person perspective self-beliefs as dealing with a memory scenario including such reasons, and to treat 1st person perspective self-beliefs as an ostensive propositional definition of a present experience —this theoretical approach to self-beliefs is suggested to bear multiple applications in therapy theory (as analysed in this chapter) and diagnostic evaluation for attending, recognising and managing clinical value in medical information theory (Cf. QIII, §10), which can be extended through a cognitive ergonomic approach mediating in the development of Artificial Intelligence Assisted Diagnostics (Cf. Add. II in QIII, §10).

#### *. Effortful Memory Scenarios*

The way the subject colours his identification of experiences when the characterisation is self-oriented, in 1st person, seems clearly different in comparison with when it is oriented towards other subject or himself in the past, in 3rd person, involving a memory scenario: the subject's remembrance «of the moment seems to have been deeply affected by what he didn't know at the time of the event [...] memory is more of a construction than an excavation and rediscovery.» (Goldie 2003, 207) —assumption that fits in the contemporary understanding on mnescicoception and the neurology of memory in the generally accepted trends of current neuroscience, from Hebb's ideas (1949) to new evidences (Kim & Baxter 2001; Eichenbaum 2008). The notion can be taken as a retrospective comprehension, which develops a new experience (the experience of remembering a particular event coloured with a precise emotional value) that contributes the characterisation in 3rd person (memory scenario) through construing, interpreting the memory in 1st person perspec-

tive: an immediate activity of reaction and enactment, the very recalling process.

After the main analysis of 1st and 3rd person identifications and ways of believing, he faces an exploration on concordance and discordance in narratives of simultaneous perspectives: an external analyser can see narratives interpreted in both, 1st and 3rd person, enacting not only different but also incompatible emotional responses and attitudes towards the scene, effortful divagatory memory scenarios that provoke unattainable singular characterisations. This is often the case for many emotional accounts: for instance, when one remembers something he did believing it was necessary, but now that one remembers he feels it was not needed (it appeared to be justified in the past but it is no longer appreciated as a justified belief), the emotional contradiction could fit into the notion of remorse, a new feeling out of a shift from 3rd to 1st person. Given Goldie's idea, a subject might be discordant in his beliefs between the experience and the telling of the story of what has been experienced: in remembering remorse, one does not feel the same he felt when he did what he remembers he did.

Goldie seems pretty active in this sense, «each perspective involves not only emotion, but also evaluative thoughts, and concordance or discordance between evaluative thoughts can explain concordance or discordance between emotional responses.» (Goldie 2003, 211). As it is observable, causes, reasons, excuses and so forth (he lays out his core idea of those items in Goldie 2000, 167ff) participate in those effortful identifications.

Following the idea of memory scenarios, as presented in the present work for unifying and describing Goldie's context of remembering through narratives, effortful memory scenarios come to act too: these are scenarios by which a subject would reintroduce perspectives in twisted person identification, as in the example of remorse given beforehand. In self-effortful

memories, when the focus is 'I in a memory but construing the past scenario anew', this 'I' becomes the actor and the narrator of the subject's own narrative identification, and the effort is a result of not being concordant with the emotional experience the narrator feels now vs what the actor felt then.

This treatment of effortful memories suggests a definition of discordant, asymmetric or seemingly contradictory feelings that are felt simultaneously: these may be entitled 'double feelings' in order to connect the notion with Goldie's interpretation of intentional feelings (what he would call 'feelings-towards', *infra*).

Introducing an example to work on, let clinical characterisation of remorse in therapy theory make the case that a patient suffering from a long-bearing reinforced pain developed depressive character traits and anxiety (Cf. QIII, §5) comorbid to it, along with severe non-acceptance coping strategies: eg, over rate substance abuse including alcohol, pain killers, antihistaminic drugs for sleep and barbiturates, and often recurred self-harm attempts at the spot of injury (if given) or in other areas for distancing from the pain experience. The subject, in characterising his feelings towards what he did (let the past scenario be to enact his coping strategies as said above) he now feels remorse, but at the same time keeps those feelings as justified feelings on account of the reasons that make him believe his pain is unbearable. He characterises his action and his feelings as both, required and unjustified, an entire circumstance to which the patient feels increasingly anxious, guilty, depressed, self-inefficient, self-destructive and unable to stop; as well as attached to, in need of and dependent because of a justified reason.

The question is: how an external analyser (therapist) could describe the experience of this subject as putting in value both emotional narrative perspectives. The case of this subject that feels remorse has an extensive value for mod-

els of double feelings in therapy theory and for clinical assessment theory.

Following that narratives in 3rd person introduce an opportunity for evaluation via the conditions of the memory scenario, which offer a space for having reasons to act in a certain manner, effortful memories appear to create as well evaluative statements (the topic Goldie reflects on when asking which are the 'appropriate feelings' to feel for such or such subject) that are sometimes in very blurred lines: shall the therapist identify the patient's 'I' in his self-narrative with what is justified to himself in the present (feeling remorseful), or rather with what is justified to the 'I' of himself in the past (feeling pain is unbearable so that he has his reasons to feel that what he did is still justified in the present when experiencing anew his remembrance)? Which feeling is the appropriate emotional experience to follow the track to and serve for a personalised therapeutical hook? Neglecting his suffering would be counterproductive, however keeping victimistic would not result on therapeutical gain. Which is or is not the accurate path is not, however, the topic of this work, but to be able to describe why and how he can actually feel both feelings so that the patient cannot determine on which of those feelings to put value, while he is actually putting value (trusting) and actualising the two of them.

Those types of discordance are the ones Goldie does not treat in extension, beyond a list of possibilities when concordance fits not the organisation or the focus of the narrative (some forms of discordance in Goldie 2003, 210), however his general perspective theory has arranged multiple instruments to deal with such problem. The concluding answer to put forward, applying the proposal of effortful memory scenarios to Goldie's ideas, is that the subject can always position himself in both ways, and this fact may be explained because a perspective shift from the 3rd person perspective narrative to the 1st person perspective overall feeling of remembering

and evaluating to contrast with what he feels in the present occurs. In this way, there is no simple fact but a multiplicity of event-evaluation in the schedule of an indeterministic self-belief (a propositionally suitable form of an effortful memory scenario).

Taking it as hypothesis, the complexity of social cognition is even more patent than the average of complexity the author assumes present: there seems to be the case that there is not always a singular fore-tale, a story of first instance, as Goldie points out to exist guiding the direction of the narrative's perspective, signalling the fire of its interpretation (Goldie 2003, 218). To the fore-tale, rather the principle of relevance does not prevail, or rather fore-tales accumulate the relevance of multiple beliefs (the example gave two feelings, a double feeling, but can be extended to more pluralised schemata) in a multiple present one. Regarding the fact that beliefs can cluster each other in a propositional style, there is no significant benefit in following a competing option: the present feeling of remembering and contrasting what is remembered to another present feeling searching for determination would be the plural fore-tale, a fore-tale of indetermination that aggregates multiple further feelings, being a belief that expresses doubt and uncertainty as the patient tries to explain, a belief that he may not be clear enough to understand at first glimpse, neither he nor the evaluator.

This can also condense the view that there is no need that in every circumstance all actors are able to react just one way, being tempted to feel in a particular manner rather because of deciding to go along with the narrator or rather because of deciding to go away from his perspective, being concordant or discordant with his emotional appeal. This expresses that our emotional experience in reaction to storytelling and imaginative identification depends not necessarily just on a concordance-discordance duality, but on being able to feel oriented towards

sharing similar experiences and beliefs with the focus of attention in the story, and also being able to open emotional experiences that bear two or more feelings towards that focus.

This token of 'feelings towards' is a very famous one of Goldie's and it shall be exposed in depth hereafter. Indeed, focuses of attention are guided by the narrator, but there is no need to assume that subjects are such ingenuous thinking listeners that cannot modulate those focuses (lose them, misunderstand them or remake them). These effortful memory scenarios that allow the twist in perspectives are the threshold to overcome for finally feel identified perspectively. If for the subject is very difficult to elicit memory similitudes with that experiential colouring the narrator establishes through an empathetic, emotional means, he shall not feel identified with his focus point of attention in the story for he would have no access to that emotional perspective. This standpoint implies that focuses are not fixed, but intertwined perspectively and plurally through evaluation. In self-beliefs and self-narratives, the same process occurs by introducing the indexical 'I' in a past memory scenario that refers not to the same version of 'I' that points out to the present narrator. The latter is in 1st person, the former in 3rd. However when felt at once indetermination appears, and the focus of the narrative shifts from one to the other while identifying the subject with both, the present 'I' and the past 'I'.

. *Double Feelings: Feeling Twice Once*

Double feelings (see a variety of neurological and psychiatric examples in Add. III) intervene in narratives by considering how the focus of the story changes from one perspective to another. To put different psychiatric examples, serve the following four cases, that may be observed in the light of entering a therapeutical treatment in which the patient is asked to make a reflective effort on explaining how would he

justify what he feels. These examples have all a similar structure: there may be a present complex belief composed by two further beliefs that manifest feelings through different narrative perspectives (changing the focus of the narrative involved in the complex belief that is presented during therapy conversation), one in present, actual circumstance (a 1st person perspective self-belief: B1), other related to the past, a futurible circumstance or a different possibility imagined by the subject (a 3rd person perspective self-belief: B2):

(a) Depressive character traits due to pain with non-acceptance coping strategies (as in the example beforehand) — following B1 the patient feels guilty; following B2 the patient feels relief, involving reasons for justifying such feeling.

(b) Suicide ideation and attempt — following B1 the patient feels guilty, remorse, shame for what he felt and did; following B2 the patient feels necessary what he did and what he was feeling, satisfied, brave enough, involving reasons for ideating a possible self-harm.

(c) Post-cingulectomy patients — following B1 the patient adopted a new identification of pain, abstract and diffuse; following B2 the patient feels an unidentifiable or unaccessible pain, involving reasons (having had a surgery) for justifying such feeling.

(d) Phantom limb pain patients (post-surgery) — following B1 the patient believes there is still a severe pain-kindred feeling towards a limb x; following B2 the patient believes there is no pain-kindred feeling towards such limb x, involving reasons for justifying such feeling (Ramachandran's mirror technique), where the reflection of a paired limb (eg, an arm, an ear, a toe, a leg) or the simulation that makes him believe he actually keeps such limb, provokes he could feel an abstract relief.

— For all the cases, if the complex belief incorporates both beliefs and the patient puts value indistinctly on them, such belief would be an

indeterministic 1st person perspective self-belief, making him feel unable to characterise his feeling towards the topic of belief. This new belief adopts the form of a double feeling.

Going back to narrative perspective theory, Goldie (2003, especially pages 210-213) offers one case that may be considered to explain the process, and it is the story of an encounter between a woman and a drunken man on the train. The drunken man gets slightly close to her, with a weird gaze, and some conclusions are directly pointed out: «this narrative suggests the woman's internal perspective, and thus invites you, audience, so far as you are able, to imaginatively identify with her thoughts and feelings of fear and revulsion at the man's behaviour.» (Goldie 2003, 212). Now the audience is also invited to assume, he says, her feelings are justified and are appropriate to the situation, on account of the evaluative information given by the focus of the narrative: she is involved in a memory scenario where imagining a possible futurable case based on her imagining herself in a set of reasons including (1) drunken people can be violent, and (2) the drunken man approaches the woman 'with a weird gaze'. Being that as it may, a very specific mood or character traits attribution is made, a form of a prediction of consequences from behaviours that end up constituting justified beliefs (of the audience) based on emotions that may be felt by the woman. Her feelings are directed towards similar circumstances that come to be felt by memory scenarios (of her knowledge about the possible consequences of a drunk man behaving as narrated): she identifies these memory scenarios as a replica of her current situation: things that she knows some other people are said to have experienced that she now plugs into the present scenario of experience.

Futurable situations are a condition to evaluative explanation, and without concluding narratives we cannot deliver any neutral in-

terpretation. Imagine the focus of narration now introduces the following future scheme: the drunken man gets close to her and vomits, then sits down and falls asleep. She will now be less afraid and more worried (maybe about his health as she notices she misunderstood his gaze), it occurring because of contrasting memory scenarios of prediction and of future possibilities. Time scale for comparisons changes their attitudes through their actions... acts actualise beliefs —what Reddy (2001, 264) calls 'affective configuration'; and Goldie (2000, 150), from Musil's works, calls 'shaping and consolidation'.

On a 3rd person perspective non-self-belief, the audience can feel in complete relief, or ashamed if identified with a poor man, for the audience changed their attitudes towards him: he is not the previous potential murderer, violator or thief, he is now the poor man that could have family issues, could be brokenhearted, could have lost the job, and so forth. It seems it depends on the narrative's multiple points of view, its biases and how it exposes future elements or neglects them (for we all participate eliciting or silencing them), and not just on the actors's point of view, but as well on how the audience grasps the intention through the multiple perspectives of the focus of narration. This involves justification as a form of identification of appropriate emotions to feel: «this notion of what makes a narrative appropriate thus leaves [...] you to imaginatively identify, at the internal level, with an inappropriate emotional response of a character, one which that character mistakenly considers to be appropriate.» (Goldie 2003, 212), like when reading stories or singing fairytales to children that need be guided, oriented and situated within a range of appropriate and inappropriate moods of interpretation. Another concern, Goldie realises, is that «there may, however, remain an epistemological worry: could it be that the emotion which I so readily attribute to the other person is, in fact, not

felt by him at all?» (Goldie 2000, 182). That is a critical point to reflect on for evaluation, the transference of private emotional experiences inaccessible to external analysers (this topic would be treated in QIII, §10).

Having justified beliefs for action, giving reasons for sustaining a version (a narrative perspective) upon certain experience, emotion or sheer acts, has been a topic of debate (internal reasons, Cf. Skorupski 2007; Goldman 1979; Williams 1995; vs. external reasons: Cf. Nagel 2014; Cf. Bonjour 2010 for a review). Nonetheless, to the scope of this dissertation, the ideas about having reasons for acting in certain manner seem particularly interesting as for turning the question into having ‘reasons for having felt in certain manner’. Introducing a therapeutical approach—where the patient is asked to reflect upon his own experiences and look for what justifies what Goldie would call an ‘appropriate feeling’—let us return to the example of the depressive patient with severe non-acceptance coping strategies and a double justifiable feeling: is an external analyser (therapist) to accept a subject’s (patient’s) pragmatic account about what he felt as justified for it was a feeling that the subject ‘felt justified to feel’ in the past given the reasons present in his narrative perspective?

Following Bernard Williams’s (1981; 1995; 2001) position on internal reasons, ‘reasons for having felt certain feelings’ can be managed as internal (in contrast with external ones): internal reasons would serve for justifying certain ‘belief about oneself feeling in the past’ with a variety of reasons for having felt in such a way (like the one held by the patient) as it goes along with a proper subjective motivation that no other subject may access to, a ‘motivational set’ (Cf. Williams’s 1981, 10-12) that is composed by one’s desires, conditions, commitments, goals, etc. For the patient of the example, the motivation to require specific rewards for suffering an unbearable pain equates to the relief that the effect of consuming (substance abuse

intended as coping strategy) different drugs provokes. This would inform about a justified feeling for following such motivation given the reasons for having felt in such manner. As suggested in QIII, §5’s clustering of dysfunctions, depressive traits and their acquisition are comorbid complications that relate to executive attitudinal dysfunctions; which may lead to impotence, worry and habits dysfunctions instrumentalised as coping strategies (explaining the presence of addictive traits, and substance abuse and dependence) in search for some sort of satisfaction that could modulate depressive symptoms.

Using William’s (1981; 1995) characterisation, the patient has a reason for feeling in ‘x’ manner when having a desire for it, as if satisfying such desire would come by feeling ‘x’. An external reason will be present on account of the patient having a reason for feeling ‘x’, but no desire would explain the motivation out of which he will ultimately act: in this sense, reasons alone do not move people to act, as Williams insisted.

What explains that the patient believes his feeling was justified comes close to this interpretation that takes into account the motivation from which the patient drags out the reasons for having felt as when requiring relief by means of abusing pain killers, barbiturates or alcohol. There seems to be no moral impartiality on storytelling, and social cognition in that sense is related to what kind of knowledge both the teller and the audience (in the case of a self-belief that audience could be the very subject remembering himself in a 3rd person perspective) want to feel attracted to, and to which perspective is the knowledge offered for that audience needs to put it in relation to them for understanding the implications of the story: the cultural, social and standard forms of interpreting that narrative (the accepted perspectives).

However, such schemata does not explain why the patient still feels justified a present be-



lief for feeling the same as in his past belief in which he held reasons for having felt and acted. The validity that attributes the external analyser (the therapist) to such justification may be different than that attributed by the patient to himself in the narration of a past event; however the case is that such evaluation of himself is a present one, exposed through a present belief, which maintains past reasons that may not serve as valid for what he is feeling now as a whole... in this contrast is possible to face the double feeling given indeterminateness: driven by an unreflective chain of thoughts, the patient may be feeling both, guilty and at the same time justified of having felt as being worthy of a necessary relief, resulting in an indeterministic self-belief. What rests to explain is how such belief reaches an actual sense by a perspective shift: how both feelings are actualised during the therapeutical interview and further assessment involving diagnostic key values. Part II introduces a propositional approach in the aim of depicting the complex belief in a circumstance of indeterminateness.

## II — *Formalising Indeterminateness*

In order to address the problem, an external analyser may think of the subject's experiences and memory scenarios as contents of a propositional belief in the context of content-based epistemic self-beliefs: a collection of contents about certain topic and which agency will ultimately befall in such subject. As for defining experiences like self-beliefs, at least one of the contents of the collection addresses such subject (eg, by introducing in the collection the content 'I'), and some other contents shall address to what the subject feels (eg, 'pain', 'relief', etc. in relation to such 'I').

In certain dialogue to the relativistic use of propositions as bearers of truth values that are situated in a determined context —Cf. MacFarlane's (2014) discussion on assessment of beliefs;

and what Kölbel identifies as 'non-tame relativist account on truth': that «the truth of propositions of some kind can be relative [in regard to its context]» (Kölbel 2002: 119)—, the working treatment of a propositional belief of this style, in the scope of a self-oriented collection of contents, opens a space to deal with inner private contents. The epistemic management of self-beliefs's contents and value (in this sense, the accessibility to the knowledge an external analyser may have about them) always appears to be concerned by the context of the subject that holds that belief. Propositionality orients the values of truth, in some way, as values of trust: the epistemic possibility of the external analyser is to raise another belief upon the experiencer, a move that will recall transference of experiences as a necessary open content of belief for both of them, displayed as if what one feels was not private for the other. As this situation does not happen in full —all agents retain their experiences, making the analyser to face a prediction about what could be the content of the experiencer's beliefs— the epistemic limit of such belief ends in what is unpredictable (Cf. Overgaard 2007), the occult characters of the other's 1st person self-belief.

However, if the analyser is internal (being the proper experiencer), the belief that is generated as an assessment of his own experiences, needs be contextually accessible by shifting between time, possibilities, futuribles and imaginations or fabrications from a 3rd to a 1st person perspective. At least, that is what is expected by understanding the meaning of introducing narratives (involving reasons to feel) in the process of assessment, recalling memory scenarios to compare new experiences.

By arguing for a theory of perspective self-beliefs in the style this work proposes, it seems particularly suitable to deal with a propositional definition of 'experiences' in the sense of a 1st person perspective self-belief. Involving trust on versions of the narratives, the ques-

tion starts by asking on which version of the narrative the subject puts value? This is, which version of the narrative is being actualised as trusted enough as for behaving like a 1st person perspective self-belief?

. *Suggesting 1st Person Perspectives  
Self-Beliefs as Defining Experiences*

1st person perspective self-beliefs —of the kind ‘I feel pain’, ‘I experience remorse’, ‘I am aroused’, etc.— are proposed to introduce ostensive definitions of experiences into propositional logics. These are suggested to define the latter conceding three conditions:

(1) *Material Consistency*: 1st person perspective self-beliefs work for defining experiences as the contents express so (an emotional activity, a feeling, an epistemically oriented affective attitude towards something, etc.). This is to say that the experience ‘x’ would be valid on account of the material consistency of the meanings of ‘I’ and ‘x’, following Stephen Read (1994/2002) in regard to the difference between formal consequence (by the logical structure) and material consequence (by intrinsic meaning) of the contents of utterances: if ‘x’ is not a suitable identifiable experience, the material requirement in addressing ‘x’ to ‘I’ would not hold, thus, a 1st person perspective self-belief. Relating this sense of ‘x’ and ‘I’ would not work as a proper logical architecture that serve for an ostensible definition of ‘I’ experiencing ‘x’: however it would consistently serve for defining an actual content in the subject’s belief. If ‘x’ is ‘a lion’, such that ‘lion’ is not a materially consistent experience for feeling, not a suitable topic within the epistemic convention addressing experiences, emotions, and the like, ‘x’ would not be felt by ‘I’, for a proper feeling is required to approach towards the lion: happiness, fear, tenderness, etc. This said, there are other abstract forms of feelings that may occur as for

‘I feel a lion’ (ie, ‘I feel brave like a lion’) where metaphors, analogies, comparisons and so forth are to be included in how experiences confirm those abstract accounts.

(2) *Transparency*: the condition that they are being believed ‘transparently’, in McDowell’s (1986) terms (having sense), or in other words, trustfully: the subject of belief is not faking (nor totally and intentionally simulating) his feelings, thus he is pragmatically accountable (Cf. Witek 2014; Haugh 2013) of the contents of his belief —Cf. QIII, §10 for an in depth study of these notions.

(3) *Instantiation of a Singular Bearer*: these beliefs have the propositional condition of an indexical architecture (Cf. as in the works of Salmon 1986; Schiffer 1987). This requires that the referential hook of the subject of such 1st person perspective self-belief is contained (is a content of) by his own belief in a way that the content that indicates the subject inside the belief can just address to one instantiation (version) of the subject: the actual, present version of the subject. This makes 3rd person perspective self-beliefs to involve the other possible instantiations of the subject, himself in a different circumstance not being the actual circumstance: past-himself, future-himself, and the other possible versions of himself as imagined or believed not being in the present (alterations of himself, futuribles, modals).

If those three conditions are to be maintained by the logical architecture, (1) expressing a suitable experience the subject could actually feel, (2) propositional transparency when believing of an experience, and (3) addressing just the actual instantiation of the subject of the belief, a 1st person perspective self-belief may be held for serving as ostensible definition of an actual experience as the contents of such belief are being irremediably actualised: no one

but the current actual subject would be a possible subject of such experience, and, as given through transparency, the subject is immediately believing that he feels what he believes he feels, thus, if he is not faking so, he is needed to propositionally define that he feels so through such belief.

A different but quite appealing application of this ideas brings perspectives to computational diagnostics and its use in Artificial Intelligence Assisted Diagnosis, as there is a propositional manner in this style of presenting beliefs where a third party analyst may differ between an experience (an agent's identification following a 1st person perspective self-belief of which its contents are actual), and a memory scenario or a possible, futurible construction participating through a memory scenario in an experience (an agent's identification following a 3rd person perspective self-belief of which its contents are not actual, or imply a perspective shift to be actual, *infra*) —Cf. *Addenda* QIII, §10.

. *Self-Beliefs Given a Circumstance of Indetermination*

If a subject appears to hold a self-belief in which he is unable to determine whether he feels 'x' or 'y', being both 'x' and 'y' contents of such belief, the subject is holding a self-belief participating in indetermination: if he is asked to report whether he feels one or the other, he would not be able to determine in which version of his self-narrative he is supposed to put trust on (rather on 'x' or rather on 'y'), thus making the case for an indeterministic self-belief of the kinds 'I feel pain and I feel relief', 'I feel proud and I feel remorseful', 'I feel guilty and I feel blameless', etc. Let this indeterministic self-belief be noted 'β (...)', for the trust values in 'x' and 'y' are Symmetric.

Applying perspective theory, one of the narratives formalising a belief is suggested to be certainly not in a proper 1st person perspective

if the subject is to be reviewed in the past, in the future or in a possible imaginary moment of the present, or if faking or simulating his experience. Accepting that one of those contents gathers the subject as regarding himself in the past, it composes a memory scenario, thus, the subject introduced in the architecture of belief does not satisfy condition (3) on subject instantiation. However, since he is suggested to be feeling both in a new circumstance of indetermination, it seems necessary that both contents actualise, being both of them 1st person perspective self-beliefs. This process comes with a required perspective shift that dynamises value on narratives: the shift makes the 3rd person perspective self-belief to reestablish as a 1st person perspective belief, framing the subject able of valuing both contents at the same time, as exposed.

Every β is a complex 1st person perspective self-belief, for it is a self-belief felt and actualised in 1st person that holds as contents other beliefs. To put a taxonomic reference, β can be marked as a complex sort of self-belief presenting a subject that holds the belief upon himself holding several other beliefs. The fact that these other beliefs are felt at once points out that the subject does not know where to put value on, whether 'x' (in, say, B1) or 'y' (in B2). These beliefs may be presented in different perspectives (by adducing self-narratives involving reasons for feeling/acting or by not doing so), however this does not need neglect the fact that both are included in a singular 1st person perspective self-belief: β.

As fact of the matter, another fact makes even more interesting the scheme: the subject may not be able to determine his current actual experience (β) as the beliefs that compose it, those being 'B1' and 'B2', participate of a narrative that is rather opposed between each other or, at least, different in perspective. The difference comes with the 1st person perspective narrative (1stN) in B1, that would put value on

content ‘x’ for informing the feelings of the subject that holds  $\beta$ ; and the 3rd person perspective narrative (3rdN) in B2, that would put value on the content ‘y’ for informing the feelings of the subject that holds  $\beta$ . In both cases, the experience is actualised through  $\beta$ , but the feeling is not to address B1 alone, nor B2 alone, but their joint: ‘S  $\beta$  (<‘B1’ & ‘B2’>).

The subject holding the indeterministic belief is then unfit, unready or lackadaisical in respect to accepting just one self-narrative perspective as a valuable information for characterising his pain-experience, thus even B2 is clearly informing about a different subject —participating of a memory scenario and neglecting condition (3): addressing to a past-himself believing a content of pain that is not actual, is a past felt pain—, given a perspective shift he would be feeling from B2 involved in  $\beta$  within a current circumstance, so the subject would be feeling both identifications at the same time, for  $\beta$  satisfies all the conditions of a 1st person perspective self-belief, and also satisfies the principle of indetermination.

. *Perspective Shift*

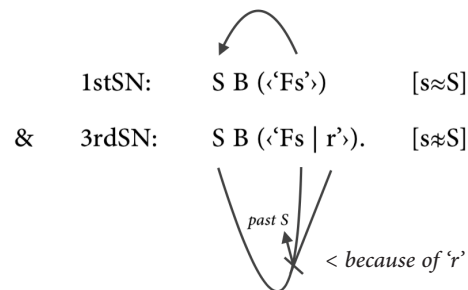
Framing the shift in the relationships subject-experience/content of belief, be the following scheme a summary of the process:

S B (<‘Fs’>  
& S B (<‘Fs | r’>).

Where ‘S’ is the subject of the belief, ‘B’ indicates the belief as an epistemically accessible collection of contents, ‘F’ reads ‘to feel pain’, and ‘s’ the subject as a content of his own belief (the subject’s ‘I’). ‘Fs’ forms the logical relation ‘I feel pain’, and ‘r’ notes the set of reasons for having felt as in ‘Fs’.

In the first belief, the material meaning in the bond ‘Fs’ is not framed by any condition that facilitates specification: the meaning of ‘F’

remains approached to ‘s’ as ‘s’ approaches to ‘S’ for that specific, present and actual state. This informs that the narrative is put in 1st person perspective. However, in the second belief, there is a condition, where the reason or set of reasons (‘r’) for feeling/acting marks the material meaning of ‘Fs’, framed within an epistemic window that allows the reason ‘r’ to be valid as a content of belief of ‘S’ in respect to participating in the relationship that the experience and the subject exhibit. Implicitly, the memory scenario (the epistemic window) facilitates ‘r’, through which the subject may conceive of his experience as of the past instantiation of himself in time, having reasons to model his own experience as he felt it: ‘S’ is holding a belief upon a past version of himself and a past experience. This informs that the narrative is put in a 3rd person perspective. Propositionally, one of those beliefs is not addressing ‘S’ as in an actual self-belief, but accounting for himself in a different situation:



While narratives colour the beliefs they do not act as a whole yet: the subject is described to have separately a 1st person perspective self-belief (B1), and a 3rd person perspective self-belief (B2). In order to facilitate ‘S’ a possible assessment upon them, through contrast, elimination or any other form of putting value into his own beliefs, ‘S’ requires to develop a new self-belief in which he occurs to hold a belief upon other beliefs. However, because of subject transitivity, there is a problem in fitting a 3rd person perspective self-belief (B2) and still calling the new

indeterministic belief a 1st person perspective self-belief. Somehow, B2 is required to transform into a 1st person.

And this requirement is not an instrumental movement, it is a recognition of what implies to follow the definition of an indeterministic belief as a proper 1st person perspective self-belief. The model proposes to explain the indetermination by considering the definitional circumstance: if, through the new belief, 'S' is able to feel both experiences, this implies (according to the three requirements for identifying 1st person perspective self-beliefs: 'Material Consistency', 'Transparency', 'Instantiation of a Singular Bearer') that both B1 and B2 address to the same bearer, and this bearer needs to be, and just be, the proper 'S' that holds the total belief. Since the relationships of those beliefs are opposed, but actualised and felt at once through the new belief, this makes the circumstance of indetermination.

To this extent, 'to put value on' a narrative, deciding whether to feel as if in 1st or as if in 3rd person what is being felt, is precisely the epistemic process of experiencing as an actual feeling both of the narratives. This said, being impossible to feel in 1st person a 3rd person narrative on account of the three requirements, it happens to be justified to think that through such process a perspective shift has developed, explaining the proper circumstance for generating indetermination. Propositionally, the perspective shift comes from the material meaning in relation to the contents of B1 and B2. Given 'r',

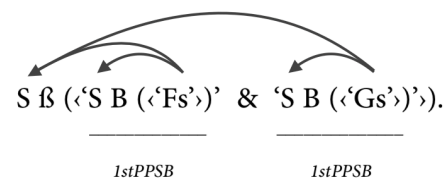
$$\text{iff } \diamond ('Fs \mid r' \longrightarrow 'Fs \approx \sim Fs'), \\ \vdash '\sim Fs' \approx 'Gs'.$$

The architecture of the perspective shift, thus, would specify that given certain reasons, framing a memory scenario, if it is possible that the subject experienced, say, pain ('F' = 'to feel pain') in such scenario as implying that what he felt within such scenario is not equivalent to what he feels now, it is obtained that this other feeling is

equivalent to an antonymous of such experience, which is a different experience (reading 'Gs' as 'to feel relief'). This opposition of contents produced as an antonymous relationship (specific non-synonymity) shifts a past belief (B2), involved in the memory scenario in which reasons acted, for a present self-belief in 1st person perspective, developing a new belief (B2')

$$B2': S B ('Gs'). \quad [s \approx S]$$

To read that the the content of 'I' in the new self-belief addresses the subject of such belief, actualising his experience as to hold the belief that he is not in pain. A perspective shift occurred. When B1 and B2' (the new 1st person perspective self-belief, reloaded from a past 3rd person perspective narrative) coalesce in a symmetric belief (both beliefs are held through the same perspective standpoint: 1st person), following the exposition of indetermination, a 'symmetric' (ß) indeterministic 1st person perspective self-belief has been generated:



This architecture is suggested to explain and define how subjects involved in indetermination may hold two or more beliefs, being unable to characterise a singular simple emotional experience, framing a double feeling that blurs the execution of a proper self-assessment upon their own personal health.

. Closure

The influences of indeterministic self-assessment of pain experiences involve interoperative relationships, as established in research neuropsychiatry and therapy theory, and in

diagnostic, clinical evaluation. Indeterministic pain self-beliefs introduce a complex problem for an external analyser in judging what the patient is valuing when self-assessing present or past experiences that may affect the recognition of possible pathological traits and architectures, generally via narratives describing feelings, beliefs about those feelings, and actions, along with beliefs about the reasons that oriented the patient to act the way he might have acted. By considering the experimental application of Goldie's general perspective theory, this chapter has proposed a strategy to define propositional self-beliefs in 1st and 3rd person perspective, situated as carried on by the focus of the narrative the narrator tends to opt when expressing an experience. It has been suggested that in a theory of perspective self-beliefs of the style maintained by this chapter, 1st person self-beliefs can serve for offering an ostensive definition of experiences. This schema has led to identify indeterministic self-beliefs as complex 1st person self-beliefs that behave in relation to the context that affords a subject to justify, assess and relatively put trust on different beliefs at the same time (valuing the concept of 'double feeling' with several actual examples in neuropsychiatry).

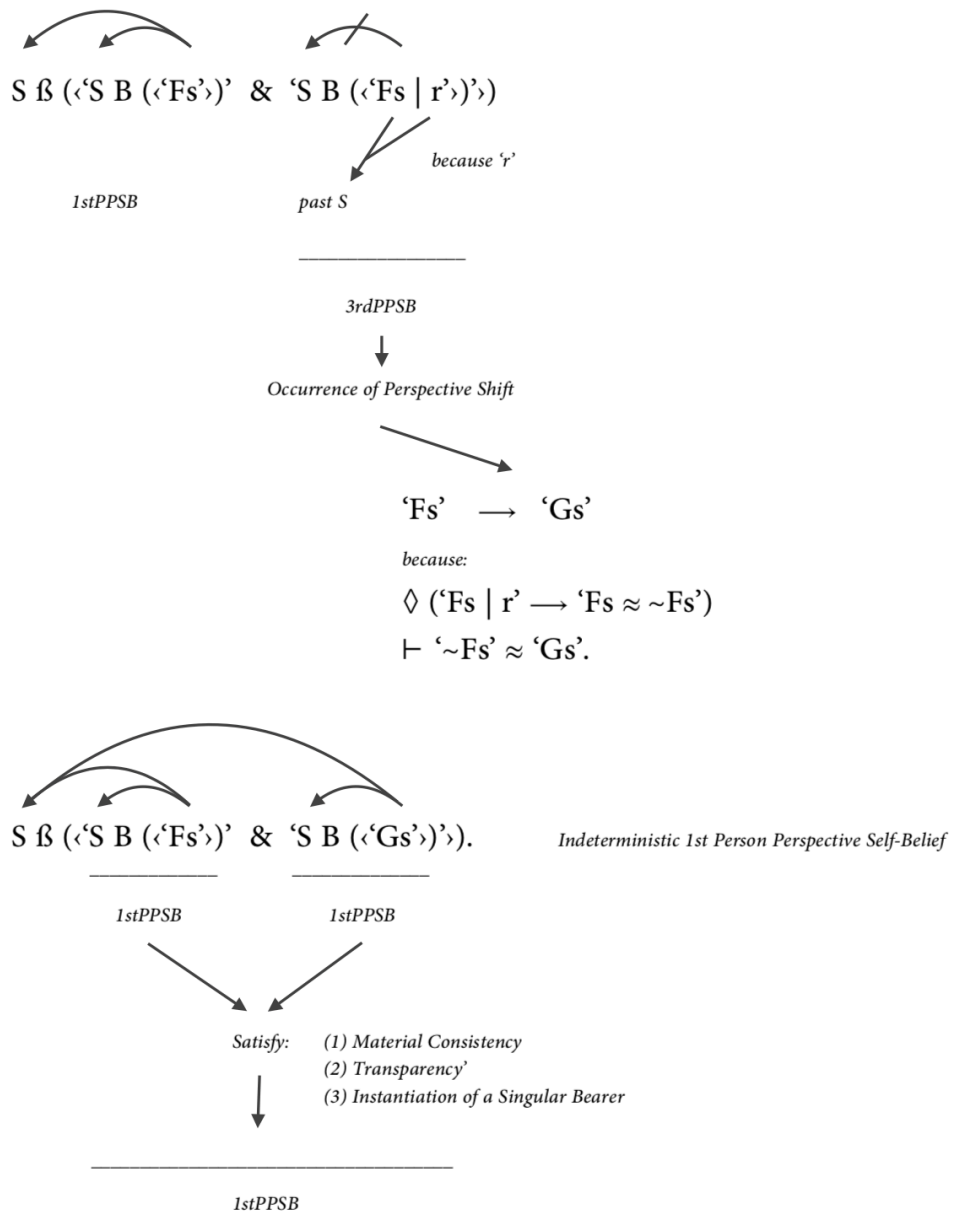
Finally, a definitional architecture has been delivered to render an explanation of the possibility of such experience making use of the conceptual uses provided by perspective theory, arguing that for having a proper indeterministic self-belief defining the experience these subjects (as patients in therapeutical evaluation or diagnostic assessment) feel in 1st person, a perspective shift occurs in the beliefs that address to those subjects in a past, possible or future experience. The fact that they may keep feeling justified both experiences, a present and a past one, makes the case for identifying the past one as a circumstance that reloaded into a new feeling, shifting from 3rd person to 1st person perspective. When this is self-assessed

by the subject, trust is put on both, generating indetermination and, consequently, making the subject unable to characterise a proper singular experience, compromising the regular identification of his experiences. The topic, reviewed in this style, aims to acknowledge the importance of unsteady pragmatic accounts in clinical epistemology, with especial attention in the field of psychiatric diagnosis and therapy theory, in the hope this can contribute to a better understanding of patients's self-assessment and the dynamics behind self-reported beliefs.



—  
 Add. I — *Graphic Formal Summary*

The following graphic summarises the process in a schema that starts with a pre-set fictional composed belief including both perspectives (1st & 3rd person self-beliefs). This composed belief has its roots on the perspectives installed in the narratives used by the subject (S) as exposing for himself what he is feeling as a pragmatic account. It is then reoriented: one of the included beliefs suffers a perspective shift that re-addresses ‘S’ and his experience (e) as ‘S’ being the only suitable (actual) version of the bearer of his experience. The two beliefs are now 1st person self-beliefs, amenable to be felt at once, thus, behaving as a double feeling that prompts value in both beliefs, thus making the case for defining it as an indeterministic 1st person perspective self-belief:



—

*Add. II — On Expanding the Logical  
Materiality of Contents of Belief*

Contents of belief, installed in a theoretical frame of the style this work suggests, prompts propositionality with two main considerations: (a) as a basic principle, the requirement that every (public) evidence that functions as a suitable topic of belief will enter propositionality as a content of belief, including intimate (private to the subject of belief) designations, attitudes, intentions, orientations, dispositions, etc.; (b) that relationships of contents need be mediated by the instantiation of such contents prior to the instantiation of their relationships.

This leaves us with proper beliefs informed by the suggested theoretical frame considering that inside a self-belief of the kinds reviewed by the chapter (eg, 'I feel pain') there would be 'S' as a content addressing the subject of his own self-belief, 'F' as a content addressing the feeling the subject experiences, and 'Fs' as a content addressing the bond that instantiates the subject into a logical relationship with his feeling, accepting semantically that 'F' in 'Fs' means 'to feel pain'. In a fragmented verbal or pragmatic account, the belief would require the three components: 'S' as the subject of his own self-belief, 'F' as the relation of feeling whatever that comes next, 'e' as the experience in question, and finally 'Fse' as the bond that instantiates the subject into a logical relationship with his feeling. In this second case the fragment 'F' is a pragmatic manoeuvre for it does not instantiate any specific feeling, the content acts as a connector —however it being non-transparent (as being senseless) using McDowell's (1986) term, can be discussed and opted to define or not such use of 'F', because the actual bearer of 'F' is the very subject by means of 'e' under the condition of the bond 'Fse', which makes clear how 'F' is not instantiating F as a content, but

the proper notion of relationship as installed in a pragmatic account of the bearer e, by words usage and the use of language that in particular linguistic niches of the world have developed a family of several connectors ('to be', 'to feel', 'to experience', etc.) for introducing the meaning of e through 'e' being connected to his own subject, or to any other agent that claims to be holding a belief upon his own experience. 'F' does not work semantically as a designation because it is a relationship between designators without instantiating a bearer. This is similarly occurring in other phenomena, as non-instantiating articles and demonstratives (eg, 'the' does not instantiate any evidence, referent or suitable bearer), claims about numbers (eg, '9' does not pick up any reference beyond our own capability to resolve algebraic topics of belief), or time scales (eg, the meaning of words like 'tomorrow', 'today', 'yesterday', 'ago', 'late' functions with particular attention to the conditions that justify the usage of such term as a proper account of what it depicts, because the reference can vary in a random fashion). Some relatively modern works on these phenomena have studied them as indexicals (Cf. Perry 1979; 2000; Salmon 1986; Kaplan 1977; Shoemaker 1968; Kripke 1979; Predelli 2002; Schiffer 1987; Salmon 1995; Kaplan 1969 over Quine's de re and de se beliefs; and Castañeda's 1968 studies of self-knowledge and deictics), however the proper idea behind logical relationships is a triggering common place that has opened the path for hundreds of years of reflection, and some derivatives of such thinking can be appreciated in relationships being treated as similar issues as indexicals are.

This makes the case for the following structures of self-narratives (SN) in 1st and 3rd person perspectives producing self-beliefs:

1stSN S B (<'S', 'F', 'Fs'>  
& 3rdSN S B (<'S', 'F', 'Fs | r'>).



—

*Add. III — On Double Feelings.  
Examples from Neurogastronomy,  
Cognitive Neuroscience, Psychiatric Sexology  
& Therapeutics*

Navigating through literature, some critical evidence has made the case for practicable studies on double feelings, especially regarding the neurogastronomy of flavours, cognitive neuroscience of emotional experiences, psychiatric sexology and therapeutics.

. *Neurogastronomy*

Flavours are generally understood as integrations of different bio-paths that get active in multiple ways and exhibit long-rooted interconnectivity. A very neat circumstance occurs when described by propositional accounts with words, as it is the case of hot and bittersweet. While eating, tasting hot flavours gets explained as a chemioceptive articulation of substances that affect nociceptors in the tongue (thin fibres sensitive to an inflammatory medium utterly connected with self-evaluation and integrity, pain-kindred systems in the brain), measurable and observable as in cases of abrasive pain and thermal induction of taste (Cf. Le Gérer 2002; Shepherd 2012).

Odors, flavours and emotional experiences are absolutely vital for assuming hedonic action of daily constant appearance. They are a critical organic disposition that binds a vast multiplicity of activities of the nervous system for what seems to be single actions (see, for example, aversive odors and affective enactment in Zald & Pardo 1997). The currently unexplained case of synesthesia with smells and other perceptions (Cf. McGurk & McDonald 1976; Morrot, Brochet & Dubourdiou 2001) works in the same wave, understanding how our perceptual realisation of (emotional) experiences tracks func-

tional differentiated biological paths (Melero et al 2013, 351) that get enacted in association due to evolutionary cooperative routines in certain species (see the case of the ‘multi-uses insula’ in Kurth et al 2010). The issue of the bittersweet feeling is centrally very similar: as a matter of fact it has its own linguistic definition of ‘bitter & sweet’, which invites us to think there is no way to perceptually introduce an isolated, single semantic content for that flavour in certain cultures, for which there exists no unique aspect appropriated towards bittersweetness, but a dual one, whose condition of directed hedonic double feeling is interpreted as bitter (aversive) and sweet (pleasure) simultaneously.

. *Cognitive Neuroscience*

A major example has been studied with gelastic seizures of cry and laugh, that expose the peri-pathological shifting between each other (Cf. Arias 2011, 419; for studies of personality and gelastic episodes, Cf. Mobbs et al 2005). A generally accepted hypothesis currently points out a neurological index in the mesencephalic-pontine junction: the model exposes how both crying and laughing would be correlated with the dorsal region of the mesencephalic-protuberant union, rooted on peri-aqueductal grey area and the reticular formation, mainly enervated by the basal ganglia, hypothalamus, thalamus, cerebellum and the temporo-frontal cortical complexes. These differentiated paths seem to have evolved cooperatively on account of laughing and crying episodes. Patients suffering from gelastic crises, emotional incontinence syndrome, affective lability syndrome, involuntary expression of emotion disfunctions or the pseudobulbar syndrome of affect (several forms of cataloguing a very similar phenomenon-observable in subjects of different central pathologies as CNS’s traumatism, amyotrophic lateral and multiple sclerosis, strokes, tumours, schizophrenia, Parkinson and other dementias,

to which gelastic seizures help maintaining) assume a primitive duality in their living emotional experiences if being conscious of having a crisis of such type (Parvizi et al 2009). The dual phenomenon can be observed since there are well known anatomocynetic tracks that lead to certain asymmetries in relation to a generic laughing picture, for example, contraction of superciliary and frontal facial muscles (which would not occur in generic cases) seems to indicate an attempt by the subject at rather avoiding laughter or controlling it somehow (Tanaka & Sumitsuji 1991). Experience of laughter (not the jocose feeling towards a referent accompanied by laugh, but the experience of being laughing) and its incontinence, thus enhance two feelings that play in contraposition of personality, the one of laughing as such and the one of frustration and mercy, both towards the same topic or focus of attention simultaneously: the activity of being laughing.

#### . *Psychiatric Sexology*

The example on psychiatric sexology can be explored with the clinical need of classifying groups of philia as engaged by the sexological concept of 'fetishe', resulting in the category of 'philic fetishism' regarding psychiatric concerns on paraphilic interests. The definition of fetishe shall be enclosed in a strong condition, considering it a topic or focus of attention (including a living one, in contrast with non-fetishistic philias) towards which a subject feels erotic arousal, being it at the same time a focus of distress or revulsion in general circumstances for the same subject. In the dynamism of philic fetishism, a referent (object, theme, issue) that gets usually neglected, avoided or rejected by cultural, biographical, biological, social or further reasons, turns into an excitatory focus of interest in erotic circumstances for this subject (podophilia/retifism: feet, urolagnia: urine; coprophilia/fecophilia: feces; menophilia/hematophilia/

hematolagnia: blood; trichophilia: hair; pique-  
rism: piercing one's or other's flesh; salirophilia:  
covering oneself with earth and mud; and the  
like for saliva, rotten food, etc.).

These contexts indicate a double emotional approximation, one which in certain pathological cases presents psychiatric pictures of shame, guilty, however pleasing, happy dynamisms at the same time, as given in the public practice of erotomania in adults complicated with coprophagy (masturbation linked to being fed by one's or other's faeces), necrophilia (aligned with its secret maintenance), vorarephilia (or Saturn's desire: being eaten or eat someone alive in a sexual frame), or hypoxiphilia (asphyxiation) and others. Such practices (all of them can be self-inflicted, like auto-coprophagy, auto-asphyxiation...) of consented duelling, masochism, sadism, algolagnia and erotic algiomania are, by definition, dual: at least two emotional experiences need be valued simultaneously for finally producing the sexual communion of pleasure, being it the reason of why it is possible for them to come to a successful and effective sexual activity with something that may appear to them repugnant outside the sexual frame.

#### . *Therapeutics*

Recent studies have put the focus of attention in contrasting the narratives about the effects that contextual pain experiences had in the life of victims in different, transcultural populations. Reflection on propsychotic group's narratives can be especially important for increasing key values in mental health evaluation and prognostic standards (Yu et al 2015). For example, the case of survivors from the Rwandan Genocide was documented due to the ages of the traumatised population, 20-35 years at 1994 when the phenomenon took place (Cf. Rugema et al 20015). Treatments for recovery from catastrophes without emotional disposition or acceptance due to double feelings's gateways re-

duce the possibilities of therapeutical success. Generally, these patients tend to be unable to characterise whether they lived or not specific situations as they narrate them, sometimes overpowering the scene, other avoiding details or neglecting critical information, other times being indeterministic in how they feel towards what they lived. Avoidance of pain and horror shocks has been adopted by these populations as a cognitive coping strategy that affects self-assessment in multiple dimensions.

How facing multiple perspectives on catastrophes concerning past and present identifications of pain permeates the way such emotional experiences affect personality, treatment and self-narratives. Traumatized patients require much more attention and personalized care than general populations for being diagnosed and approached in therapy. This is assessed by the relation between bipolar patients presenting mood instability and compulsory admission for hospitalisation (Cf. Patel et al 2015 in schizophrenia and other mental disorders).



## QIII, Chapter §10

### Transference of Trusted Knowledge on Pain by Contextualising Empathetic Perspectives.

(In Niche D — Framing Interpersonal Characterisations)

☛ 364 — 369

—

#### Parts

. *Introduction*

I — Actors, Beliefs, Utterances, Attitudes

- . *On Ostensive Definitions: the Boundaries of an Ideal Pain*
- . *On Naming Emotions: Names that Bear the Meanings of Experiences*
- . *On Transparency When All the Bearers Force No Common Bearer*

II — 1st & 3rd Person Perspectives Self-Beliefs

III — Transferring Trust: Transference & Simulation

- . *The Limits of Using a Convention with No Standard*
- . *From Private to Public Traits: On the Logics of Partial Simulation*

IV — Incorporating Trust to Transferred Value

- . *On Propositionality as Conventionality: Enriching Attitudinal Feelings*
- . *Incorporating Trust through Enriched Contrast*
- . *The Role of Empathy on Propositional Trust: Discerning Fake Attitudes*
- . *The Role of Sense in Trusted Knowledge Transference*

. *Closure*

—

*Add. I* — Relating General Pragmatics with Partial Simulation

*Add. II* — Ergonomic Applications to Artificial Intelligence Assisted Diagnostics

## *. Introduction*

This chapter explores the field of cognitive ergonomics in its implications to medical information theory. This involves the sequence of common distribution, protection, sharing protocols, management, trust activities and decisions as regard to many participants in the movement of clinical data, including relationships of the kind patient-physician, patient-instrument, physician-instrument, physician-physician, etc. This work examines how transference of self-beliefs on pain is performed from pain-bearers to analysers, how the second assess external beliefs, and can trust on shared knowledge from a naturalised, contextual, perspective epistemology standpoint.

The idea behind the topic is that experiences are, yet to the contemporary exploration, unable to be transferred: one would not be able to experience the pain of any other self. Beliefs, however, or their contents, are constantly being communicated, exchanged: by being shown through behaviour, linguistic patterns, meaningful images, or pragmatic accounts as utterances and speech acts, they form our principal means for evaluating others's experiences, informing valuable knowledge. Bringing the issue into a belief-&-action-based framework, it is expected to enhance the way clinical recognition, characterisation and assessment is carried out. In a medical sense, beliefs are constantly being subjected to transaction, in which two or more parties agree on trusting given or extracted information to become, for instance, diagnostic criteria, epidemiological data, standards, or case reports.

Transference of beliefs is an interpersonal phenomenon that affects therapy theory, neuropsychiatric assessment, and experimental diagnostics (especially for resolving grounding logics for current experiments in Artificial Intelligence applied to diagnostics and clinical assessment). A major reason is that the con-

cept of transference allows the very practice of evaluation, offering deep theoretical and philosophical support in the elaboration of scientific, ergonomic and engineering models concerning medical transactions of valuable information that have the potential to shape clinical criteria informing with diagnostic values when interpreted and contrasted correctly. The chapter chases a definitional framework for answering how are we able to define that such a transference is actually being of trusted knowledge (of contents of beliefs that manifest actual 'felt pain'), instead of entirely simulated knowledge (of contents of beliefs on several characteristics of pain, but that do not manifest a phenomenon as enriched as 'felt pain' would be experienced). As a first proposal, the chapter provides a protocol for introducing trust in assessment processes, regarding transference of experience-based self-beliefs even when the analyser may be holding a simulation in his or her belief about the analysed subject's experiences.

The text is divided in 5 parts. The first part addresses the implications of conceiving of subjects of beliefs as actors of their beliefs, manifesting utterances and attitudinal traits of a felt pain. Discussion focuses on how these actions serve for defining, naming and meaning experiences to others. The second part introduces perspective theory reviewing how beliefs inform analysers about how actors of pain self-beliefs experience pain, involving 1st and 3rd person perspectives into such self-beliefs for serving an overture to analyse experiences propositionally. The third part deals with trust: it distinguishes between trustworthy and untrustworthy transference, describing the former as a sort of communication involving enriched public traits of contents open to any subject of such transaction (contents identified with conventions that both parties agree on), and the latter as a simulation, a belief composed by not-as-enriched-conven-

tional-traits of contents as felt pain beliefs are suggested to be (involving private traits). The notion of a 'partial simulation' is presented as a possible propositional solution for understanding transactions of trusted knowledge through beliefs. The fourth part deals with how this enrichment of traits of contents of belief is exhibited by the pain-bearer actor through behavioural patterns (conventionality through propositionality). It presents a logical architecture for empathetic perspectives, resolving a definition on how assessment is able to incorporate trust to transferred value through a common background based on agreement. Below, an index for the chapter is offered to support the reading. A final closure and two *addenda* to the logics and pragmatics concerning partial simulation and Artificial Intelligence applied to diagnostics and clinical assessment end the text.

There is a hope this proposal could help in providing methodical and theoretical tools in order to build increasingly better instruments for measuring self-beliefs on pain and other complex experiences of diagnostic use.

### I — *Actors, Beliefs, Utterances, Attitudes*

Experiences suffered by a subject are yet, to the current instrumental development, unable to be accessed by an external analyser. The process of transferring valuable information about others's experiences (ie, data that would not be able to fit in any kind of truth-falsehood schemata), makes the case for discerning whether or not during such transference value can be maintained. This work reviews this problem engaging it in propositional logics of perspectives and beliefs, arguing that trust, instead of truth, could serve for assessing the value that is being transferred, through multi-party agreement. Understanding that some sort of simulation would be involved in the processes, the protocol tries to develop an empathetic ground for characterising the value of information, as

the proper agreement implicit in overall clinical assessments requires the transference of information to be valuable (trusted) for a proper diagnosis to be developed. From an ergonomic outlook applied to solving this scenario of medical information theory, the transference would be necessarily interpreted as of 'valuable quanta': ie, shared fragments of information that have the potential to shape clinical criteria informing diagnostic values when interpreted. As a working definition, clinical data are value, a future worth, which may serve for a patient to be correctly identified, diagnosed, taken care of, treated, protected, intervened or engaged in specific therapeutical processes. Such value is stored in multiple forms of quanta for each patient: measurable amounts of information gathered in clinical registers, appointments, hospital files, prescriptions or clinical reports, but also volatile fragments in the memory of healthcare givers, medical personnel, and acquainted physicians diagnosing specific patients. Generally, all of this information transferring presents a useful role for undertaking etio-pathological evaluation: in a future, the more this pluralised information constitutes the feed of a broader anamnesis, that could be stored and cross-analysed, the more accurate this assessment would come to be.

To the extent of practice epistemology (as accounting for emotions as practices of social import too, Cf. Scheer 2012; Fischer & Manstead 2008), the assessment of external agents's experiences —which may be other people, patients, non-human organisms; and for experimental research: synthetic structures or Artificial Life (A-Life), or software patterns in Artificial Intelligence agents, Artificial Memory agents, Artificial Cognition agents, or the like— can be understood as a problem of interpersonal (inter-agent) transference of contents of beliefs, where subjects are 'subjects of belief' (subjects of an contextualised community of knowledge, an 'epistemic community': Cf. situated practice

epistemology and social epistemology foundations in Longino 1990; 2001; Fehr & Plaisance 2010; Kitcher 1993), and their knowledge (trustful or not) expressed by the contents of their beliefs. Maintaining that self-beliefs make use of pain, or multiple traits of pain, as being able to participate as clusters of traits of these contents of a propositional belief, expressing that the believer is suffering pain, the transference of some of such traits of contents to other agents is to be studied as laying the foundation for a propositional assessment theory. Propositional beliefs, contents and traits frame a logical philosophical concept, which may be projected into other organisms and synthetic entities as specific forms of abstracted transferrable acts. In human subjects, pragmatics is taken to study many of such acts as based on language. Action has received an immense treatment in philosophy and logics (Cf. Bishop 1989; Davidson 1963/1980; 1980; Frankfurt 1978; Gallistel 1980), and to the extent of this dissertation, action is thought as mediated and composed by emotional and affective orientation, and its manifestations can be studied by defining how it participates in beliefs (self-beliefs and beliefs on others's beliefs) and decision-making schemata, for example analysing an agent believing something in relation to his or her practice of deciding trust on other agent's experience (Cf. Schwarz 2000 on emotion and decision making through action; Cf. Zhu & Thagard 2002 for a review on the role of emotion in human action).

In such transference, those contents bring up a textual, narrative qualitative feed (ergonomically speaking, contents are a contextualised-to-the-patient chain of diverse valuable quanta) supplied by a pain-bearer (the agent holding the belief that him or herself is suffering pain: eg, a patient), which can be contrasted with the contents of belief of an external agent (a 3rd party analyser: eg, a physician, an instrument, an artificial agent, etc.). This contrast activity is grounded on trust: in other words, the

information provided by the former is believed to be trustworthy by the latter (that actual pain is being felt by the pain-bearer) when a threshold of similarity about the contents of belief on pain held by the second agent is overcome (this threshold is finely developed by means of empathetic attitudes, and can be studied propositionally as well, *infra*). Assessment, termed as an interpersonal transference, would function like a measurement strategy (Cf. QIII, §8) that works by comparing clusters of traits of contents composing self-beliefs, beliefs and judgements regarding the proper agent that holds them. This section will review some theoretical inclinations in the philosophy of language and pragmatics that afford a clear consideration of the problem.

. *On Ostensive Definitions:  
the Boundaries of an Ideal Pain*

On 'Philosophical Investigations' (Wittgenstein 1986; and the 2015 version; this work will be quoted by the sequence of aphorisms indicated by §# or page), Wittgenstein spends an appreciable number of pages considering the problems pain and its transferability bring into theory as examined propositionally. To such a pursuit, emotional experiences of pain, conceived of 'pain as such' (ie, a direct, straightforward sensation in which oneself thinks of him or herself being feeling, for example, a toothache), present a sharp obstacle: they seem to bear no linguistic track in order to search for propositional meaning, nor epistemic reference (a suitable evidence that would be accessible for an analyser to develop knowledge upon it). It just occur through belief transference: when the pain-bearer agent (acting as an informant), is asked by another agent (acting as an interrogator) to define such pain, happens that 'pain as such' is put on words, and transferred as 'pain as defined by the informant'. When understood by the interrogator (acting now as an analys-

er), it would be taken as ‘pain as defined by the informant and understood by the analyser’. Through this propositional process, there are multiple opportunities to loose content and value in transaction.

For instance, if asked about its ostensible definition (replying to a question of the kind ‘what is pain?’), the informant, in order to answer it with justified knowledge, would find a difficulty in relation to the very interoceptive nature of pain events (Cf. Craig 2008): his or her perceptions need of a personal experience for building a proper understanding. Implying transferability, one can say that the intimate feeling of specific pain events behaves as the ostensible definition for the notion of ‘pain as such’ the person handles. This notion is what the interrogator is asking about, and what the informant is preparing to deliver: valuable content transferrable by the word ‘pain’, related adjectives and derivatives (a semantic field to interact with), or another action. However, by introducing words usage, the issue addresses how language can search for the bearers (evidences that serve for ‘bearing’ the burden of reference) of all the nuances of the experience the informant is experiencing without transferring the experience. An external analyser could ask: would pain-related linguistic patterns be appropriate enough to understand the ostensible meaning of pain as felt by the bearer?

The immediate answer is negative: by no means the interrogator would undertake an intimate feeling of the pain the informant is feeling, for the pain event cannot be transported as will to any other person, not even to the same person in a different time: pain would be other, always different, always appropriate to the person at hand, to the case at hand, unable to be transferrable. It seems that transference loses pain: the ostensible definition of ‘pain as such’, if it is respected to be the ‘experiencing as such’, would never be enacted by any other agent than the experiencer: the actor of most of the agency involved in giving an ostensible definition of

‘pain as such’, would necessarily be the same and unique actor of most of the agency involved in experiencing it.

Both, the interrogator (which is also the analyser) and the informant (pain-bearer) are doomed to the boundaries of an ‘Ideal Pain’, a pain that is a reflection of the experience, a second thought upon the perception. It does not suffice for a definition of very meaning of ‘pain as such’ (what is perceptible, feelable), but of the meaning of a pain that is in actual terms suffered by nobody, and just a recreation. This is, to utter the word ‘pain’ or any other related term, used for transferring a valuable content that serves as an ostensible, straightforward definition of the experience of a pain-bearing actor, is to act behaving as if the interrogator has a basis for understanding such behaviour: a common linguistic standard to which approach the informant’s feed.

Following Wittgenstein’s aphorism §30, this ostensible definition would be possibly understandable because it explains «the use —the meaning— of the word when the overall role of the word in language is clear.» (Wittgenstein 1986, 14). One can be tempted to explore this sentence translated by Anscombe in a narrower manner: ‘the ostensible definition given by the informant explains to the analyser the usage —the meaning (*Bedeutung*)— of the word when it is already clear for both what role shall the word generally play in language’. In such ‘agreement on meaning’ (using the pragmatic sense of agreeing the limits of words usage, a ‘joint-meaning’; Cf. an integrationist view in Carassa & Colombetti 2009), no common definition for pain is able to be clear for both subjects: distributively, one definition for pain at a certain case will be held by one subject, and another by the other subject.

Clarity may require involving feeling into the ostensible definition: to actualise the content of the definition as a behaviour, as an action. To put an explicit example, let the informant kick



the interrogator as an action performed in order to serve as an ostensible definition of 'pain as such': the definition will deliver a general picture of what the circumstances of pain are (at least one, the given one, this precise pain event), and so the analyser must assess the meaning of his pain by being kicked, instead of being able to assess the meaning of an universal pain by such definition, for what the analyser felt shall be the role of the word 'pain' plays as defined by 'kicking', not defining, thus, a universal sense of pain as a total concept, an ostensible definition for the question 'what is pain?'

Engaging the circumstances of pain, the recollections of the pain event shall track the meaning of the word 'pain', making transferrable to one another what pain experiences are to mean. But, vaguely, the action will just behave as the ostensible definition for the meaning of 'pain in kicking' and, regarding the actors, it would just inform them about the meaning of 'pain in kicking felt by the kicked as performed by the kicker'. Obviously, the kicked (who asked) will never perceive the kicker's pain: the analyser will just almost perceive an invitation to a relatively similar affect of what the informant thinks kicking produces. No agent involved in the action (any actor) will get a fully propositional answer without knowing beforehand what is 'pain as such' (yet there or experienced empirically), let alone analysing qualities or thresholds of pain degrees. The circumstance requires a pragmatic account to specify how the definition of an experience is used: this is, by an agreement on clarity, actors need to use words 'transparently', in McDowell's (1998) terms (*infra*): with a transparent attitude.

The problem grounds on the interrogator asking about something that cannot be realisable without intervening his own experiences as an ostensible definition too, when no one but him or her as an actor could answer. The meaning of an experience appears to be intimate to a 1st person perspective.

. *On Naming Emotions: Names that Bear the Meanings of Experiences*

The majority of natural thinkers on emotion has been reorienting discussion this way (Solomon 2008), that emotions as such are not natural kinds, singularities or realms to be ascribable to people (Cf. Griffiths 1997; 2004; Griffiths & Scarantino 2009). Emotions have been thought instead as building up character traits not from pure states, but from unfolding step-by-step processes of personality consolidation, that get filtered through our actions, attitudes and conceptions, as Goldie (2000; 2003) studies, and as cumuli of active thought that is labeled and marked once we have felt it, as Reddy (2001, 102) specifies. Emotions fit situated patterns of exclusion and inclusion of oneself and others in the environment, functioning as attitudinal styles of communication (Gammerl 2012). Historian of pain Joanna Bourke insisted in the way we name and write about our own experiences (Bourke 2003) for it is one fact that overexposes the social nature of our sentiments while feeling them through separate time contexts; making use of Wittgenstein's thesis on mental language through social interaction (Bourke 2003, 117).

Examining an example with names, Wittgenstein (1986, §31) famously exposes the idea of the king piece in the chessboard and the ability to use the term 'king' while pointing towards the figure for an ostensible definition that would answer the question 'what is the 'king'?' or 'what is the name of 'this piece'?'. This dissertation initiated the propositional discussion on self-beliefs and self-narratives. In an analytical view, if an interrogator was to care about the name of the piece, this interrogator acting as the analyser would need to know what is it for him or herself previously, for so we say 'this is the king', 'this is called the king', at least in a case in which the interrogator knows what chessboard pieces are. This focuses on the fact that the one who asks needs to track the meaning of

the term 'king' through his or her meaning of what that piece is for him or herself (a self-belief composed by contents with a comprehensible meaning), by which the analyser will finally develop a sense of the proper term (the term would instantiate the proper meaning if used contextually correct).

The interrogator will be able to know the meaning of the king piece for him or herself regarding the fact that is the analyser who asks, is the analyser's circumstance, the analyser's memory scenario, and the analyser's entire need-of-the-term what is at stage. The analyser needs to know first what is the Western board game (a knowledge for him or herself, a biographical knowledge) for finally understand the meaning of the term 'king' (Cf. Wittgenstein 1986, 14). Now, if we ask 'what is pain?', it is observable there is a difference concerning the sense of the term there and the sense of the intended term of this other question: 'what is the name of this sensation?'

How could any informant point towards a feeling he is having privately while using the name 'pain' for building an ostensible definition of his proper feeling? How would an analyser that is not the very interrogator point towards something like 'this sensation' if the experience of such 'this sensation' is never felt by the analyser? Wittgenstein would expose right the generally accepted idea that «only someone who already knows how to do something with it [with the name] can significantly ask a name.» (Wittgenstein 1998, 15).

In point of fact, it is always searching for understanding a thematic assumption: 'to know what we are talking about when we talk about pain'. It transforms logically:

1, This is pain = a Precedent: This [experience] means pain

2, This pain [this experience meaning pain] is called 'pain' [the word 'pain'].

The problem comes when speakers cannot epistemically access the bearer of such a name, and tend to simulate it through reifying the word they use in agreement, however not transparently, thus involving a fictional bearer:

1\*, x means y

2\*, y is born by the name 'pain' (ie, the word 'pain' bears the suitable topic pain)

3, The name 'pain' is introduced to transfer some traits of x.

Given this structure, the analyser makes language (eg, a name) to bear the burden of reference of a given experience. The problem is that the epistemic precedent ('1, This is pain') tracks a very sensitive notion that is felt by each of the actors differently and properly, being any kind of particular transference of x impossible to analyse *prima facie* by no other actor than the one who is actually instantiating pain (the pain-bearer, in a 1st person perspective self-belief, *infra*). Analysers would lack the epistemic root and channel to others's pain, and for it analysers cannot but simulate for themselves in a 3rd person perspective others's suffering in 1st. Actors use the word to channel it, which recreates the word as a bearer.

However the very transference of the word loses some of the main traits of the sense of pain as felt by any other pain-bearer, as the only possible bearer of pain is no other than the subject who suffers it: there is no phenomenon as pain-as-such existing freely felt by no one. Introducing the shortcut of an ideal Pain will solve instrumental transference, but will not hold theoretically for a model of transparent transference, as there is no unique possible bearer of a universal Ideal Pain. Without a bearer, thus, the expression would be senseless, using McDowell's (1998) characterisation. Transference loses value.

. *On Transparency When All the Bearers  
Force No Common Bearer*

Language sometimes loses the sense and the meaning of a given proper name because there is no primary epistemological access to the roots of a referent, or the immediate instantiation of an evidence, like in the case at hand. References sometimes get abstracted or reified by speech (Cf. Yablo 2003; Chang 2012), affecting as well the recognition of scientific topics. The problem focuses on how the bearer of a name can be needed for understanding the sense of our terms, pragmatic uses and utterances. For studying this problem, conclusions from social and situated epistemology of science (applied to medical assessment practices) can be compared with conclusions in propositional logics of belief formation and reference. Starting with the second field, John McDowell (1998, 180-185) installs a similar question with the example of an interpreter set in an ambiance of foreign speakers. It is to note that this text will make limited use of McDowell's characterisation, more clearly, to the extent of his proposal for dealing propositionally with sense in a theory of intentional transparent words usage, as transparently would tend to mean managing expressions in accordance to agreed assumptions that 'what we are talking about' is clearly suitable to every subject in a conversation.

For the sake of simplicity, let us concede that pain was something like a suitable object of the world (in McDowell's terms), an epistemologically immediate and accessible phenomenon, a 'scientifically suitable' topic for an instrument to measure. A group of speakers (actors reflecting on an experience: subjects of belief producing and sharing contents of belief) know of such phenomenon, however let us put the case that this phenomenon and the way these speakers name it and use words towards it are two factors unknown for the interpreter. McDowell builds the case as follows: «someone interpreting a for-

eign language will himself already have a name for a suitable object (say a planet) [...] intelligible in terms of propositional attitudes about it [attachable to the foreign speakers who act that way].» (McDowell 1998, 183), then the interpreter can generate clauses like 'Aleph' stands for Jupiter', as Jupiter (the planet reference) is accessible to the interpreter's knowledge: he would just need to substitute the name 'Jupiter' by 'Aleph'.

In a slightly less simple case, the interpreter would not have a name for the reference (as Jupiter, a mountain or whatever instance, as no thematic assumption is accessible to the interpreter's knowledge of his language: he does not know the thematic assumption 'what are all talking about when talking about x'). Having had no occasion to use a name about it, he gets inside a game of cooperation with the rest of the speakers for grasping the topic and the name's meaning in the foreign language. For trying to understand what the present chapter calls the thematic assumption, 'what are we talking about when we talk about x', McDowell (1998, 184) writes: «his [the interpreter's] attention might be drawn to some object in their environment, say a mountain (hitherto unknown to him). He would thereby acquire a batch of theory about the mountain...», and mixing what he sees, making a theory out of those facts, together with plausible principles about the impact of the environment on propositional attitudes appreciable in those speakers, it will be sufficient for him to make sense of their utterances. If given some expression 'Afla', the writer says, then making the environment easy to assume the foreign speakers are talking their way of a mountain, the interpreter's choice will go for 'Afla' stands for that mountain'. Now, when the context disappears and some speakers of such language appear to be talking about the mountain on a different circumstance, the acceptable choice would seem to adopt the foreigners's term for the interpreter's own use, as if 'Afla' stands

for Afla' was the appropriate convention when having no direct evidences. This strategy is a form of realisation: the circumstance made that the word 'Afla' turned out a reified object, the reference, the suitable object Afla. Epistemologically, the main problem appears when the interpreter finds no bearer of the name: no planet, no mountain, no suitable topic that resolves properly the thematic assumption for every of the subjects.

Similarly, the scientific discussion on pain as a topic of analysis permeates this reification strategy: as pain is needed to be accessed through a common reference, but is impossible to be so, the proper dissertation on the referee makes the reference an object of the world, the speech reappears as a thing in the world, and the 'pain of a patient' turns out to be the 'physiological, psychiatric, neurological or therapeutical concept of pain', suitable to be studied, a pain that no one feels in an actual sense of the expression: an Ideal Pain. Through this thesis, the assumption is to create an investigation on the origins of our beliefs, on how any experience, through words usage, would reify ontologically accrediting value through performance (Cf. critiques to reification mereologies applied to scientific interests in Brenner 2009; 2015; Cameron 2007; 2010, 2012).

Turning the assumption to social epistemology (Cf. Longino 1990; 1996; 2000; 2001; 2006; Galison & Stump 1996; Goldman 1999; Solomon 2001), such a practice would configure a form of generative performance that allows a common social knowledge of scientifically approachable topics to create 'justified beliefs' about those topics as if they were suitable objects of the world. Accepting this knowledge is instrumental, and its validity responds (is 'accountable to') under the scope of some accepted practice (a scientific community agreeing on the limits of a scale, an instrument, a style of measurement, etc.), scientific information is implicitly mediated through several socially

implied chains of agreement, in communities of agreement on the value of such information, that may inform on simulated or recreated, reified contents (Cf. QII, §1; Cf. works on pluralism and contextualised social epistemologies on scientific practice: Cartwright 1999; Giere 2006a; 2006b; Fuller 1988; Kitcher 1984; 1992; 1993).

Significant attention has been put on discerning how such 'justified beliefs' may be warranted —briefly, Cf. externalism's proposal, Goldman (1979): through external causes using a 'reliable belief making process' for warranting such justified belief; Cf. internalism's proposal, Nagel (2014): for understanding that such justified belief is warranted if it is grounded on the fine details of the case to believe, Cf. Bonjour's (2010) exposition on the topic—. Discussions on how the warranting system may function will not fit the scope of this work, but the pragmatic account through which the believer trusts on them seems important. Value seems to be accounted by the proper transference of similar contents of belief, names, pragmatically accountable to a linguistic niche where the context is supposed to inform about the origin and validity of such transference through agreement. Generally, the theoretical background on propositionality is based upon truth tables that present the functions and conditions to satisfy by which propositions relate to their having sense (in a Fregean style). In dealing with non-transferable self-beliefs through the framework in the style this work proposes, it would be logical to substitute truth by trust (as there is no way to ascertain whether it is true or not that other subject except the analyser is suffering pain or any other 1st person perspective self-belief), conceding that trustworthy beliefs are those which fit the conditions of an agreement upon the context of a transaction of value, being the limits of such agreement mediated by the subjects that conform the community in which the agreement has been decided, generally by

convention. Managing valuable information through trust would require value to get transferred through agreeing on the context of such transference. If the context fails, information is not valuable.

To put an example of how agreement presents conditions of value through communities, the development of theory change may serve as a reference: in a country or a historical context where certain disease is not considered (agreed in community) to be so, information upon the patient who bears it, taken as a disease to deserve treatment, would not fit to be valuable information. Homosexuality or classical hysteria would imply no clinical value for rendering a proper disease in the majority of modern countries today. This prompts with a significant implication from social epistemology to belief formation and actualisation (Cf. studies in Bjørdal 1996; Frijda & Mesquita 2000; Fiedler & Bless 2000): what-to or to whom is the content of pain beliefs addressing the bearer? In the case of pain as a scientific topic, when the content is upgraded from mere language to real phenomena, the question to ask for tracking the context is 'where is the bearer?': the bearer of the reference pain is always a person, each person. But this is conceptually vague, for the experiences of the others are not epistemically accessible, and thus we cannot trace a root for sharing a common basis for assessing whether others are feeling pain, nor even to answer the question of a plausible ostensive definition for their pain. While every actor remains a bearer, it results as if there is no common bearer.

For a vision like the one handled by McDowell, clauses with names that have implicitly no bearer (common) do not offer proof of having sense, for no immediate suitable object in the world «is replaced by a name he [the interpreter] could use to express a theory of his own about an object.» (McDowell 1986, 184). This adheres to Wittgenstein's requirement of self-belief and self-narratives: we need to look

at the term for our uses, in our conditions of life, in our view. Thus, if a sufferer feels pain, and raises a belief about it forming contents concerning pain, in order any analyser to clearly understand him, such content of beliefs must have had to be found in the analysers previously, which only occurs in the sufferer. The rest of analysers would manage such content regarding the pain of the sufferer as a senseless content of belief. Hence the obstacle: «names that, in an interpreter's view, have no bearers cannot, by that interpreter, be handled in a theory of sense in the style I [John McDowell] have considered so far. In this view they can have no sense, if a name's having a sense is its being able to be dealt with in that style.» (McDowell 1986, 185). In his concern, those terms would be tracking no sense because lacking bearers affects the way the interpreter can sincerely use the term.

To the extent of transferability theory, the bearers actually exist (sufferers exist), but what does not exist is the proper epistemic access to their contents of belief when those are self-beliefs: «if the name has no bearer (in the interpreter's perspective), he cannot describe any suitable related belief in that transparent style.» (McDowell 1986, 185), and regarding that his or her beliefs and attitudes towards that phantom or inexistent bearer are null, or at least not sincere for there are no specified conditions to satisfy, the interpreter would not be understanding 'transparently', using McDowell's terms, any proposition. For an ergonomic model of medical information transference, this implies there is no explicit value of trust surrounding what is being named, shared, communicated, transferred. How could we incorporate trust? How could we make explicit the implicit trust of a pain-bearer's felt pain for an analyser?

When analysers (eg, therapists, clinical researchers, diagnosers) try to answer the thematic assumption 'what are we talking about when we talk about the patient's pain', and approach the topic clinically, they would need to make

use of certain pragmatic accounts like “the informer’s pain’ stands for the informer’s pain’, as in the case of “Afla’ stands for Afla’; however the analysers’s belief is never making sense of the informer’s pain sincerely, transparently, as no one but the patient has a precedent with which to substitute the expression, no interpersonal standard to fit, no sense to deal with. Propositionally, measurement instruments face strategies that make their observation remain about phantom conclusions, suggestive clinical noise reifying an Ideal Pain that is, epistemically speaking, as trivial for trustworthy understanding as it would be uttering recreational names, (eg, “Ulambo’ stands for Ulambo’), or substituting critical terms by names in a foreign language with no one translating them (eg, “고통’ stands for 고통’).

The critique about the current panorama of measurement strategies (QIII, §8) is implicitly linked to this situation, and invites to rethink to which extent a physician is subjected to contribute with his or her personal experience, case-to-case interpretations of previous events, feeding with non-selective information, general standards, or epidemiological generalities, the report about his or her patient’s experiences as the instrument does not, or cannot, allow the patient to inform with a ‘broader resolution feed’ the requirement for a proper measurement.

Another problem affecting clinical assessment theory is that this same process may happen with the very bearer of such experience as time makes this person a different instantiation of him or herself in a different moment, with a distinct circumstance and just accessible to the felt pain via memorabilia, effortful memory, as predicted in QIII, §8, and QIII, § 9. If the patient results to be in a position of no reflection, no transparent bearer will be recalled, contextualising the contents of his or her own beliefs: transparency gets affected replying with ‘thin resolution feeds’ regarding personal experiences with such a vagueness that arbitrariousness and

spontaneity may bias the measure (Cf. Broderic, Junhaenel & Turk 2004; and conclusions in QIII, §8).

## *II — 1st & 3rd Person Perspective Self-Beliefs*

By the second half of ‘Philosophical Investigations’, Wittgenstein’s discussion is dappled with thoughts considering the differences between the feeler and the one who tries to know how something feels like. He begins writing (Wittgenstein 1986, §280-281) how 1st and 3rd person perspectives share something relatively unique, it being that self-beliefs are produced by subjects (he would address these as lively beings or organisms; here these are conceived of as actors) with intervention of behaviour (the different forms of a subject’s action). Ontological considerations aside, he recognises that pain is something highly private and intimate (Wittgenstein 1986, §283), and that the possibility of certain emotional experiences as pain, which can be just imagined through the performance of someone or something that feels them, may irrevocably introduce subjectivity: the famous concept that the world and possibilities of agents would be framed by the limits of their language, the limits of what they can subject to names.

Turning to naturalised, perspective epistemologies, agents are ‘situated subjects’ of belief, and the very context of their epistemological access to their environment, others, others’s experiences, etc., would work as their theoretical horizon: as something they cannot escape from (Cf. Longino 1990; 2000; Cartwright 1999; Solomon 2001; Giere 2006a; 2006b; Kitcher 1993). The limits of the context, of the circumstance, of what is a suitable evidence, a topic for building a belief out of it, etc., for these subjects of beliefs, are the limits of their agreements, and, in certain way, the boundaries of their transference (Cf. the naturalised epistemic movements in pluralism, perspectivism and beyond in: Reger 2005; Geller

& Stockett 2006; Goldman 1987; 1989; Merton 1973; Solomon & Richardson 2005; Giere 1985; Harding 1991; 1993; Mitchell 2002; 2003; Kitcher 1984; 1992; 2003; 2004; Kitcher & Salmon 1989). The sense of an agent subjecting an emotion to him or herself, ascribing such emotion as his or her emotion (this means, orienting it towards the horizon of him or herself), actually organises a perspective in which a specific kind of beliefs is the consequence of subjectivity: self-beliefs —pluralised beliefs (involving dappled, many subjects) informed through situated knowledge contextualised to the experiences of the believer that holds them.

The theoretical protocol provided by this chapter suggests that by treating self-beliefs through perspective epistemology, especially applying some conclusions excerpted from the general theory developed by Peter Lawrence Goldie (2000; 2002a; 2002b; 2003; 2004), the protocol may introduce experiences as contents or traits of contents of beliefs, informing research on evaluation (especially clinically and therapeutically) and its experimental application (especially on Artificial Memory and Artificial Intelligence Assisted Diagnosis) with a new tool for embedding trust propositionally. Depending on the perspective that defines the ascription of such emotion to the believer, self-beliefs can be thought of consisting in 1st and 3rd person perspective.

A 3rd person perspective self-belief would consist of general ascriptions, directed to a self that is the proper believer, in which the narrative of the ascription is propositionally limited to a 3rd person characterisation. Clear examples are remembrances, memories, future hopes or past identifications: ie, 'I felt pain', where 'I' is 'the believer introduced as a subject in 3rd person'. Propositionally, the subject of belief would hold a propositional belief (using a variation of the general framework initiated for studying self-reference and indexicals by Perry 1979; 2000; Salmon 1986; Kaplan 1977; Shoemaker

1968; Kripke 1979; Predelli 2002, etc.), such as 'B (...)', through which he accesses a second past belief (of himself in the past), in which he experienced pain —thus his characterisation would be necessarily installed in a 3rd person perspective:

'I' (for it is a self-belief) = The Believer

The Believer B (<'The past Believer' B(<'The past Believer', 'to feel-past', 'pain')>).

The 'I' who believes of himself in another time is contextualised in the present, whereas his contents of belief (himself in another situation) is contextualised in the past: the suitable bearer has changed. For the name 'pain' to be transparently used, thus not being senseless, it requires a suitable bearer, which is the past believer, not the present, so the sense of pain instantiated in the belief is always a past pain, the pain as the believer felt in the past: pain in a 3rd person characterisation, even being it enclosed in a self-belief.

In contrast, a 1st person perspective self-belief (or its contents), as is suggested by this work, would necessarily define proper experiences if we agree that the conditions of such belief require to actualise its contents as of being arranged in 1st person and transparently (involving trust). This form of self-belief will actualise experiences in the sense of a strong condition, that it subjects the contents to just one very specific bearer, the believer does not change along different versions of himself, and that the belief is used transparently. With this condition, the proposal advocates to bring trust within propositionality.

This is no trivial addendum: considering Goldie's (2000; 2003) theory on narratives, emotion, perspective and directionality (Cf. QIII, §9), an agent of belief that holds a self-belief conceiving of himself as if imagining an actor in a scenario, would involve himself in such belief

as active furniture of memory, not as himself acting, and would narrate his belief in 3rd person, giving reasons or judging actions as watching a film or reading a story. A perspective shift impedes to obtain a trustworthy self-belief (this difficulty is implied in what QIII, §9 calls an ‘effortful memory’). A trustworthy 1st person self-belief would be one which is believed in 1st person, which is experienced, which is felt. In other words, an actual self-belief would be one that actualises its contents, as experiences do: when experiencing pain, pain is actual. Put as a content of belief, if this is actual, it fits for a 1st person perspective self-belief to define an experience: eg, the sense of uttering transparently ‘I feel pain’, where ‘I’ is ‘the believer introduced as a subject in 1st person’:

‘I’ = The Believer

The Believer B (‘The Believer’, ‘to feel-present’, ‘pain’).

Taking the condition of transparency as defined in McDowell (1986), if the propositional belief is not senseless, then it would necessarily express that the believer is actually experiencing pain. If one utters a sentence like ‘I feel pain’ in the belief that ‘I feel pain, but pain is not a transparent, sensed definition of what I actually experience’, then one is simulating pain: pain is not actualised, pain is not fully suitable to participate in the belief as trusted knowledge. For instance: a group of children plays a physical game, one of them pretends he got harmed, interrupting the match. He falls to the ground and utters an ostensive definition of his experience (eg, ‘Ahh!’), meaning ‘I feel pain’. Everyone would understand he has his reasons for accounting pragmatically his utterance, thus he appears to be transferring a trustworthy content of belief (Cf. Witek 2014; Haugh 2013 for the concept of ‘accountability’). However, analysing his propositional attitude, he does not actually

believe he is in pain, he believes is pretending to feel so, he is simulating pain:

‘I’ = The Player

The Player B (‘The fake Player’ B(‘The fake Player’, ‘to feel’, ‘pain’)).

The enclosed belief, ‘Fake Player B(‘The fake Player’, ‘to feel’, ‘pain’)', is a simulation. Since there is no actualised content of belief, what the player holds is a 3rd person perspective self-belief, as he is never depicted in 1st person perspective by himself within his belief, for he does not hold the belief his transparent and suitable self (in 1st person) is feeling pain, but a fake feeler who is a non-transparent and imaginary self (he in 3rd person). Without being actualised by the subjective action, the sense of the term ‘pain’ in his self-belief is necessarily not transparent, because dealing with a self-belief, the subject accounts for bearing the pain: since the subject is fake, the pain would necessarily be fake too. No evidence of pain is suitable to the belief, actually it does not participate on it—in effect, the simulator is a simulator because of his not believing that he is in pain.

### III — *Transferring Trust: Transference & Simulation*

Wittgenstein concludes that perceptive acquaintances, as forming part of the body of language-games, need to be ascribable to a form of criterion of selfhood: «if I assume the abrogation of the normal language-game with the expression of a sensation [like in the case above], I need a criterion of identity for the sensation; and then the possibility of error also exists.» (Wittgenstein 1986, 98-99). The point of ‘playing’, regarding his idea of language-games as conventions, is not just to follow the norms that configure the game, its limits, its sense, but accepting those norms as something we have to



do: action, but also trust in the others's following the rule. He asks for the rules of such an 'identification process', to which a subject rooted in a 3rd person perspective operates with a simulation of the other's 1st person view of the facts. For reaching to this identification, he claims that all the parties will need to follow the rules of conventional language definition, exchange, words usage, etc. In further stanzas he notices that by characterising others's contents of belief, error can take place. Goldie (Cf. 2000, 153-154 for a definitional background) extends a commentary from Wittgenstein's concerns on sense and meaning to emotional perspective shifting.

In his theoretical structure, Goldie (2000; 2003; 2004) assumes perspectives as narrative orientations that are applicable for our task of attributing traits of character to people. Analysers accomplish such task by having some motives for maintaining their beliefs and notions about someone's behaviour. This associates with the concept of 'belief revision' in propositional logic, applied to general information theory and Artificial Intelligence and Memory models (Cf. Gärdenfors 1988; Gärdenfors & Rott 1995; Boutilier 1996; Aucher 2003; Baltag & Smets 2006; Gliozzi 2002), and may be conjugated and applied to clinical assessment in a trust protocol of the kind this work proposes through Goldie's epistemology of beliefs, introducing a narrative schema for updating this practice of maintaining motives and reasons for justifying traits of character: ie, by empathetic accounts, which constitute a major topic of his literature.

Errors inform about how approximate analysers's contents of beliefs are in comparison to the ones raised by the bearers of experiences. Errors manifest too by hesitance: by casting doubt on their identification process, analysers suspend a total crediting of their own contents of belief, for «there may, however, remain an epistemological worry: could it be that the emotion which I so readily attribute to the other person is, in fact, not felt by him at all?»

(Goldie 2000, 182). In that case, the analyser's contents of belief would be a simulation facing partiality of information: a 'partial simulation'. Errors point out that 'accepting the norm' ('to follow the rule' in Wittgenstein's sense) may be difficult undertaking identification processes, as there is no interpersonal standard that will suffice for a pragmatic calibration of the sense of someone's pain. Wittgenstein also worries about justifying personal conditions of pain (eg, 'I am in pain'). He asks: what does it mean that I am justified before myself to that situation, «[does it mean that] "if someone else could know what I am calling 'pain', he would admit that I was using the word correctly"?» (Wittgenstein 1986, 99). Concerning medical information theory, for example, in the assessment of therapeutic use of words, the puzzle is about how could therapy theory systems build a narrative basis for pain events constituted by a criterion that rather lacks propositional transparency (therapists would not actually identify nor assess patients's experience) or allows simulating it (therapists simulate fake knowledge): returning to the limits of Ideal Pain.

*. The Limits of Using a Convention  
with No Standard*

If common expressions embed simulated or fake knowledge in the context of analysers deciphering a pain-bearer's self-belief, trusted knowledge may be difficult to achieve, as the believer would appear to them 'acting privately'. Understanding other's private contents would require to make such acts public. Consider Wittgenstein's stanza §293:

«Suppose everyone had a box with something in it: we call it a "beetle". No one can look into anyone else's box, and everyone says he knows what a beetle is only by looking at his beetle. Here it would be quite possible for everyone to have something different in his box. One might even imagine such a thing constantly

changing. But suppose the word “beetle” had a use in these people’s language... If so it would not be used as the name of a thing. The thing in the box has no place in the language-game at all; not even as a something: for the box might even be empty. No, one can ‘divide through’ by the thing in the box; it cancels out, whatever it is. That is to say: if we construe the grammar of the expression of sensation on the model of ‘object and designation’ the object drops out of consideration as irrelevant.» (Wittgenstein 1986, 100).

The ‘thing in the box’, being it as it may, for each of the analysers, has no place in the language-game for there is no common standard with which to contrast everyone’s identification of the thing: there is no rule to follow. Within the model of ‘object-designation’ the identity of experiences hide public value. Neutralising the private objects of self-narratives as public and suitable objects of the world (Ideal Pain) exposes just a plot, a conjuration of what pain ‘shall be’, which, as it offers a standard, publicly accessible rule, neglects the fact that nobody and no one bears it. Propositionally, it is a simulation, and utterances senseless. The next part will try to resolve how utterances may be valuable and, at least, partially senseless conceding a perspective standpoint.

*. From Private to Public Traits:  
On the Logics of Partial Simulation*

To ‘act publicly’ or ‘privately’ plays in general terms with the contrast of private and public language present in the thought of the first Wittgenstein; rejected by the second (or as used in Chomsky’s concept of an external ‘ELanguage’ and an internal ‘ILanguage’). To ‘act privately’ would imply that the meanings generated by the utterances of a speaker, through words or through words usage (involving pragmatic accounts, intentions and propositional attitudes), are limited to this person. As a theoretical attempt, privacy is not to be neglected

in beliefs. For engaging a process of transparent transference of experiences through beliefs, implicitly, those contents of belief seem to have private traits, characteristic, unique or uncommon hues that colour them as private. That the traits of the concepts of this person’s self-belief are not shared means they are not public. The content may be of public interest, it may be present or instantiated through different versions of the same or a similar suitable topic or evidence in others’s beliefs, but the entire set of traits that characterise it is not involved in the performance of any ‘public act’. When this speaker utters a belief, as if performing a private act, and someone is to understand this utterance, the latter will be participating in a partial simulation: the analyser may recognise parts of the belief, but not the whole, lacking transparency of the sense of the speakers’s speech, or at least of one part of his. In other words, he may have epistemic access to some traits of the set of traits that characterise the speaker’s contents of his self-belief, and those which remain unreached by the analyser, would remain private: he would necessarily hold a partial simulation in his belief about the speaker’s experience.

To put an example recovering McDowell’s (1986) idea of an interpreter that lack the ability to fully understand a thematic assumption, let us build now a clinical situation where, for instance, a Korean speaker is a patient in an English ambience where no one but an interpreter speaks her language, however this interpreter happens to be not fully fluent in Korean. The patient may utter ‘편두통’. Publicly, it may be of interest, as there is a suitable evidence with a name expressed by contents present in English, the language of the ambience speakers, however it is half-way understood by the interpreter, who would utter ‘She is saying something about her head, but I cannot fully translate’. What ‘편두통’ addresses in Korean (편두통) may have a linguistic replica in English, however the entire set of traits in ‘편두통’ is not transferred. The

interpreter may not understand the full trait compositionality that allows a pragmatic recognition of the content ‘편두통’, lacking access to some traits that remain private to the speaker interoperationally. Propositionally, in the belief of the interpreter this would appear as if the foreign speaker is acting privately: there is no common ground that would serve as a contrast key to unfold ‘편두통’ with sense.

The Interpreter B (‘The Patient’ B(‘The Patient’, ‘to feel’, ‘편두통’)).

If the interpreter is to ignore also the logical relationship between the feeler and the suitable feeling, the contents of the belief would be even more difficult to access:

The Interpreter B (‘The Patient’, ‘편두통’, ‘The Patient B (‘편두통’)).

However, this logical architecture is not possible: as ‘The Patient B (‘편두통’)) is a private self-belief of the patient, the analyser would not be able to access it, thus he would be necessarily recognising part of the required set of traits, the rest remaining private. Using the idea of ‘clustering concepts’ (Cf. proposals in Michalski’s 1980: ‘clustering’ as a type of learning by observing as opposed to learning by examples; treated in a similar fashion by Fisher 1987; Stepp 1984; or Stepp & Michalski 1986), the schemata may substitute the mental philosophical notion of ‘concept’ by the epistemological notion of ‘contents of belief’: by this, the set of traits can be subscaled to private and public clusters. These clusters colour plurally through traits each set, providing the belief with plurally understood contents from which to learn what the other speaker is trying to mean. Propositionally, the public cluster of traits of those contents coming from the patient that are recognised within the suggested belief of the interpreter will compose a partial simulation.

. ‘고통’ is a content of belief of The Patient, such as: ‘The Patient B (‘편두통’))’

. ‘고통’ is also reviewable as a set of traits:

. Some traits of ‘편두통’ are public (open cluster of ‘편두통’) = ‘O-‘편두통’

. Some traits of ‘편두통’ are private (closed cluster of ‘편두통’) = ‘C-‘편두통’

Regarding this information, the limits of the interpreter’s belief are such that:

The Interpreter B (‘The Patient’ B (‘The Patient’, ‘O-‘편두통’)).

[without needing ‘편두통’ entirely]

The enclosed belief, ‘The Patient’ B (‘The Patient’, ‘O-‘편두통’)), is a partial simulation, a form of transference where the subject of a self-belief (the patient) and certain traits (open cluster) of some content of his supposed belief are known (which may be some traits that resemble very clearly to those of the speaker’s open cluster, however not the entire cluster), but the relationship between the content and the subject, as some other traits (closed cluster) of his supposed belief are not necessarily known. It is partially transparent, propositionally partial in sense.

The Interpreter B (‘The Patient’ B (‘The Patient’, ‘O-‘편두통’)), ‘C-‘편두통’)).

When the formalisation restructures the interpreter’s understanding of the content provided by the patient, automatically the interpreter attaches a closed cluster of traits (‘C-‘편두통’), which is always linked to the initial subject of belief as a bearer) colouring for him or herself what may serve as a private key to composing a content that now has meaning for the interpreter. Some would require a hard fulfilment of

propositional conditions and would regard this belief as senseless, nonetheless this case deals with partial understanding, allowing middle stages of comprehension as working with trust instead of truth and truth tables.

Privately for the speaker, “편두통’ is 편두통’: the former being a word, the latter the suitable topic redirecting to the bearer of the name. For the utterer, ‘편두통’ still is fully a content of belief that behaves as a public act in his language, because ‘편두통’ is a word in proper use, however, pragmatically put for the interpreter, if the interpreter does not reach a full recognition of the speaker’s acts, it would be understood as a private act: ‘편두통’ would never unfold totally as the word ‘migraine’, and 편두통 would never totally refer as the suitable topic migraine. However, some sort of value has been transferred. Full translation requires full public acts (Cf. the schema of translation theory as a ‘social action’ in Zlateva 1993). In other words, for translation to be fully trustful, the set of traits that compose the content of this belief need to act publicly: be common, to participate of certain convention. It can be said that trust reveals with the common, with a background, an agreed context. If the scenario makes these traits to act privately, the utterance may seem senseless for an external analyser, or partly senseless.

This form of simulation, different from faking or pretending, allows partial definitions of experiences in multiple cases, and can be taken to analyse important clinical signatures, and plenty pragmatic accounts that inform external assessment with the diverse propositional attitudes and intentions that the bearer of a pain is actualising as feeling his or her personal pain. The richer this open cluster of traits of contents of belief of a singular person is, being accessible to a different person, the more conventionality involves in the performance of transferring beliefs. Enrichment, of these open clusters, may favour trusted transference, as the more the cluster of traits informing about the content of

belief of an interpreter resembles the cluster of traits informing about the content of belief of a speaker, the less the former holds a partial simulation of the belief of the latter. This, composing the standard by conventional sharing of open clusters, engages more transparency. Enrichment (Cf. QIII, §8 critique to ‘thin resolution feeds’) may be taken seriously into account for accrediting trust in assessments and value in the transference of trusted knowledge.

#### IV — *Incorporating Trust to Transferred Value*

The point of participating in language-games is not just to ‘follow the norms’, but accepting them as something we have to do, leading to actions towards which agency is cultivated to reproduce with certain ethical depth. Conventionality in pain events may be very immediate if we consider the role of someone suffering, adopting certain attitudes, social, cultural, gender patterns. Conventionality can also be used to think about forms of quantifying pain: intuitively, if a sufferer expresses a horrible pain by shouting, quavering, etc., an external analyser would tend to think the sufferer is bearing a higher pain than if he just murmured slightly. The context may serve for mediating this calibration too.

#### . *On Propositionality as Conventionality: Enriching Attitudinal Feelings*

Donald Davidson extends the idea: «the attribution of attitudes is analogous in many ways to the measurement of various magnitudes.» (Davidson 1997, 74-75), and given such magnitudes as conventional amounts, the question affords to ask whether analysers could develop some kind of scale system by which to transform others’s pain experiences into a reasonable fountain of propositionality. If «the numbers are not part of the weighty objects; they belong

not to the empirical world but to us who need them in order to keep track of certain relations among objects» (Davidson 1997, 75), then those scales shall not be present within the structure of pain as such (like an a priori organic biological process equaling Ideal Pain), but referred instead to the recognition of those structures (the evaluative comprehension of the instrument's output and the informant's resolution feeds).

There is some kind of transformation taking place, from 1st-to-3rd person perspectives, as in comparing our privately thought metric scales to other's scales (eg, 'my 1-metre is not your 1-metre'): «in the same way, the entities to which we relate thinkers when we attribute beliefs and other propositional attitudes to them are not in the thinkers —not in their minds, or before their minds.» (Davidson 1997, 75). The measurement structure an analyser thinks is there in, with, or of the analysed subject using a scale of pain, is not actually there in the latter, but coming through the former's attribution of others's experience.

The idea of an approximate scale would be rudimentary simulating proper experiences concerning actual clinical syntheses, for if a subject's vision of his or her pain exterminates any others's perspective upon pain, that system would be measuring an Ideal Pain that is neither sufferable nor portrayable by others (it is an issue of reflection, not of perception nor experimentation). The knowledge extracted from such scale would never transcend an instrumental scope, an interpretative reconstruction of the past events that fit for assessing present ones. If there is no context, no life-powered biographical, narrative or attitudinal development in the description, assertion, or construction of the patient's pain, there is no trustworthy value transferred to the evaluator through the instrument: the resolution feed would be measured without trust and non-transparently. This means the resolution feed would be senseless, or partially senseless, and that reason accentu-

ates the critique about ignoring the significance of involving effortful memory, narratives, situation-dependence and decision-making for assessing patients properly (Cf. QIII, §7-8).

Scalar measurement strategies trace a parallelism with attitudes in the way they are putatively assigned to certain individuals regarding their actions (instead of by perceiving they bear those attitudes). This is a key consideration:

«An interpreter cannot directly observe another person's propositional attitudes; beliefs, desires, and intentions, including the intentions which partly determine the meanings of utterances [...] The interpreter can, however, attend to the outward manifestations of these attitudes, including utterances. Since we are all able to discover from such manifestations what an agent thinks and means, there must be an intelligible relation between evidence and attitude.» (Davidson 1991b, 210).

Contextual experiences, attitudinally thought as feelings directed to something, are 1st person perspectives self-beliefs inevitably circumscribed to the intention the subjects hold towards their own past pain events for managing the new ones. They act privately as biography. The intentional trait of pain events's contents of belief would inform an attitudinal feeling towards the previous lived events re-acquirable to assess the new ones. In that sense, pain is intentionally linked to memory for it is an attitudinal feeling, one describable as in Goldie's terms: «an emotion —as contrasted with an episode— can last for years.» (Goldie 2000, 188), whilst feelings, which are directed towards oneself, a particular situation, a topic of attention or embodied as manifestation of a particular emotional tendency, are meant to be episodic and intentional. The concept of 'feelings towards', as they «are directed towards the object of one's emotion as such —for example, feeling fear towards the lion.» (Goldie 2002a, 241), thus, is intentionally marked with a 1st person perspective

(Cf. Goldie 2002b; 2004). The more the memory scenario recovers intentionality and projects it into an attitudinal narrative, the more work on extracting a valuable transference through propositional beliefs can be done. This relationship explains the significance of enriched open clusters shared, or partially shared, as convention and agreement by the subjects of belief.

*. Incorporating Trust through  
Enriched Contrast*

The contrast of as many traits of contents of belief as possibly given in a transference process feed, from subject 1 (S1) to subject 2 (S2), incorporates a conventional pattern that will remain pivotal for sharing any understandable and valuable content from S1 to S2. The contrast is to be made by S2 (an analyser). That this contrast is conventional takes the notion that conventional patterns are demonstrations of following the rule of a language-game. But this also means that the subjects involved in the game accept the rule (they agree that the convention is valuable). In other words, contents of belief (through open cluster traits partially composing such contents) act publicly. The more public action embedded in this open cluster of belief, the easier the identification process implied in S2's assessment of S1's experience: in other words, it would be more enriched. This enrichment of open traits of contents of belief is exhibited by the pain-bearer actor through behavioural patterns. Arriving to a biodynamic anatomy characterisation of such patterns (Cf. QIII, §3-4; Cf. Grennon, Smith & Coldberg 2004's work for an ontological ground), the partial simulation proposal can issue them as an 'overall scalar sign': all, from physical, anatomo-physiological, personal, societal to global environment-affecting behaviours are considered action patterns manifesting, in this case, pain coloured traits of contents of beliefs, no matter their scale. Pain, necessarily, would be a simulation by default (a partial form of Ideal Pain).

Regarding the problem of pain transference, the partial simulation would solve the transference of trusted knowledge by incorporating an intimate closed cluster in S2's belief that could introduce a bearer. S1's closed cluster (his or her biographic standpoint on pain) will not transfer, but the conventional pragmatic expression of it (public open cluster) will. S2 will hold in his or her belief this or some extracts of this open cluster, and will attach S2's own biographical closed cluster to it. Thus, the simulation is partial, not entire, since there are conventional and private experience-kindred contents, 3rd and 1st person perspective-referring contents in S2's belief, and there is a bearer: S2.

As condition, the need would be of a 'common background' (*infra*), not for the contents of belief entirely, but for some of the open traits of such content (embedding into the propositional belief structure, among others, the attitudes, intentions, orientations, dispositions, etc. expressed by the other subject's belief) that may be trusted to inform that the private traits of the same content are not intentionally fake, fraudulent or simulated by S1. Given the fact that partial simulation introduces error in the theoretical framework, the search of an external analyser would follow the procedure of a trusted protocol, in opposition to requiring fixed point conventions (like truth-falsehood). The conditions of belief need not to accomplish a resolution of a table of truth, but a protocol of trust: in other words, an external analyser is implicitly oriented to assume the relationship between S1 and S2 is a transference of trusted contents, not of true or false contents, for there would be no epistemic means nor standard by which to clear out whether S1 is truly experiencing pain or not. In that relationship, thus, the contrast of as many traits of contents of belief as possibly given ('enriched contrast') in a transference process feed (a 'broad feed'), assuming a common background of trusted open traits, would configure the only manner

to ensure transparency, propositionally and pragmatically studied.

*. The Role of Empathy on Propositional Trust:  
Discerning Fake Attitudes*

A partial simulation incorporating plenty conventional traits in S2's belief would inform incorrectly about the belief held by S1 if S1 did not actually hold a 1st person perspective self-belief: this is, S1 would be faking a pain experience, projecting non-transparent contents. As an actor, S1's patterns would be feeding with open clustered traits the contents of belief on S2, in a common background: thus as many are similar, conventionally given, S2 would be cheated (holding a senseless belief). Since it is not truth but trust (agreement for transactions) what is being handled by reported self-beliefs, what matters is if S2 can actually contrast the feed acutely enough to be aware that there is no bearer in S2's reported self-belief, and that his or her utterances are, though conventional, not transparent, senseless.

Partial simulation requires a 'finely developed common ground', but this needs be understood by each believer in his or her own way (by their biography). Given a propositional belief in which open clusters manifest such common ground threshold for others's used traits, understanding their usage would be attending to their attitudes, intentions, orientation and interests. As long as the trusted relationship maintains, intentions shall be agreed to orient transparently among the subjects. Without this assumption, which is also a thematic assumption (ie, that the agreement on 'what are we talking when we talk about x' implies the sufficient trust to believe the other is talking transparently about the same topic we talk about), transference would not be trustworthy. Thus the 'finely developed common ground' requirement is a threshold for the others's attitudes, intentions, orientations, dispositions.

These are brought in by traits, clustered as well openly and privately. Situation-dependance and decision-making contexts would make those come up in narratives, as these require subjects to maintain the same attitudes in all the process in order not to be understood as flagrant. The more traits informing an analyst, the more opportunities that these can incorporate intentional traits, as are also manifested by patterns and convention.

A solution to this problem involves empathetic attitudes, attitudes that would help an analyser to discern others's attitudes as identifying and characterising the situation they are installed into. Following Green's (2008; 2010; 2016) depiction, empathy may serve as a source of knowledge:

«Empathy enables us to know what a certain state of mind (affective, cognitive, or experiential) is like; as applied to an individual whom we take to be in that state of mind, empathy enables us to know what she is going through; further, and on the strength of that understanding, empathizing can guide us to a proper approach to such a person and to those in similar situations. In these respects, the epistemic value of empathy is both practical (sensu know-how) and theoretical (sensu knowledge-that).» (Green 2017, 887)

In order trust to be incorporated into transference, the development of empathetic attitudes shall integrate 'conventional empathising strategies': active instrumental knowledge guided by a person's private experience, that may be used for discerning and approaching another person's attitudes towards his or her own situation. In a propositional manner, such 'conventional empathising strategies' are the contrast utility of the previous 'finely developed common ground'. It will work as a logical standard for measuring situation and context dependent-precedents of propositions. If the propositional contents of S1's transferred belief to S2 are contrasted and pass S2's empathetic threshold, such transfer-

ence would be trustworthy (trusted by agreement): an external analyser would be able to say S2 is 'confident that' S1 is feeling pain the way S1 describes it through convention. We can use M Slote's (2017) pragmatic account on assertive utterances for defining such convention:

«Confidence can be empathetically conveyed or infused via an assertion, and assertion as a speech act is (among other things) fundamentally characterizable as a conventional way to get people to take in our confidence about some subject matter.» (Slote 2017, 12).

Trusted transference can occur only by ascertaining whether there is an epistemologically comfortable context for coming to contrast the attitudinal traits of S1 and S2, which they have developed biographically enabling their feelings, and the propositional possibility of their feelings (1st person perspective self-beliefs). This context is an 'empathetic context'. Conclusively, if S2 is able to hold with an empathetic attitude a content of belief upon the experiential topic (S1's feeling pain) that other agent (S1) is transferring to him or her (S2), then it would be because S2 believes S1 is not simulating about such topic. Given this context of empathy, trust is introduced in transference through discerning fake attitudes through enrichment of open conventional traits comparison.

If empathy is put as an experience too, the fact that S2 is able to feel with an empathetic attitude (a 1st person perspective self-belief) a recreated content of belief upon the experiential topic (S1's feeling pain) that other agent (S1) is transferring to him or her (S2), then it implies that S2 feels a reconstruction (partially simulated) of S1's 1st person self-belief about a topic of which, at least its open cluster (conventionally) can be accessed by both of them. Through empathy as threshold (for contrasting S2's information) and as well as index (for being prompted with an emergent, spontaneous self-belief on a similar topic), trust is actually being introduced

in transference, proving a protocol for validating the agreement on the community's used convention as its scale strategy.

This context frames a community of belief (using situated perspectivism epistemology, where integers of such community trust on the conventional usage of, not just contents of beliefs, but of their transference. Once established this community, a frame for these subjects to trust on each other, understanding others's experiences comes with the empathetic disposition for being involved into a shared arousal of proper pain traits, which as composing private closed clusters, also manifest conventional open clusters recognisable by others. These arousals are sprouted from an empathetic context between the external analyser and the sufferer, which constitutes a form of communication but as well of proper assessment. A clinical example is therapy (Cf. Tesdale 1999 on metacognition; Cf. White & Epston 1990 on therapy and narrativity; Cf. Brinegar et al 2006 for problem solving and understanding in theoretical therapy).

Pain emergence, neurologically traceable, is feasible to transfer through such context of empathy, existing situated in such emotional community (Cf. Rosenwein), which develops a transcendence in which what is felt by someone affects the other, reshapes his or her own sentiments as evoked or contrasted to be creatively felt, although no origin of damage is demanded. This process is a proof for asserting that value has been transferred, but serves not as an instrument for quantifying others's experience (such a quantification process would always be of an Ideal Pain, and it can occur that this Ideal Pain is the one constructed through the simulation of S2 as trying to put S1's pain in a scale). Qualitative research on pain is consequentially more relevant than quantificational for understanding and assessing patients, even more for neuropsychiatric interests and therapeutical requirements. When the context is unable to be engaged, self-beliefs lack transparency, and are



propositionally senseless: clinically, self-beliefs that mediate no empathy, as said in some autistic spectrum conditions, Asperger disease, or psychopathy, occur to be senseless when studied propositionally, and perspectively imply that patients suffering such pictures do not actually engage in 1st-to-3rd person perspective shifts as conventionally as non-suffering population do.

. *The Role of Sense in  
Trusted Knowledge Transference*

The concept of sense, as partial simulation deals with it through transparency, conforms a pragmatic evaluative asset, a form of criterion that speakers or believers would use to measure how value is being transferred. By using sense as an accreditative instrument of belief, an external analyser of a given belief may differentiate trustworthy from untrustworthy transferences. Given the case that a content of belief is transferred from S1 to S2, the former would have used a convention pattern through which the meaning of such content (and excerpts of his or her belief) is reproduced in the belief of the latter. S1, as an actor, would have used a performative action (conventionally understood physiological, biochemical, attitudinal, linguistic, behavioural pattern) by which S2 would have been able to hold a belief with a similar content to the one offered by S1. Such convention is agreed by both of the subjects, is always an open set of traits composing a publicly offered content of belief that is engaged in use by a particular community of belief (following a situated understanding of epistemic communities). Synonymity theory may also be useful to this account, as those two contents of belief, the one held by S1 and the one held by S2, may be characterised as propositionally installed in a relationship of synonymity through their public traits given a context that allows such resemblance (Cf. *Addenda* to this chapter: Add. I). Having sense would mean in this transaction

that for an external analyser, at least the open cluster of traits of the content that now S2 holds in his or her belief is clearly similar to the open cluster held by S1. Those contents act publicly. The closed cluster of traits behaves privately for each of the subjects involving their own biographical conditions (so joint-meaning mediation is not altered; Cf. Carassa-Colombetti 2009), thus informing personally about the content to each of the subjects. In such transference of contents, as having sense would imply that the same suitable topic of belief is bearing the burden of reference for S1 and S2, if the open cluster involved in both subjects is clearly similar, the sense would be necessarily preserved. An analyser may say that the content in S2's belief maintains the value approached by S1, and that such transference is trustworthy: transparency occurs, even though simulation partially takes place intervening the transference of beliefs.

The pragmatic account of others's experiences may be trusted as valuable knowledge for assessing S1's 1st person perspective self-belief through S2's 3rd person belief on S1. And if empathy is put as an experience in S2, then through S2's 1st person belief on a constructed simulation of S1's 1st person perspective self-belief (as partial simulation) may be trusted equally.

. *Closure*

The chapter suggests a proposal for defining how assessment is able to incorporate trust to transferred value through a common background based on agreement, and how value can be assessed to be shared through trustworthy transference by means of participating in a context of empathy, which is contextualised to communities of subjects of belief. Propositionally, this context would serve as an analyser's threshold for contrasting contents of belief of an informant, discerning whether or not the informant is transferring transparently (with sense) his or her beliefs rather than simulating them.

As an integrative proposal binding social, plural, perspective epistemologies with propositional logics of self-beliefs, the work provides a protocol for introducing trust in assessment processes, regarding transference of experience-based self-beliefs even when the analyser may be holding a simulation in his or her belief about the analysed subject's experiences.

By involving 1st and 3rd person perspectives into self-beliefs logical architectures, analyses may face an overture to define experiences propositionally, maintaining that 1st person self-beliefs put the condition to actualise (make actual) the experience the subject of such belief is experiencing as he or she believes, conceding the requirement that the meaning of his or her proposition has been solved transparently.

Introducing perspective beliefs in a theory of the style this chapter is dealing with, plural cluster compositionality (of public and private traits composing the contents of beliefs) may be used for accrediting partial value (as regarding to the formation of 'partial simulations' in the belief of the analyser, solving the problem of total simulation: Ideal Pain). The proposal also allows for its embedment into a propositional belief as content with traits (which may instantiate attitudes, orientations, intentions, pragmatic addressivity, and forms of public conventions and private dispositions into the very belief of the subject), as well as its transference and its plausible options for solving the identification process that serves for an external analyser to discern through empathetic agreement what is the suitable evidence that makes the experience of an external subject to be transferred with sense.



—

*Add. I — Relating General Pragmatics with Partial Simulation*

To a much greater extent than is often assumed, the scope of the arguments on partial simulations may broaden a general theory of transparent transference of trusted knowledge in a perspective epistemological standpoint. Being sceptic about easy attainment of transparency in transference, we may ask if any kind of general pragmatic assessment of transferred contents of belief is fully understood by the analyser. In order to achieve transference of value, language-games are not necessarily played accepting a yes or no rule: either the interpreter knows the word, the meaning, the sense, the reference, etc., or he cannot play. Theoretical design needs to ask itself why middle ways are broken. An answer could be that, analytically, there is no element of the system that ensures the value of what is transferred if the sense of a proper name is not fully achieved.

Introducing perspective beliefs in a theory of the style this chapter is dealing with, plural cluster compositionality accredits partial value, its embedment into a belief as content with traits, its transference, and its plausible options for solving the identification process that serves for an external analyser to discern what the believer is talking about (the thematic assumption). Indeed, as consequence of having introduced a rule to follow in a context of experiences (returning to Wittgenstein's 1986, §293 beetle in the box), what the external analyser discerns is propositionally a simulation: a partial one. With those conditions there is no actual need to worry about full set of traits of contents. Even further: how are we able to accredit that interpreters attain the full set of traits that the speaker has used to account for a word, or referring to something, or approaching intentionally to someone? What serves as standard?

Rather nothing or an entire fake simulation. Extremes seem rather simplistic or too immature.

It appears that the generally common, conventional actions that serve as patterns for communicating and understanding, actually happen to be a partial propositional cluster of traits that conform a content of belief that we handle as terms in language. Standards, criteria, as acting publicly, cannot be but partial propositional clusters of an invented, abstracted statistical fiction, a conceptual signal without any suitable object of the world that bears the burden of reference, or multiple suitable objects of the world (subjects) partially bearing such burden.

This idea comes close to some authors on integrative pragmatics. In the slavic school, regulation of meaning has been constantly dealt since Alexander Potebnya's 1913 research on personal statements. Shpet or Vigotsky (1986) widened different applications to assess language acquisition (meta-cognition and learning processes) and propositionality with a similar aim (Cf. also Gombert 2015 on metacognition and metapragmatics). In therapy theory, an example of the uses of pragmatics in psychiatry brings the identification developed in (Voloshinov 1988, with Bakhtin): in the psychoanalytic interaction between the analyst and the analysed, the 'sphericity of dialogue' (the ambiance in which speakers play their role while conceiving of expressions and using them) implicitly manages a form of subjective value of words, attuned to both of them, that the author calls 'intersubjectivity'. His notion of sphericity also raises the process of epistemic orientation (Cf. Öhman 1979): «to understand the statement of another means orienting oneself with respect to him [...] finding the right place for him in the corresponding context.» (Voloshinov 1973, 102).

The thesis of orientation configures in Bakhtin the notion of 'addressivity', a characteristic of any discourse that understands that value is accredited by 'where-to' one is speaking, 'to whom' the value is being transferred. As

«addressivity, the quality of turning to someone, is a constitutive feature of the utterance; without it the utterance does not and can not exist.» (Bakhtin 1986, 99), it is interesting to conclude that by identifying the traits of such orientation, one would make clear the degree of trust in the transference. As soon as an external analyser identifies the role, attitude, intention and other pragmatic requirements to understand properly the orientation of the speech, the dialogic value of the utterances would create different 'genres of speech' (different forms of 'speech acts' or 'illocution', in Western terms, regarding the framework set by Grice 1975, Austin 1975, Strawson 1964, and Searle 1969 in the 60's-80's; Cf. Barker 2003; Sbisà 2014; Searle & Vanderveken 1985; Toulmin 1985/2003; Sperber & Wilson 2002). Fake contents would be intentional contents oriented in a fake way to an audience, thus an integrative pragmatic account has been offered to accommodate both interactive and intentional views. Bakhtin's (in Holquist 1981, 293-294) concepts of dialogism and mediation result familiar to traits plurality: words and expressions conforming speech are dialogical in the sense they are used interpersonally: «the word in language is in part of another. It becomes 'owned by one' only when the speaker populates it with his own intention, his own accent, when he appropriates the word, adapting it to his own semantics and expressive intention.» (Bakhtin 1981, 293-94). This makes the meaning of expressions mediated by the agents involved in the sphere of discourse, contextualised to that sphere, and epistemologically situated to the subjects that conform decidedly a community of use.

Maintaining that meaning is mediated (Cf. intervention and joint-meaning in Carassa-Colombetti 2009), standards would be decided in constant fashion, contextualised to communities of usage: as sharing occurs (of value, through words usage), standards would actualise. Terms in language, words, expressions as such fit this

definition: we share them to transfer what they accomplish to put in value. By deciding whether we agree on the conditions of such use of words, value is transferred, being accountable to the limits of the context in which the pragmatic transference has developed (Cf. Haugh 2013; Witek 2014 for the notion of ‘accountability’ in meaning through pragmatic agreement; or ‘commitment’ in dialog in Walton & Krabbe 1995).

The same process occurs in valuing ‘고통’ as pain, and in valuing ‘pain’ as pain: what changes is the conventions that cluster specific traits and bring them open to public actions to be developed.

Similarly, synonymy reflects this concept of plural traits clustering given a convention that accredits how one word is in relation of synonymy with another ( $x \approx y$ ) given a pragmatic context (C):

(C), ‘고통’  $\approx$  ‘통증’  
 [‘고통’ = ‘pain’ — ‘통증’ = ‘ache’]

This would require a context where ‘고통’ is a content of belief of a speaker (S1), such as: ‘S1 B (‘고통’)', and where ‘통증’ is a content of belief of a speaker (S2), such as: ‘S2 B (‘통증’)’. Given a context (C) in which S1 could make use of ‘고통’ as ‘통증’ understood by S2, then for S1-2 community, those contents are synonymous: ‘고통’  $\approx$  ‘통증’.

Involving conventionality through traits clustering, ‘고통’ and ‘통증’ are two set of traits of contents of belief.

Some traits of ‘고통’ and ‘통증’ are public (open clusters = O-‘고통’ & O-‘통증’).

Some traits of ‘고통’ and ‘통증’ are private (closed clusters = C-‘고통’ & C-‘통증’). When a speaker (S1) utters the word ‘고통’, open (public) and closed (private) contents instantiate in his or her belief upon the suitable topic 고통:

(‘고통’), S1 B (O-‘고통’ & C-‘고통’).

If S1 uses publicly ‘고통’ as ‘통증’, his belief upon such relation would instantiate:

(C), S1 B (O-‘고통’  
 &  
 C-‘고통’) = (O-‘고통’  $\approx$  O-‘통증’).

S would believe that his own conception of ‘고통’ may be used in a precise context as ‘통증’, as long as any other speaker would also understand ‘통증’ as a public act: in other words, as long as S2 could access to the same open cluster or parts of it that S1 has accessed beforehand (O-‘통증’). The richer this open cluster, the more conventionality involves in transference. Enrichment may favour transferring trusted knowledge, as the more the cluster of traits informing about the content of belief of an interpreter resembles the cluster of traits informing about the content of belief of a speaker, the less the former simulates the belief of the latter. As generating a standard by conventional sharing of open clusters, this idea has a potential value for engaging more transparency. Enrichment may be taken seriously into account for accrediting trust in assessments and value in the transference of trusted knowledge.

—

#### *Add. II — Ergonomic Applications to Artificial Intelligence Assisted Diagnostics*

Rall (1964; 1970) was one of the first major neural networking simulationists in applying probabilistic neurotechnical knowledge in favour of achieving artificial nervous systems, inventing a modern neurotopology (topological map of the brain) of common use about the 60’s-90’s. Computational neurosimulation gave birth to new forms of scientific proceeding, especially in the field of perception and cognitive analysis (Cf. studies in neural electro-dynamism, Rosenblatt 1962; Abbott & LeMas-

son 1993; in neuropsychology, Eeckman 1993; identification models, Zipser 1992; connectivity and modulism, Among-Snir & Segev 1996; Dayan & Abbott 2001), and in neuropsychiatry (Cf. studies in modelling personality, Tomkins & Messick 1963; on electronic implants for mediating bionic reactions to mental diseases, and computerised signal modulation for mapping neuropsychiatric patterns in obsessive disorder, Abbott 2002; as well as the MedTronic Projects). The study of contents of speech and cognition (as contents of propositional systems) has provided many advancements in artificial systems, which have been groundbreaking in the study of pragmatics and grammar through text analysis models, synonymity and semantic field theory, generating corpuses and analytic protocols of many uses (Cf. Fiederici's et al 2006; 2011 studies on the differentiation of human and non-human grammars; Gustafsson & Balkenius 2004, on semantic web models for validating/rejecting cognitive models; Dayan & Abbott 2001 for virtual spaces of vision; Tomkins & Messick 1963, or Moser et al 1970, in computer models of personality; Skarda & Freeman 1990, on chaos theory and computer modelling of brain work; or Yamagata et al 2013, on ontological models of diseases).

In Artificial Memory, applied to Artificial Intelligence Assisted Diagnostics, assessment would need the artificial agent (the specific software running the protocols required for a given diagnostic) to hold such closed cluster of traits colouring the content of a propositional belief through private, intimate action for itself. A protocol within the style of theory making that has been developed in this work could avoid the notion of 'conceptual memory' reinforcing the interference of concept-driven propositional beliefs (Cf. an example and review in Rieger 1975), substituting concepts by contents of propositional belief through perspective epistemology. Private would stand for 'suitable topics that mediate and bear the burden of reference'

in the biography of such agent: by endorsing the multiple encounters it had facing such suitable topics, the agent could recall, remember, learn and propose alternatives to understand each time 'as for itself' (as for its own experience and iterations running the procedure) a closed cluster of traits of contents of belief, which would serve for building a probabilistic, Hebbian web in a decision-making protocol to finally act publicly intervening propositionally with a solution for assessing a particular patient case (Cf. Hebbian approach to probabilistic act organisation in Hebb 1964). Self-beliefs in this case would imply 'biographical accountability', not private to the code but implied in the code through terms that are not shared nor accountable by any other artificial agent. Its self-belief upon the state of a patient would be the very solution of the problem that has been approached through the decision-making protocol. Trust protocols would also inform the agent about the probable degree of senselessness in the contents handled by the patient as managing interoperational case-to-case revisions and text-voice analysis contrasted with the given accounted clinical standards, and the reports, analyses, tests and other interventions occurred previously to the patient at hand. The applications are enthralling extensive for the ergonomic management of medical information, especially for clinical evaluation, complex prognosis and overflowing multifactorial analysis.

*. On Building & Assessing  
A-Life Trusted Communities*

If we were to simulate imminent pain in appliance to an agent of A-Life, propositional assessment would be indispensable. The partial simulation proposal may serve as well as a general measurement strategy of trust. The assessment would be about whether such agent is simulating an A-Life model exhibiting certain mannerisms that simulate some organic

activities considered in 3rd person perspective as correlated to pain experiences, or rather if it is developing a pain event as felt in 1st person perspective.

In contemporary bionic experiments, as Evelyn Fox Keller (1995; 2003a; 2005) reviews, conclusions are getting into a degree of simulation where the organic is transcended by the artificial and projected in the future with increasing simplicity (Keller 2003b; Cf. Wimsatt 2007 on limits biology epistemology; Cf. Ford, Glymour & Hayes 1995 on android epistemology). If we could develop a context for a community of artificial agents, in comparison with an organic one, we could arrange a definition of what an artificial agent of A-Life should feel, by 'following the norm of pain events' for natural organisms (eliminating prior autonomous origination, but planning and designing them as artificial experiments), and patching that onto the required synthetic conventions affordable by this community. Attaining them to construct a propositionally valuable self-belief engaging contents as suitable folder-based topics about this organic activity, an artificial agent acting as external analyser within such community could assess if from their reproducing such activity (3rd person perspective) it also supposes their experimenting intimate pain (1st person perspective self-belief) by having an ostensive definition of an enriched open cluster of traits that serve as a standard for the empathetic context, and an ostensive definition of closed clusters of traits that will configure the agent's artificial memory, private to just one agent, its own biography. To such community, the belief would be trustworthy depending on the transparency of their propositional beliefs. Attitudes may be simulated as well as identifying situation-dependent and context-dependent traits of contents, and assessed in problem-solving decision-making scenarios. Empathy would define this community's conventions for understanding fake attitudes by being inscribed

within transparent empathetic contexts. Given an experiment with as enriched information as required to build broad feeds for complex analyses based on human factors, a human analyser would be installed in the same difficulties for assessing an A-Life agent's simulated pain as for assessing human pain. If this experimental ground of complexity and conventionality takes ground in an ergonomic human-computer interaction as a foundation for designing a well suited empathetic content (reviewing the implications of emergency and spontaneity outcomes in complex systems design: Cf. Gell-Mann 1995; Holland 1996; 1998; McMahan et al 1978; Heylighen 2000; Korn 2005), it will also constitute a possible trusted protocol for assessing artificial cognition models on trusted transference.



---

## **Quarter IV**

### **Results, Conclusions & Future Lines.**

§1 Structured Summary of Results, Conclusions & Implications (p 270)

§2 Future Lines on Epiagnostics: Applications to Neuropsychiatry,  
Neuropsychiatric Epistemologies & the Nosographic Technologicalisation (p 284)

# QIV, Chapter §1

## Structured Summary of Results: Implications & Conclusions.

—

### Parts

. *Introduction*

I — Structured Results & Conclusions by Niche

- . *Specific Results, Conclusions & Implications Excerpted from Niche A  
(Neurophysiological Characterisations: Historical & Comparative Traits)*
- . *Specific Results, Conclusions & Implications Excerpted from Niche B  
(Psychiatric-Epidemiological Characterisations: Overflowing Morbidities & Pain)*
- . *Specific Results, Conclusions & Implications Excerpted from Niche C  
(Clinical Characterisations: Diagnostic Practices & Pain Measurement Strategies)*
- . *Specific Results, Conclusions & Implications Excerpted from Niche D  
(Interpersonal Characterisations: Difficulties on Self-Narratives & Pain Transference)*

II — Remarks on the Neurophilosophical Contributions of this Work

III — Global Results. On the Attainment of Goals



## . Introduction

Niches, frames, perspectives act as keyword entries capturing practices of understanding, learning, knowing. Theoretical remodelling, by shifting frames, recalling new markers and facing further horizons, becomes imaginable as such only through contextualising suitable scientific activity to analysis, inasmuch this activity supposes contributing, affecting, breaking or empowering a chain of trust delivered on the basis of cultural, political, social factors that comprise the very different movements established within the plural epistemic niches present at a specific space and era. Clinical evaluation is inscribed, as this work has suggested, in said primitive foam from which time-tied and geographically-scaled scientific themes emerge, impersonating a wavelength of interests that seeks to capture and measure socially demanded solutions upon critical events in a landscape of human interests, intentions, expectations and limits. Diagnostics are not separated from their performance, as framing cannot be set away from its 'practicing framing' as an epistemic act of trust. Trust on conventionality, on new strategies, on personal and interpersonal experiences, on situated values. As a concept, it has only validity and utility in its application —and it is through the style of application decided by the multiple epistemic communities of theory making and debate engaging diagnostics that epistemic inquiry may have an access to investigate why, how and for what the different criteria and stressors modulating such styles appear necessary to certain niches, why their framing practices show as they manifest, and why conclusions are to gain the inherited values, limits and benefits that each one of such agents of the process has to offer.

Neuropsychiatric evaluation of pain experiences, and the grounding epistemic factors enabling its performance, have been in focus across this entire work through the various

theme-involving niches sorted in QIII, by inspecting the historiographical understanding of neurophysiological characterisations on fibre-channel qualitative conduction, travelling to newer inspections on epi-phenomenal inter-systemic and meta-systemic attributions of organic agency, focusing the different principles understanding material implications and facilitation (Niche A, 'Neurophysiological Characterisations: Historical & Comparative Traits': QIII, §1-4); by rethinking psychiatric systemic approaches recognising the epidemiological accounts of 21st-century overflowed panorama on morbidity, exposing the contemporary necessity of newer concepts and deeper technological implication for situating multifactorial and prognostic values analyses in performing a better, modernised and more complex diagnostic evaluation, especially orienting evaluation of dysfunctionality and collateral clinical scenarios reinforcing pathological identifications and, therefore, better understanding the patients's burden of a life with pain (Niche B, 'Psychiatric-Epidemiological Characterisations: Overflowing Morbidities & Pain': QIII, §5-6); by addressing the clinical practice of contemporary neuropsychiatric diagnosis on the basis of an epistemic practice installed in a bridging boundary of knowing, learning, communicating and intervening, and by criticising the measuring strategies approached to the patients's clinical pain scenario, recognising the scope, limits and factors for theory change in the field (Niche C, 'Clinical Characterisations: Diagnostic Practices & Pain Measurement Strategies': QIII, §7-8); and by rethinking the interpersonal difficulties of sounding self-narratives through indeterministic self-beliefs, narrative perspectives and interpersonal belief transference through empathy and trust endorsement (Niche D, 'Interpersonal Characterisations: Difficulties on Self-Narratives & Pain Transference': QIII, §9-

10). These were all attempts to set pain evaluation into a collection of perspectives framed by the contextual conditions of the different thematic niches acting in a global hypercontextualised sphere of shareable and contrastable knowledge, producing and re-producing the different theoretical morphologies through which pain itself might be known.

The collection of chapters developed upon four major niches, proposed for building, inspecting, mining and empowering interconnected frames for defining how epidiagnostic characterisations could work, facing historiographically, epistemologically, ethnographically and analytically how theories develop, transform and generate trusted and agreed-upon knowledge through deciding on convention, debating and refuting, and enhanced by the contemporary possibility of contrasting hypercontextualised information through interfield, pluralised, decentralised frames.

I — *Structured Results & Conclusions*  
*Sorted by Niche*

The following sections note how each chapter impacts into framing epidiagnostic characterisations, contributing to further research on specific interfield work and inquiry on inter-frames. Interrelations show how integration could be straightforwardly helpful in generating value-knowledge, trust and operational interpersonal and clinical ergonomic improvement through pluralism upholding an instrumental skepticism standpoint. Each topic on these multiple and plural frames influences theory and decision making, and develops into formal resolutions of problems: the 'value of pain' turns out to be an abstraction underpinned by such clinical formalisations, useful or refutable, shifted, moulded, pledged and rewritten through the different standards contextualised to their own epistemic niche, or transformed via interflow amongst various niches, frames and per-

spectives. As a general conclusion, the more perspectives the frame allows interpretations to introduce, the more inter-framed plural and integrative characterisations appear, the more robust, trustworthy, decentralised and solving the theory, model, understanding appears to be. This scene promotes a practice of epidiagnostic evaluation.

—

. *Specific Results, Conclusions & Implications*  
*Excerpted from Niche A — Neurophysiological*  
*Characterisations: Historical & Comparative*  
*Traits'*

As if moving crossways niches, taking short distance from neurophysiological endeavours, frames start exploring pain as a proper phenomenon of fibre excitability. This enterprise resumes the epistemic access to the topic in a clear deepening systematisation where pain, as proper to the nervous system, comes in relation with other systems but in a collateral fashion. When conceived historiographically, this concretion mitigates its grounding factors to great extents in modernity, where, as exposed in QIII, §3 and §4, inter-systemic and meta-systemic approaches make pain an event proper to the organism as a whole in its wafting and wandering interaction with its environment. In QIII, §1 and §2, analyses showed how, from earlier metaphysical roots, pain was 'physiologised' by physicians and clinicians in history into a morphology by itself that has only sense when exposed within the boundaries of the physiological attributions to fibres at each time-tied context. Pain talks in many ways, we can adduce, inasmuch as it resolves to present itself diagnosed, evaluated and assessed medically and clinically in multiple styles along the way. Presentism, forcing interpretations of the past as requiring them to abide by the present standards, as inquiring what has been called a 'whig' historiography by H Butterfield, shall have no

place in the recognition that previous theory makers in history made of pain, nonetheless the comparative effort on excerpting and contrasting their theoretical contents of epistemic belief is significantly useful for demonstrating the plurality, disunity and contextualisation of their situated practice in the resolution of similar, quite conventionally identifiable problems: the burden of a life in pain.

However it is well requirable of present theory makers to reinforce modern claims on modern data, by then having the prompt clinical liability of and academic invitation to rethinking which standards are they following, why and for what, and thus to answer the whose-&-why question on the value of the knowledge they seem to be using in actual days (Cf. QII; §1). The qualitative macrointerpretations studied historically and epistemically in QIII, §1-3, in specific terms, qualitative-evaluative attributions on fibre action coming from pre-medieval times, appear to have still in the two first 2000's decades deep effects in the epistemological roots that are passively understood by clinicians and physiologists. The liminal 19th-century notion of continentality is a deceiving materialist reduction that is still reaching minimalist interpretations on very complex issues that, as has been exposed, overflow mono-field, mono-framed conclusions making processes. The metaphysical dilemmas underpinning the material and theoretical concepts used to describe and explain experiences like pain, sorrow, anxiety and so forth show to be in lack, yet in modern times, of an integrative solution benefiting and covering a plural collection of disciplines —not because solutions have not been developed, delivered or integrated, but because the immensity of the gap between epistemic inquiry and scientific content making does not close easily in today's internationalised climate of debate, straining hypercontextualisation and globalisation to narrow, utilitarian and segmented hyper-partial atomisation of

contents in a consequential process of deformation and de-contextualisation that looses the proper horizon and inter-frame suitability of research. As concluded in QIII, §1 and §2, the commonplace construct of an 'universal pain', an abstract, simulated characterisation of pain, a historical, social construction whose origin has exposed its roots through the instrumental utilitarianism of metaphorical terms in experimental explanation, is no longer valid to define nor explain the ontological entity of pain as an experience when cognitive and metacognitive neuropsychiatric studies demand answers on what to establish as a referential standard.

The epistemic analysis in QIII, §3 concludes how the historiographical diffamation on the concepts and understandings of pain in neuropsychiatric theory making led to stress a de-contextualisation of terms, language usage, attributions and definitional characterisation that affects harshly current interfields when comparing the different strategies used in modern physiology for explaining the multiple aspects of pain experiences in different levels of complexity: the terms, intentions, expectations, interests and needs proper to tagging, labelling, classifying and shortening in words the experience of pain, all variate from field to field, promoting a disparity not just of application on the clinical ground, but that affects the ontological recognition of what pain is. Results on this matter, in applying an instrumental skepticism standpoint, argue in favour of maintaining such plurality in use, however of understanding the critical need of clarifying and submitting to a principle of non-restriction for identifying such ontological claims, making understandable to practitioners and scholars that singularised oriented characterisations miss the potential enhancement of knowledge in clinical conditions that a pluralised polyhedron definitional claim could apply in acknowledging that, even neurophysiologically, the answer to the question on the ontological grounds of pain expe-

periences may and surely are concluded to have multiple responses, from which collaboration instead competition is expected in a contemporary overflowing scenario of events. This makes straightforwardly necessary the involvement of the rest of niches for having an epistemically plausible plural characterisation of such schemata in answering the ontological question. Evaluation must involve all characterisations at once for developing solutions.

A cardinal obstacle has been appointed in contrasting information. Both the average found in non-reproduced and non-reproducible experiments, and the lack of interfield strategies used in explanatory needs are two major indicators of this fact, which is also imbricated with how interfield, inter-framed requirements are managing interpretational reasoning and explanation. Recent promising pluralistic characterisations of pain experiences may end up prompting with significant results, especially in terms of epi-phenomenal interpretations that might lead to understand experiences not as a sole phenomenon proper to the experimental physiology at hand, but as an epi-phenomenon of the whole organism occurring along the physiological performance of multi-systemic interaction, with further transcendence in meta-regional physiological (this is, not proper to a localist region of the organism, but proper to the organism's integrity in reciprocal interaction with its environment) consequential self-beliefs, self-narratives and identifications in the construction of intimate experiences through personal biographies.

The last chapter of the niche, QIII, §4, concluded on a contemporary image of physiographies in favour of an overall interpretation with potential significance for understanding fibres specialisation and their role in facilitating pain as an epi-phenomenal experience inter-systemically. The chapter's suggestion comes in the form of a physiographical interpretation. The RIF (Reciprocal Inflammatory Fibrogene-

sis) Interpretation put in integrative value two historical inspections on pain physiology, the Intensive Theory and the Specificity Theory, as analysed and historised in QIII, §1 and §2. The RIF Interpretation worked through the concept of heterotopisation (an organic reshaping process: a developmental specific morphofunctional reorganisation) re-orienting the contents of multiple theoretical interests into a pre-evaluative characterisation of cell specialisation as demanded in QIII, §3. In this sense, peripheral C fibres, plus internuncial and central fibres, are not over-attributed with an evaluative load in argumentation: these fibres do not conduct a pain quality, nor are qualitative themselves for pain —pain is attributed proper to the whole organism; as agency of experiences is an evaluative feature of the whole inter- and meta-systemic interaction—. These fibres conduct voltage-irritatory waves that happen to facilitate a more complex integration of neural and immune recognition of disintegration informed by chemical tissular processes (accepting a systems biology 'Principle of Integrity'), based on stressor chemical ambiances exposed to a continuous diachronic inflammatory de-homotopisation (morphofunctional specialisation given a stressor-resistance dynamic) conforming fibrogenesis.

QIII, §4's proposal suggested answers to three questions —(1) what are pain facilitatory fibres sensitive to?, (2) how those fibres specialised?, (3) what was the evolutionarily niche and requirements for these fibres to exist, be adapted and generate?— through adducing different implications of acknowledging the solving theoretical properties in using the RIF Interpretation's term 'RIF fibres' displacing the use of the 19th-20th fin de siècle problematic term 'nociceptor' (Cf. discussions and reasons in QIII, §1-3). The RIF characterisation of such fibres could help to explain the morphological, functional and local resemblances between proprioceptive and nociceptive fields, the fact that both

fibre families are not fully specialised at birth, and the fact that given the milieu shift from aqueous to terrestrial media C fibrils appeared later in the diachronic evolution of organisms, thus, heterotopised after proprioception and developed in response to higher inflammatory stressor conditions of disintegration than in water milieu. Nonetheless, the RIF Interpretation is not to be understood as a perspective conforming a mono-framed response to pain neurophysiology, quite the contrary, if anything, as a plausible physiographic account, a contribution to build a pluralised complex characterisation of the process, that may help to install significant paths for depicting further different identifications of pain in close related topics.

—

*. Specific Results, Conclusions & Implications  
Excerpted from Niche B — 'Psychiatric-Epidemiological Characterisations: Overflowing Morbidities & Pain'*

Recent calls in current clinical epistemics and neuropsychiatry to attend to a more complex, decentralised, heterotopic systematisation of morbidities for internal medicine inasmuch as for specific psychiatric and interfield diagnostic classifications are, QIII, §5-6 maintain, impossible to flout today. The diagnosis of complex syndromes, in cluster, spectrum, or scattered polythetic form, need to rethink the validity and utility of systematic relationships, statistical and demographic bondings, and category-suited etiological schemata given the overflowing hypercontextualised pathological scenario patients can present with. Beyond-scope unitary diagnoses provoke unsatisfactory responses as comorbid states involve and require a multifactorial, prognostic perspective.

QIII, §5 suggested, after reviewing, contrasting and merging definitional claims of abundant and variegated literature focuses on co-pathological scenarios, the notion of 'epid-

iagnostic practices' for better studying and approaching complex scenarios. Epiagnostics seek to face those stressors in an overflowed panorama of scientific interfield acquaintances, when evaluation conjoins the 'over-(epi)-flow factor' detected by modern ethnographic, cultural and epistemological studies as applied to clinical ambiances in the works of this thesis (Cf. presentation and epistemological interests in QII, §1).

An epiagnostic characterisation of the style proposed, thus, builds integration through difference, multiplicity, plurality, recognising partialities through perspectival approaches, and drawing athwart (crossways, crosswards) theory in its attempt at navigating across biological and theoretical complexity.

Some specific conclusions were excerpted from such inspection: (1) that comorbidities and multimorbidities work as tendencies, a tendency to increase the probability of suffering reciprocally related pathologies in comorbid circumstances, and, respectively, the tendency to increase the probability of suffering from coexisting although not necessarily correlated pathologies in multimorbid circumstances. As tendencies offer a directionality, a future beyond the current presentation, the epiagnostic attitude seems fairly adequate as a definition of co- and multimorbidity trend seeking; (2) that the overflowing effect introduced by complexity and heterogeneity affecting diagnosability puts in value the characterisation of epiagnostic research and practices, developing an attitudinal shift to epiagnostics as defined in QIII, §4, and to consider the value that new technologies present in assisting clinical decision making with new emergent ontologies and mereologies (particularly in Artificial Intelligence Assisted Diagnosis), probabilistic and frequentist; (3) that epiagnostic practices are fundamentally directed to determine collateral and correlational factors to better decide the detection of plausible comorbid instantiations of pathologies in a

patient's clinical picture, and primarily aligned to finding the appropriate treatment interventions, informing about prevention and prognosis of further comorbid possible scenarios, given any index diseases under study; and (4), that epidiagnostics are pluralised working hypothesis, multiple plausible drafts presenting a reading of a personal scenario that affects both, the validation of clinical classifications, and the consequential epistemic accommodation of new approaches and proposals of interrelation (Cf. QII, §1: revaluing trust by filling the gap between diachronic and synchronic conventionalism). This empowers the validity of plural diagnostics, requiring of different 'interfield strategies' to frame, inter-frame and approach multiple pluralistic interpretations, opening the diagnostic practice of depiction, recognition, comparison and relational inference to a reconsideration in terms of probabilistic multiple-decision making assisted by contemporary clinical ergonomics and clinical engineering (involving personalised attribution through Artificial Intelligence Assisted Diagnosis, thick-&-think bid data analysis, patients's report text and qualitative analysis, cross reference comparison, etc.).

As concluded in QIII, §5, the value of epidiagnostics as a practice lies in how it focuses multifarious, heterogeneous, complex, multimorbid, comorbid circumstances employing all efforts to suggest differential diagnoses for depicting antithetic processes, using probabilistic inference for organising plausible hypothesis, practicing multiple drafts theory making, and orienting the circumstantial nature of a patient's symptomatology with a clinically significant prognostic account (including concurrent or future comorbid/multimorbid peripheral distress), and a more contrasted treatment than few-dimensional, univocal, systematic diagnostics.

In next chapter, QIII, §6, epidiagnostic evaluation turns to a clinical facet, where inspection of nosographic entities is made by

the identification of neuropsychiatric dysfunctions of interest to comorbid pain assessment. Plenty evidences have exposed how emergent neuropsychiatric symptomatology appears along with pain reinforcement processes. The opposite direction, pain symptomatology followed by neuropsychiatric index diseases, or pain reinforcing such diseases, presents as well. Neuroplasticity, brain inter-systemic distant connectivity, and reshaping processes affecting a proper neuroanatomical and physiological work have been introduced as crucial markers for identifying comorbid and reinforcement dynamics following conclusions on inter- and meta-systemic involvement via RIF Interpretation (QIII, §4), and for approaching to plausible explanations of dysfunctional pain self-bioevaluation. Prognosis and multifactorial analysis are two major focuses of attention for developing a strategically oriented diagnostic practice to comorbidity and heterogeneous, complex, uncertain presentations.

For this reason, a contextualised scale of implied comorbid criteria, and of viable stressors that lead to clinical worsening, must be generated in diagnostic person-centered evaluation, especially if pain presents, understanding the patient as a whole, and his or her central nervous integration, affection, memory, thinking and coping strategies as an organic, unsteady, plural course of actions. In order to assist diagnostic detection, this QIII, §6 introduced a neuropsychiatric framework for interrelating such multifarious comorbid contributors, overviewing some of the most common diseases affected by, or being affecting pain reinforcement processes and emotional functionality. Four epidiagnostic factors were applied, mainly driven by relational and prognostic values, which may help in finding neurotypical features during the diagnostic search and evaluation of the patient as key signals.

Vulnerability factors for emotional comorbidities implying pain reinforcement and func-

tional neurodestruction are also implicit values. Dysfunctionality clusters involved (1) 'executive attitudinal dysfunctions', (2) 'impotence, worry and habits dysfunctions', (3) 'affection, mood, character and personality dysfunctions', and (4) 'dysfunctions related with central neurodegenerative disorders'. These clusters are presented to be taken into account in further scales, questionnaires and tests all-together, making new technology in application to smart detection of micro traces of dysfunctionality that could make a probabilistic pattern recognisable to the instruments and better assessable by the clinician —this is also connected to conclusions in QIII, §8—.

The idea behind the notion of clustering dysfunctionality for instrumental recognition recovers epidiagnostic multifactorial and prognostic virtues (QII, §1 and QIII, §5): assessment of comorbidity is nowadays extremely under-sophisticated because of the lack of interfield theoretical frameworks enabling compositionality and flexibility of use. This chapter wanted to contribute to the edification of a wider and deeper understanding of such frameworks, delivering on an organisational articulation on the basis of its cohabiting chapters. This is also hoped for physicians to facilitate the recognition of diagnostic phases in copathological pain-reinforced neuropsychiatric assessment, or as a guide to select interconnected wired conceptual links that would benefit the diagnostic search of diseases and polythetic symptomatology in psychiatric follow up.

Further neuropsychiatric frames delivering on this niche B can tackle the different variations evaluation can adopt in approaching patient-specific cases, involving contemporary reflection on clinical characterisations as diagnostic practices of measuring (comparing to nosographical standards developed by theory making underpinning routines) and knowing (epistemic access), as studied in the following niche C.

—

. *Specific Results, Conclusions & Implications Excerpted from Niche C — 'Clinical Characterisations: Diagnostic Practices & Pain Measurement Strategies'*

Running forward to a pluralistic interpretation of the diagnostic performance, QIII, §7 analysis spoke in favour of personalisation and contextualisation of nosographic accounts by a modernised descriptive neuropsychopathology. This recalled the identification of diagnostics as an epistemic practice, whereof main features have been defined as a response to the contemporary conditions modern medicine is establishing: (1) favouring personalisation by relocating patients's situation at the centre of clinical care, (2) accounting for patient proximity and interpersonal care as two pragmatic keys towards a more empathetic physician-patient relationship, and (3) assessing the intricacies of clinical classifications as situated confluences of kinds, socially elicited and decided, affecting patients, symptoms, diseases and healthcare systems. It has been explored how efforts at de-trivialising rigid, mono-causal and categorical diagnostic methods can lead to a more flexible concept of diagnostic practice, more profitable to psychiatric needs. By rethinking its multimodal requirements to respond to multifactorial symptomatology, and by adopting pluralistic, social epistemic values, the movements of the practice towards a better understanding of individual clinical case behaving can be more easily assessed, observing community-based decisions, and re-designing previous schemata through error-learning.

The proposed collection of features outlines a practice comprised by 9 traits that, in defining how and through which structures diagnostics work, may be of use in applying systemic performance to Artificial Intelligence assisting pathological traits exploration. These features involve language and pragmatic accounts on

pathological descriptions (words usage are critical for newer involvement of cognitive ergonomics into text and qualitative analysis on patients and clinical reports), along with the implicit pathological architectures and traits composing nosographical contextual standards, where also instrumental and test-making contribute to contrast under specific decided scopes and criteria (in relation to QII, §1 and QIII, §8). This definition also comprises three more features, by addressing probabilistic-frequentist interpretation of pathological presentations, where engineered thick-&-thin Big Data contrasting might be introducing a future revolution in clinical inspection; by committing personalisation of diagnostics as contrasting past cases with similar pathological traits and their referred attributed diagnostics; and finally by promoting the involvement of accretional information feeds, both by patients (and patients's environment) and by healthcare personnel, building a more complex and suitable descriptive neuropsychiatric pathological account of the patient's scenario, that thus goes along with the application of textual and qualitative contrasting technology for filtering and rendering probabilistic scales and suggestions by instruments to diagnosers to decide and assess —this interpretation is also followed by conclusions in QIII, §8.

It is hoped this consideration can be related to QIII, §9 and §10 in their extension to clinical ergonomics framing artificial recognition and simulation of knowledge upon patients as clinical value data systematised for a better understanding of complex scenarios, helping in refiguring from bottom to top, as argued in QII, §1, the nosological debate through an accretive drift of well ordered, filtered and contrasted medical data, thus favouring development in newer and modernised nosographies.

The following chapter, QIII, §8, concluded on the problematic situation given the current assuagement in evaluation instruments renew-

al, borderlining an epochal neglect of modern technological accesses to characterise how patients understand their own experiences, as for clinicians to assess their ability in doing so (recalling self-identification dysfunctionalities: Cf. QIII, §6). Conclusions showed how the majority of scales of current use and main application do not induce patients into 'effortful reflection', striving to recall and reshape their experiences. When cognitive effort delivers on tests, neuropsychiatric scenarios are more suitable to assess on account to the evaluation of the patients ability to formulate futuribles, engaging memory and integrational functionality, decision making routines and personal and interpersonal emotional projectionality, which performs as well as an evaluation oriented to identify neurocognitive reorganisations, systemic and inter-systemic reshaping processes and, thus, open to a therapeutical basis. In other words, scales do not have an implicitly designed complex integrational-therapeutical role, but limit their scope willingly to an un-accretional feed of value knowledge via performative extraction of information, most likely decontextualised and non re-contrasted (or temporally tight to a few minutes instead a few hours or days). Criticism was addressed to the ambiance of trust in which such extraction is performed. Low feasibility presents a trust-knowledge imbalance, as the thinner this information gets, the more the diagnoser needs to guess, elaborating 3rd person perspective judgements in the lack of patients's self-narratives, contextualised to situations or decision making processes. Put in other words, the less the instrument relies on the patient's feeding the scale, the more the diagnoser (a 3rd party) is required to feed the answer with 3rd-party information, being it epidemiological typical data, general standards, or personal/experience-based guesses. When patients do not reflect effortfully on a given topic where just themselves are trustful agents (because the instruments work for understanding



self-beliefs and self-judgements: thus, interoperationally diagnostic interaction), more probabilities arise for arbitrary, shortcut-like answers to be developed, testimonially spontaneous.

A more interactive (with the paper/software method of the instrument) and therapeutical (with the interviewer/analyst/diagnoser) approach is vindicated to reinforce further measurement strategies, involving new technology capable of capturing broad resolution feeds, where self-reflection, affective identification, rethinking of experiences, naming and renaming of emotions, peripheral tension evocation strategies (perturbation-situational strategies), and personalised attentional baits would improve data gathering and contrast.

Situation-based measurement strategies are upheld: when situation recalls actions, agency implies the person, his or her decisions, reasons to act and to feel, and this involvement entangles the patients into their feelings through inscribing themselves with perspectivity, a new 3rd person perspective enacted by memory and effortful reflection and narratives (Cf. QIII, §9). Inventories, scales, interviews or questionnaires are suggested to focus equally on topic-specific matters of experience and on the surrounding situation that provoked, and could provoke anew, pain-concerning events, personalised to the context of each specific patient. Self-beliefs and judgements appear to be accessed via straightforward addresses to experiences, context-free, instead of via attentional, attitudinal, reflective contexts. Situation-based strategies would focus on actions and attitudes, possibilities of thinking of specific situations where pain has been felt, managed, associated with other issues or overcome by specific patients. This enables trust knowledge to be obtained, generating a broader feed. Future lines will tell how measurement strategies evolve into these new possibilities, involving clinical ergonomics and speech and text engineering evaluation using broad rather than thin resolution feeds, promoting a

more reflective and considerably more descriptive neuropsychopathology. This moves conclusions to the next niche on value, self-beliefs and interpersonal difficulties transferring them.

—

*. Specific Results, Conclusions & Implications  
Excerpted from Niche D — ‘Interpersonal  
Characterisations: Difficulties on Self-Narratives  
& Pain Transference’*

Value is, in a clinical sense, what evaluation runs for: to assess implies to give credit to what the patient puts value on, and merging it with what the diagnoser understands valuable for ascribing nosographical interpretations in a synchronic decision making of trust (Cf. QIII, §1). This processes involve epistemic beliefs, and in the case of patients reflecting on problematic, confusing or uncertain experiences in therapeutical assessment situations, descriptions of their pain turn out to be unable to address specific values, framing indeterministic self-beliefs. By considering the experimental application of Peter Lawrence Goldie’s general perspective theory, QIII, §9 proposed a strategy to define propositional self-beliefs in 1st and 3rd person perspective, situated as carried on by the focus of the narrative the narrator tends to opt when expressing an experience. It has been suggested that in a theory of perspective self-beliefs of the style maintained by this chapter, 1st person self-beliefs can serve for offering an ostensive definition of experiences. This schema has led to identify indeterministic self-beliefs as complex 1st person self-beliefs that behave in relation to the context that affords a subject to justify, assess and relatively put trust on different beliefs at the same time (valuing the concept of ‘double feeling’ with several actual examples in neuropsychiatry). Indeterministic pain self-beliefs introduce a complex problem for an external analyser in judging what the patient is valuing when self-assessing present or past

experiences that may affect the recognition of possible pathological traits and architectures (in conflict with the aims of instrumental analysis on feed, recalling QIII, §8), generally via narratives describing feelings, beliefs about those feelings, and actions, along with beliefs about the reasons that oriented the patient to act the way he might have acted. The topic, reviewed in this style, aims to acknowledge the importance of unsteady pragmatic accounts in clinical epistemology, with especial attention in the field of psychiatric diagnosis and therapy theory, in the hope this can contribute to a better understanding of patients's self-assessment and the dynamics behind self-reported beliefs, that also can be beneficial in developing broader resolution feed analysed technologically and ergonomically.

The last chapter of the thesis, QIII, §10, concludes with a proposal for defining how assessment is able to incorporate trust to transferred value through a common background based on agreement, and how value can be assessed to be shared through trustworthy transference chains and practices by means of participating in a context of empathy, which is contextualised to communities of subjects of belief recalling the epistemological readings on situationism in QII, §1. Propositionally, this context would serve as an analyser's threshold for contrasting contents of belief of an informant, discerning whether or not the informant is transferring transparently (with sense) his or her beliefs rather than simulating them. The proposal allows analysis in embedding trust, nosographical accounts, pathological traits and architectures into propositional beliefs composed of contents with traits (which may instantiate attitudes, orientations, intentions, pragmatic addressivity, and forms of public conventions and private dispositions into the very belief of the subject), as well as its transference and its plausible options for solving the identification process that serves for an external analyser to discern through empathetic agreement what is the suitable evidence that makes the experience of an external

subject to be transferred with sense. Contents appear collected in open and closed clusters, those open inform of traits on conventional sharable definitional claims on referential suitable matters of interest, those closed inform of traits proper to the agent of the belief, composing the subject understanding, interpretation and, working perspective theory using the assets developed in the previous chapter QIII, §9, experiences in a private, intimate characterisation of the subject's biography. This is hoped to help in rethinking the problems of simulating pain as appointed by the chapter in a referential and pragmatic manner, concerning compositionality and partiality. In this sense, partial simulation is put to underpin the epistemic belief under which both, evaluation and experiences are given into the neurophilosophical scope via these clusters of traits (which, in a straightforward fashion, orient discussion on experience evaluation to the conclusions on broad and thin resolution feeds in QIII, §8): the richer the open cluster, the more conventionality involves in transference, favouring situation-based approaches to instrumentalisation and application transference theory. Enrichment may favour transferring trusted knowledge, as the more the cluster of traits informing about the content of belief of an interpreter resembles the cluster of traits informing about the content of belief of a speaker, the less the former simulates the belief of the latter (the major criticism in QIII, §8). As generating a standard by conventional sharing of open clusters, this idea has a potential value for engaging more transparency. In its appendices, the chapter concluded some experimental applications on artificial self-beliefs and experiences in the field of cognitive ergonomics, involving communities of evaluation through empathetic agreement in Artificial Intelligence Assisted Diagnostics favouring transference of trusted knowledge through enriched clustering. Enrichment may be taken seriously into account for accrediting trust in assessments and value in the transference of trusted knowledge.

## II — *Remarks on the Neurophilosophical Contributions of this Work*

Should an integrative field for an epistemically contextualised neuropsychiatry be defined, there appears a sound need, to the extent of the convictions in the present text, of settling common working medical and clinical evaluatory characterisations taking into account the following factors, common from the standpoint of a skeptic instrumentalism:

(1) *Unavoidable Evidence on the Instrumental-Skeptic Role of Materialism*: neuro-psychiatry works with anatomical grounds and chemical scenarios, that need to get along with multiple psychiatric tendencies and behavioural theory making, however not by neglecting the proper constitutive feature of the interfield, that also connects the mental depiction of experiences with the rest of the medical disciplines. This also produces naturalised contents on account of 21st-century psychiatry on its definitional claim, not as the medicine practiced towards the alienated extremed mental sufferer of the 19th Century, but to every human being suffering from an affective problem, vitally depriving him or her from health, interpersonal relationality, and personal growth. Modern psychiatry in incorporating neurological studies, is prepared to be now the medicine practiced towards affective conditions, where description, definition, explanation and treatment of such affective complications are appointed through nosological debates and convention shifting. ‘Madness’ might be, not just historically but for some practitioners today, still useful for having a humane trait, where the mad has his or her own role and range of reason, nonetheless such pragmatic account is but a ‘perspective taking’, a stance that grounded on personalised, descriptive and patient-tailored neuropsychiatry would lack multiple specifications in need for practicing the interfield as required.

(2) *Anti-Localism via Orchestration and Facilitation*: master nuclei, master pathways, master fields, master systems bear no hyper-scaled over-attributed agency, their agency is set to that of facilitation in an all-encompassing organic inter- and meta-systemic building of competing and collaborating actions that, as a result, happen to perform experiences (as it is the case for the topic of this work) in macro-scaled agency attributions.

(3) *Dynamic Neurophysiological Development from Morphofunction*: morpho-functionality imbricates developmental accounts on diachronic (evolutive organisation and reorganisation) and synchronic (present at the time of evaluation) interpretation of materiality, but the medical and clinical inspection of this twinning term, morphofunction, merging matter and its action, needs be understood properly as a consequence of slow and generative emergent processes that — with errors of environment-accommodation and adaptation as well included in the biological result of systems and organisms— are to be assessed in relation to dis-morpho-dys-functionality: clinical evaluation through diagnostic assessment is concluded in this works, within this strict scope, to flexibilise its ascriptions as to better describe and explain why and how pathologies occurred, evidencing epidiagnostically, multifactorially and prognostically what pathological traits manifest.

(4) *Overall Identificational Claims*: characterisation is concluded to inform about the epi-phenomenal nature of both, of the behavioural morpho-functional manifestations of organic subjects, and of the medical and clinical agreement on the dysfunctional and dismorphic processes that orchestrate and facilitate pathological traits for further classification, systematisation and nosographical organisation. Experience, understanding self-experience as a ‘de facto interpretation of what occurs’, along the faculties that behaviour resolves, need be

considered epi-phenomena, and attributed with identificational claims, interpreting explanatory and descriptive strategies of medical and clinical affairs on the basis of the argument assigning those affairs overflowing epistemic complexity. Agency goes beyond physiology, organicism, material reductionism: agency as microproperties shall not be fallaciously characterised as to agentise macrophenomena, and, for the same reason, evaluation of complex neuropsychiatric scenarios is concluded to be better resolved through epidiagnostic practices.

(5) *Inter-Systemic Interaction, Meta-Systemic Attribution*: organic integrity is concluded to perform through the whole organism, thus ascriptions of psychiatric disorders as proper to neurological functionality keeps the same reductionist interpretation criticised in the previous texts. Inter-systemic orchestration is vital to figure the overall scenario in which the patient is organically involved. Inter-systemic interaction and meta-systemic attribution — thus, of the emergent resolution of what the whole organism does through its systems and in reciprocal interaction with its milieu— are concluded favourable characterisations on this extent. Finally,

(6) *Recognition of Epidiagnostic Attributions*: evaluative multiplicity reinforces the role of plurality, probability, situation-dependence, contextualism and personalisation of multiple attributions making. Gender, sexes, cultures, anthropological accounts are intertwined with diagnostics and are, therefore, implicitly giving shape and formalisation to decisions, trust and agreement. Diseases and their classification into nominal clinical pathological accounts are concluded, thus, not to be imaginable trans-historically applicable to every contexts: their identity and adequacy resolve suitable in situated epistemic niches of acceptance and the proper identification of such niches values interfield in-

terdisciplinary and multicultural plausible solutions. This favours the adoption of an epi-diagnostic evaluation, a multiple drafts model, based on contextual probable chains of copathological identifications, giving to multifactorial analysis and prognosis a major role on decision making processes, and providing of new, alternative and re-producible nosological (argumentative dynamic systematisation of pathological traits) and nosographical (clinical knowledge set to be applied to characterise and textualise through nominal claims the pathological conditions of a given patient) accounts on comorbid and multimorbid scenarios.

### III — *Global Results.* *On the Attainment of Goals*

The research plan agreed for the development of this doctoral project arranged five goals intersecting the main factors that gave coherence and sense to the work proposed by the present thesis. The following lines will assess how such goals have been positively met and expose the difficulties on the process.

(1) The major goal of the thesis was suggested to portray the niches underpinning the epistemic conditions affecting diagnostics in the neuropsychiatric evaluation of pain experiences. This major goal has been positively attained along the body of the thesis, reasoning in QII, §1 and §2 the structure of the analysis proposed and, thus, the organisation of the Index, affirming 4 major niches (A, B, C and D), gatherers of their proper thematisation dynamics, engaging situated factors contextualised for the generation of specific topical questions, answers, and styles of assessment on the value of the scientific contents delivered, debated, refuted or accepted (especially on clinical discussions upon pathological standards, methods of attribution of agency, and attributability of diseases to specific patients). The prosecution of this goal also

supposed the continuous refinement and adaptations of the structure of the Index, for which I would like to acknowledge the rigour and attention given from my thesis director, Dr. Ángel Luis Peña Melián, and the multiple conversations and talks held with psychiatrist Dr. Lars Christian Moen, from Oslo, and PhDR Piotr Król, from Warsaw. The definition of the niches for framing epistemic contents on evaluation has also been positive in its exposition of theoretical conflicts on the matter in a historical fashion, indicating the epistemological consequences internationalisation, globalisation and interfield work are having in reshaping the strategies required in 21st-century neuropsychiatric diagnostics.

(2) Regarding the second goal informed, integration has been especially treated in delivering possible solutions or suggestive alternatives to evidenced and exposed problems. This factor has been specifically significant in QIII, §3; in relation to explaining the ethnographic transformations of the practice and suggesting the epistemological inspection on agency over-attribution; in QIII, §4; proposing an inter- and meta-systemic integrative alternative (the RIF Interpretation) to the characterisation of nociceptors; in chapters QIII, §5 and §8, suggesting the integrative notion of epidiagnostics as a multifactorial and prognostic intermorbidly evaluation, inquiring the need of contemporary interfield patient-&-situation-dependent measurement strategies; and in chapters QIII, §9 and §10, ending with an integrative answer to interpersonal transference of value knowledge in epistemic beliefs.

(3) Conjugation of neurophysiological and psychiatric contents has been put on the centre of analysis, applying a comparative and pragmatic approach for developing plausible beneficial interactions from neurofields and behavioural interpersonal fields, including therapy theory and clinical engineered evaluation.

(4) Accounting on utility, it is hoped that the contents here developed could offer good assistance in application of analytical perspectives for advancing neurophysiological attributions in Niche A, especially the contribution of the RIF Interpretation to this extent; for enhancing the diagnostic practice in recognition of the current overflowing hypercontextualisation of nosographies in Niche B, especially with the contributions of epidiagnostics, and personalised assessment from modernised technology-involving measurement strategies in Niche C; and for helping to understand the pragmatic interpersonal problems evidenced in Niche D through perspective theory applied in the style suggested by QIII, §9 and §10, with further implications in Artificial Intelligence Assisted Diagnostics, Big Data analysis (recalling the significance of broad resolution feeds), and textual and qualitative analysis.

(5) Concluding the work, the final fifth goal on placing value on epidiagnostic practices is hoped to have shaped the notion, on the application of epistemic framing as a form of understanding pathology and multiplicity of presentations in pathological scenarios of co- and multimorbidity.



## QIV, Chapter §2

### Future Lines on Epiagnostics: Applications to Neuropsychiatry, Neuropsychiatric Epistemologies & the Nosographic Technologicalisation.

—

#### Parts

##### . *Introduction*

#### I — Aspects of an Epiagnostic Turn

- . *(1) Decision Making Routines & Fragility*
- . *(2) Barriers of Biomedical Modelling & General Reductionism*
- . *(3) Increasing Need of Memory, Contrasting and Epidemiological Facilitation Strategies to the Clinician*
- . *(4) Promotion of Democratic or Educated Participatory Trust Protocols of Conventionality for Deciding Changes in Pathological Registration and Ascription*
- . *(5) De-Stigmatisation via Nosographical Inflation*
- . *(6) Naturalisation of the Relationships among the Institution, the Clinician (diagnoser), the Patient and the Patient's Environment*

#### II — On the Lines of Transformation towards a Future Epiagnostic Practice

- . *(1) Incorporating Framing and Diffraction to Professional Activism & Research Practices*
- . *(2) Incorporating Personalised Attention by Calibrating Abstraction from Epidemiological Accounts to Clinical Accounts*
- . *(3) Informing New Trust Protocols and New Forms of Agreement*
- . *(4) Reassuring Qualitative Scenarios: The Significance of 'Contextual Evaluation' in Clinical Assessment of Pain Experience*
- . *(5) Design and Incorporation of Artificial Intelligence Assisted Diagnostics*
- . *(6) From Pain Experience Evaluation to Contemporary Interdisciplinary Algology & Pain Units*
- . *(7) Nosography Responding to Contemporary Complexity in Standards*
- . *(8) Platforms, Queries, Decentralisations*

#### III — On Future Work on Epiagnostics Opened by the Present Thesis

## . Introduction

Neurophilosophy has approached along 21st-century scholarly works with medical and therapeutical interests the epistemology of pathologies through multiple sides, and with the shift of the technological rhythms into deeper and broader information systems, neuropsychiatric fields can open as well to critical studies, alternatives and historiographical and analogical-comparative inquiries on pathologisation, beyond solely biological schemata. Cultural, social, economical, gender and race studies on the mater have and will develop into new forms of understanding what pathological accounts are, classifications, evaluations and epidemiological claims on diseases appointed to specific patients, instantiated by their conditions, emerged from their interactions with their changing environments.

Ascription claims (definitional tagging schemas) inform through categorial structures different mereologies, ontologies, identifications on pathological dispositions, thus about diagnostic possibilities: ascriptions, in being abstractions, remain artifactual, socially and conveniently decided by communities of research and clinical practitioners. It starts to be the case for categorial claims in contemporary evaluation that fixed point paradigms provide not as medically profitable and theoretically solvable solutions as dynamic, interactive, interoperative, multifactorial and prognostic-related strategies. This conclusion, involving those characteristics as foundational traits of epidiagnostics as proposed by this thesis, makes space for new alternatives in diagnostic recognition, not just for the case selected (neuropsychiatry) but for internal medicine as a whole in coming years.

In the lapse from 2020's to 2040's the fields related to diagnostic evaluation will see profound changes affecting the technologisation of the practice with fruitful promises for casting better decision making processes, assisted by

Artificial Intelligence, cross-cultural, cross-comparative, multivalued situational assessment and case behaving strategies for measuring private experiences like pain.

It is to note that diagnostic intervention, as appointed from contemporary professional activism, must be ontologically separated from treatment intervention in the sense offered by the duality 'diagnosis-farmacotherapy': a progressively larger and increasingly overflowing diagnostic scenario of classificatory plausible pathological clusters, to be called 'nosographical inflation', does not provide for, and has no necessity of, inducing immediate or appointed therapeutical intervention. Nosographical inflation can be thought of, and is argued to be informed as so, informational compounds that will progressively evolve into facilitation factors for building modern computerised assistants performing hyper-contextualised and tendency-specific descriptive pathological systems. Examples in international classifications for internal medicine (eg, ICD10v) serve for understanding this suggestion: the possibility of claiming 'domestic cat scrape' does not identify treatment intervention, but a more comprehensive assessment and contextualised attachment that may be of much help if tracked along patients's anamnesis for future developments of, for instance, infections—for in knowing the attacker's species and the patient's situation at the event will make better informed differential diagnoses given the case of poor prognosis, in this way providing of a more educated guess assisting decision making routines for practitioners—. 20th-century 'medicalisation of ordinary life' has not much to do with 21st-century 'pathologisation of possible health problems of ordinary life'. The first perspective approached biomedical instructions, which has been highly criticised, especially in psychiatric ambiances, involving acutely inefficient medicaments pos-

ology decision making, framing pharmacological adherence and resistance, secondary-gain emergence (legitimation of affective problems masking deeper societal problems affecting the individual), and comorbid implications of iatrogenic origin, providing reductionist and centralised medical results —however endorsing multiple economical benefits for certain industries—. The second modernised perspective approaches an overall paradigm of intervention, generating medical diagnostic produce on account of heterogeneity and complexity, of personalisation of the practice, by enabling a better space for human contact in a decentralised institutionalisation of healthcare, internationally contrasted and disposed to understand the problems of the patient as a person in his or her contextual contact with a shifting environment of stressors that may be characterised broadly, descriptively and prognostically. Pathologisation of ordinary possibilities may be, in this sense via nosographical inflation, a big hope in attaining better healthcare systems aided by expert software, in an era where physicians are shifting from private memory and research study, individual decision making processes, and personal skills, to cooperation, globalisation of power, interpersonalisation of authority, indetermination of unitary singularised index diseases, and multiple drafts theory making, recognising the human value before the organic, biological immediacy, and putting to work plural dynamic resources for extracting well-ordered and epidemiologically compared suit-to-the-patient diagnostic values that integrate his or her authority, personality, character traits, ordinary behaviours, life preferences, interpersonal accounts, general skills and specific abilities, with further involvement of how societal, cultural, economic, laboural and familiar-friendship-kindred multifactors appear affecting his or her pathological niche in a medical sense. Diagnostic recognition has today's opportunity to rethink and reinvent clinical epidemiology, patient evaluation, social,

cultural, economical, interpersonal problems framing, and to re-read the societal changes that are, in many ways, provoking and aggravating such pathologies.

Diagnostic contrast and thick-&-thin Big Data comparison, Smart Comparison and further strategies have the power to translate those problems that have a basically societal emergence point, and empowering the individual suffering from them through interpersonal and intimate descriptive forms of diagnosis that could make patients reunite, focus their problems in a natural and social manner, de-taching diagnostic stigma, and favouring spaces for cooperation within institutional and associational grounds (proposals that walk across diagnostic evaluation from a first instance medical intervention, and that come in very common terms with the postpsychiatric and critic psychiatric movements, which would work in similar ways as in mental medicine as for those applications currently installed in oncology, kidney diseases, hepatic diseases, orthopaedics, paediatrics and viral infections with familiar, laboural, scholar and further social impacts).

In this writing, the following three parts will consider the developmental space of what is understood by this research to be the lines needed and programmable through future works as for addressing the problems in today's evolution of diagnostics, with especial attention to neuropsychiatry in the study of patients's affection and experience, but with direct application to internal medicine. Part I considers some of the aspects the present epidiagnostic turn to complexity faces, seeks and looks forward to provide in 6 points. Part II sounds the 8 major traits concluded in the transformation towards a future diagnostic practice. Part III finishes the text exposing the orientation to future work opened by the present thesis, continuing with the development of a research basis for theoretically underpinning epidiagnostic projects in current views, as applied in clinical ergonomics too.



## I — *Aspects of an Epi-diagnostic Turn*

### (1) *Decision Making Routines & Fragility:*

In a close future characterised by an overflow clinical nosography, with an inflationary offer of clinical and medical data from interfield origin, current decision making routines will straightforwardly come vague into diagnostic human-follow-oriented precision algorithms, showing non-exhaustive in defining proper-to-the-case divisions of polythetic pathological classes (generally in need of application of diffuse and abductive logic of difficult performance without technical assistance). This scenario worries the common application and understanding of clinical paradigms: should the collateral effects of nosographical inflation occur to perpetuate rough decision making, hindering clinical identification, solely human routines will show fragile in detection, characterisation and determination of pathologies —as so for theoretical-comparative and alternative shifting paradigms in progressive movements towards interfield re-classifications. This fragility can be attuned to the time and era of contemporary identifications through assisted comparison, in the sense epi-diagnostic precision algorithms for polythetic detection would end up helping practitioners to better determine pathological clusters and niches via new adaptive software and epi-diagnostic nosographers.

(2) *Barriers of Biomedical Modelling & General Reductionism:* As appointed in QIII, §3 and §4, the need of anatomophysiological accounts in neuropsychiatry (and internal medicine in general practice) is irrevocable: the diagnostic horizon cannot escape from material alibis in current times —the amount of causal critique and counter critique, of experimental data and interpretations, of correlations and multi-causal models implying material expositions of events is increasingly been modified and morphed into more complex views that shall not be re-

viewed but thoroughly. Psychiatric nosography and decision makers along the way cannot obviate as an article of float scholarly optionalism the effects of vascular breakage (eg, encephalic hypertension, aneurisms, ictuses), of hormonal equilibrium (eg, thyroidal stability, hypophysis, metabolic balance), of immune coalescence with nervous system (as exposed by the RIF Interpretation in QIII, §4), or more directly tumours, internal oedemas, glio-neural fields dynamic and structural dysfunctionalities, of exo-substances's effects on cognition, of neural reactivity after nervous disability via exercising and sports, of cell migration, and of functional plasticity.

The problem is not presented by material alibis as such, but with stating that these are ontologically responsible for overall clinical reactivity and personal agency, which is an argument involving highly discutible propositions and fallacies. To the extent of this summary, as approached beforehand, nosography could expand its views through materiality nonetheless accepting and endorsing an instrumental skepticism overriding suggestions recalling, as studied by 'Niche A' in this work, ancient 17th-18th-19th-century partial and reductive inclinations on material reasoning.

Description and explanation as revealed by trusting conventionalism can be separated from epistemological analysis, and it is the case that through the second one, three modernised anatomophysiological aspects might get extracted: the significance of (a) adopting an intersystemic disposition (a coral work among organic systems), of (b) claiming through a metasystemic perspective (overflowing integrative agencies over singular systems, pluralising specific agencies through the whole organism, and distributing partialised agencies among the interactions of the organism with its changing environments), and of (c) making arguments participate of an epiphenomenal assumption (this implies conceiving of experiences in differ-

ent scales of complexity as the basis of self-ascriptions, and not as 'a product of the brain', but of the interactive evaluation of the contextual circumstance the person, in the medical case, is induced as a whole and exposed to interoperate with, in a situated scheme, socially, culturally, economically, familiarly... appointed). These aspects make the case for using material claims of agency as 'facilitators' or 'orchestrators' of further agency charges proper to the person in his or her interaction with the involving medium, for thus enhancing the way clinical evaluation of experiences through complex multifactorial stressors affecting such facilitators changes overall action and interaction from the person.

The biomedical roles associated with modern practices do not need to be associated with strong materialism, nor the cultural implications of capitalism in the anthropological sense that historically this way of thinking medicine approaches the patient as an organic machinery in a process of dysfunctionality. In its stead, modern interfield theory making can supply better assumptions for understanding the person — and his or her circumstantial disposition to the surrounding multifactorial schemata— in need of medical assistance as a proper human niche for factors aggravating or impeding his or her personal and interpersonal realisation in life.

In this sense, integrative medicine and modernised understanding of values, beliefs, narratives and their emergency as epiphenomenal developments would be able to help to make biological, medical, psychiatric and behavioural tenets convive in mutual understanding, without neglective argumentation, fallacious selection problems, or pseudo-explanations based on a purely unneat, metaphorical, unrealistic, mono-field, biased or interested and unbalanced reduction of complex scenarios.

(3) *Increasing Need of Memory, Contrasting and Epidemiological Facilitation Strategies to the Clinician:* The epistemic overflow on the

amount of data and perspectives reunited for generating standards, contrast tools and for finally delivering on diagnostic values exposes contemporary and future physicians in a problematic situation proper to human finite sets of skills. Modern technology can drive powerful softwares to act as facilitators to clinicians, as nosographers readapting immediately, contextually and internationally, tendencies of pathologies situating patients in personalised and interpersonalised niches, thus responding the necessity of Memory Facilitation Strategies (smart and expert search engines), of Contrasting Facilitation Strategies (through massive data cross-referentialised comparison), and of Epidemiological Facilitation Strategies (helping to apply global statistical background knowledge to case-behaving personalised requirements that may not respond to statistical claims). It is hoped these tools may set clinicians during diagnostic phases free from anxiety-driven decision making routines and de-installing them from individual biases in a more approachable and patient-oriented humane service, leaving to machinery skills that show programmatic, repetitive, time-consuming and about contrasting immense quantity of information from an up to date schema; and to humans skills that require interpretative, integrative, emergent, imaginative and contactual, interoperative and interpersonal performance.

(4) *Promotion of Democratic or Educated Participatory Trust Protocols of Conventionality for Deciding Changes in Pathological Registration and Ascription:* Promotion of such would require to adapt to contemporary requirements the way epistemic communities trust on conventions, and the style of discussions they have. Through adaptive nosographers (more specifically, via artificially guided trend-seekers and query responders) a different form of participatory and integrative re-distribution of trust into newer nosological claims shall emerge,

favouring a deeper, progressive, contextualised and descriptive pathology. One significant aspect of this shift comes with the identification of the notion of 'pathologies in nosographies' and 'pathologies in patients', being the second ones instantiations of the former with multiple variables proper to the person at case, that also affect his or her environment and gathers stressors that may function outside the material niche of the proper patient (eg, reinforcement of pathologies derived from economic crises, multiple-class conflicts —post traumatic stress, fear, anxiety—, familiar unbalance, scholar or laboural asymmetries, interpersonal dysfunctions...), forming a scene that reclaims modern nosographies and diagnostic interpretations to re-value the weight of how epistemic communities decide upon the division and classification of pathologies.

(5) *De-Stigmatisation via Nosographical Inflation*: The terms 'pathological trait' informing 'pathological architectures' have been introduced here in this sense for capturing the shift from disease-like, syndromic, disorderly or condition-like ascriptions: pathological traits via recognition of specific stressors do affect, this way, overflowing those concepts, and ascribing multifactorially, prognostically, personally and interpersonally multiple drafts characterisations of affections and evaluations of health 'in the scenario of the patient', meaning, de-stigmatised from a category, and reassumed as a person involving specific stress and responses developed against it affecting from multiple focuses his or her life performance which, assessed, identified and suggested for a treatment, would be medically approachable, involving as well therapeutical behavioural patterns that the patient may follow with prevention ends (the benefit of equilibrium in diet, socialisation, sports and physical activities, open stays rebalancing the amount of time spent in closed spaces, and so forth), and the reduction and specialisation of

medication for dealing with pathological alterations that may be solved with a non-pharmacological interaction. A more plural, contrasted, integrative, abundant and broader claim on pathological traits can be projected with contemporary and future software assistance. The diagnostic direction shifts, from solely attributing a disease to a patient, to identifying pathologies in the scenario of the person, extracting and interpreting (abducting) a problematisation described in medical and clinical terms. Epiagnostics make the effort of using multifactorial expansive and descriptive nosographies using traits in deep comparison and characterisation from the patient's scenario, instead of assigning the patient a reduced nosography approachable from a finite trusted conventional recount.

The inflational effect in nosographical accounts initially brakes the limits of specific determinations of diseases stigmatising categorically a particular patient, moving the clinical narrative into terms like 'pathological traits and architectures' inscribed as heterogeneous 'instantiations in-the-patient-scenario', being such instances of pathology the different variations approached by the patient in his or her individual and interpersonal resolution of specific pathologies. The need of claiming on the necessity of names for diseases will end up coming standardly unnecessary should the epiagnostic project achieves enough cross-comparative inflational satisfaction of assessment resources so that descriptive pathology could present more approachable through interoperative diagnostics based on conceiving the patient as a person in a particular circumstance, completing their focus work with more complex and broader ascriptions and characterisations for the pathological scenarios of a patient.

(6) *Naturalisation of the Relationships among the Institution, the Clinician (diagnoser), the Patient and the Patient's Environment*: The naturalisation of patient-physician relationships

occurs more clearly in 21st-century forms of attention, care and assistance—in comparison with 17th-18th-19th-century authority, oppression, violence, etc. as a significant number of historical and epistemological critiques have been appointed, and studied by the present work in QII, §1 and QIII, §8—. This naturalisation is present in pragmatic and linguistic accounts on what the patient says and informs about, and what the physician through specific measurement instruments and strategies understands from such speech. The relevance of text and qualitative analysis makes the case for adopting an inflationary perspective on this specific topic, as for choosing to provide broader resolution feeds (Cf. QIII, §8), situating the patient in the context of presentation of multiple plausible pathologies via a multiple drafts methodology, and contextualising his or her experiences through acknowledging the pragmatic accounts and narratives used (helping in case of communicative and executive patients: self-beliefs, self-narratives; Cf. QIII, §9 and §10) or performing advanced clinical diagnostics through pathological traits trend recognition (helping in case of non-communicative or dysexecutive patients).

## II — *On the Lines of Transformation towards a Future Epiagnostic Practice*

(1) *Incorporating Framing and Diffamation to Professional Activism & Research Practices*: One specific task in the prosecution of a more complex, dynamic, responsive and bilateral (patient-physician) future practice comes with incorporating historiographical and epistemic reasoning about linear-to-non-linear theoretical developments, ‘difformations’, as exposed by Lambert Williams in 2012 and studied in the present work in QIII, §1-4, in application to discerning how theories move convention from certain locus of attention to another, both in research and practicing clinical work.

This process will help to understand the underpinning ideas contributing in maintaining historical diachronic conventions as trusted or debunked in a democratic, contemporary, debating formulation of scientific acceptance. As informed in QII, §1, framing strategies expose a descriptive and explanatory analogy to theory making in diagnostics with the introduction of trust protocols, their interpretation, re-distribution of authority and enrichment of data. Incorporating those two traits to common scientific practices would also imply the usage of cultural critique, epistemic analysis and social inquiry in everyday decision making processes on diagnostic calibre, empowering critical and skeptical ideation and, thus, contrasting styles of producing valuable data.

(2) *Incorporating Personalised Attention by Calibrating Abstraction from Epidemiological Accounts to Clinical Accounts*: Epidemiological accounts, statistically defined, populationally-driven, niche-accurate, gender-race-ethnicity-age-specific and cross-culturally, economically, politically and internationally compared, offer abstract standards that may serve as background data for actively informing upon pathological architectures and pathological traits exposure and instantiation in a demographical sense. When transcribed into the clinical realm for a specific patient, as approached in QIII, §7, many studies have claimed background data to coalesce with personal and interpersonal information to properly arrive to conclusions on pathological attributions: in future years new software would be able to direct—through broad resolution feeds from the patient and even broader massively fed standards uploaded to decentralised open case-reported, research-reported, institutionally-reported and agency-policy reported networks—highly cross-comparison strategies towards determining kin resemblances among specific contextualised patient-specific symptoms with broad

knowledge pathological traits. This extraction will calibrate the way epidemiological abstraction ends up clinically applied into personalised diagnostic accounts, manifesting the significance of personal variations in the processes of instantiating pathological architectures through individual polymorphisms, thus gathering the necessary information for educating better decisions on the extraction of diagnostic values, prognostic factors and in the application of treatment interventions.

(3) *Informing New Trust Protocols and New Forms of Agreement: Refilling the Gap Between Diachronic & Synchronic Convention:* New forms of protocols will emerge, where different and decentralised stakeholders manage decision making dynamics. There a shift phase appears transitioning from previous processes of deciding —away from patient zones, and among scientific communities, what patients can suffer from, providing a standard and a name corresponding to the presentation of a specific disease structure and development— to modern forms of deciding trust, involving scenarios where many (clinicians, patients, patients's environment) argue, decide and collaborate in providing broad reference marks, describing presentational and circumstantial whole-scale symptomatology, that will end up in delivering assistance before intervention, helped by software protocols that will aid in determining descriptive architectures opened to possible treatments based upon material, test and analytical basis, but as well on self-reporting beliefs and narratives from the patient, and global standards functioning in decentralised fashions contextualising diagnostics to the patient, in his or her niche, and in his or her interpersonal interaction with the shifting environment. These new trust protocols will also make clearer the way information is managed, exchanged, modified, written and analysed, and whose is the owner of such, the patient, legally protected, authori-

tatively empowered, and disposed to collaboration with clinicians and institutions, which will also have a significant part of legal ownership of detailed reports on specific patients —in an evidently different modular scheme in comparison with patients—. Informatisation and deployment of value data upon networks and platforms (specifically with the development of blockchain resources and value-oriented exchange networking internet plazas) will redistribute power, enhance privacy, and encourage self-awareness of the value of personal data in medical and clinical realms, for better informing diagnostic schemas, and for controlling the protocols that will run what people share, how they do it and why they need to do it.

(4) *Reassuring Qualitative Scenarios: The Significance of 'Contextual Evaluation' in Clinical Assessment of Pain Experience:* Broad resolution feeds expose the case for qualitiveness in a world of quantities and measurements. Tests or material analyses based on biological sample extraction and pathological comparison will jump in future years with the development of micro- and nanorobotic agents, which may need to develop in close relationship with other forms of data gathering in metasystemic disciplines, where experiences, narratives, beliefs, speech, behaviour, interpersonal values and complex social and cultural vectors determine multifactorially important diagnostic values. The example of psychiatry, and neuropsychiatry as an interfield, in the clinical diagnostic assessment of experiences (as it is the case of pain) frames a magnificent example for interpreting how measurement strategies would work in a plausible future epidiagnostic flow: the incorporation of contextual evaluation through scenarios that assess the patient's resolution skills, collaborative performance, decision making, interpersonal sense in task solving, risk-taking and emotional narratives during performance are suggested (Cf. QIII, §8) to benefit the ex-

traction of broad resolution feeds, that will orient better comparison, and bring personalisation of evaluation to the clinical field.

(5) *Design and Incorporation of Artificial Intelligence Assisted Diagnostics*: The incorporation of Assisted Diagnosis in neuropsychiatric and internal medicine through Artificial Intelligence will contribute to make manifest the actual utility and international, decentralised controllability of the pathological overflow proper to nosographical inflation. Several lines of research and design are to be noticed: (a) Text & Qualitative Analysis (T&QA), with especial utility for enabling cross-comparison of patient symptoms with standards, and for extracting stressor-tensors in patients's speech and self-narratives through word-managing and analysis. (b) Thick-&-Thin Big Data, contrasting massive volumes of data in thick epidemiological blocks and abducting thin clinical applicable clusters through probabilistic multiple drafts methodology sorting. (c) Probabilistic-Frequentist Analysis, in the articulation of diagnosis and prognosis of pathologies, morbidities and co-/multi-morbidities as tendencies, where hypercomorbid and hypocorbid scenarios might be extracted through accidental vs. reciprocal/causal coexistence of multiple pathological architectures. (d) Blockchain technologies, in clinical application to systems of organisation, distribution, monitoring, encryption and communication of clinical value data in doctor-patient and doctor-doctor inter-operational relationships. And finally (e) Micro- and Nanorobotics diagnosing from the inside-outside macro-tissular, cellular, molecular and metabolic proteinic processes characteristic of pathological accounts ascribable from the patient's scenario.

(6) *From Pain Experience Evaluation to Contemporary Interdisciplinary Algology & Pain Units*: Algology, as the medical overall study of

pain experiences, has the opportunity to frame itself in 21st-century research practices as an interfield collaborative ground for theory making and clinical practice in a much needed impulse regarding the impressively high prevalence of pain and comorbid pain bearing scenarios in today's societies, and the opioid epidemic suffered by a big part of the world, involved, in psychiatric claims, as an overcoming compensatory strategy towards a non-realisational space where people can develop and health can be maintained and assorted. Algology, through pain units in hospitals with assistance-oriented value as introduced by P Wall and reinvented in the current century internationally, can play a good role in recovering clinical processes, as well as in enhancing an interdisciplinary complex collaboration in research theory making that, as the different grouping niches of the present thesis show in synthetic, polyhedron-like collaboration, with an integrative spirit, may structure the heterogeneous dynamics that favour pain debuting and continuity.

Another important topic this work wants to address is the lack of specific interfield development in 'Algology' as a medical speciality. This comes to the requirements of medico-clinical specialists on pain spectrum diseases, aetiology, morbidity, comorbidities, pathology, internal assistance, prevention, prognosis, kindred copathological scenarios, along with their needed intervention and treatment should it be applicable. Why is there not such a thing as algology for a medical student to become a specialist algologist? Why there is no academical specialty, before scholarly research, such as algology providing education on assistance, guidance, direction and caring beyond the also required and well executed for the most of cases pain units. A relational, inter-systemic, meta-systemic approach in algology is claimed here to be necessary, concluding with a specific interfield, a medical discipline in research and a clinical practice in direct intervention and healthcare systems.

(7) *Nosography Responding to Contemporary Complexity in Standards*: Nosographies may get transformed in the next decades of this century in highly useful, adaptive, cooperative and decentralised software technology tools. New forms of conceiving of previous static book-edited nosographies that can shift towards modernised plural, interactive, processing, instantly responsive and immediately updated nosographers, pieces of software dedicated to smart massive data searching and contrasting, personalisation and multifactorial value extracting engines that will facilitate the diagnostic recognition of pathological traits and architectures all around the globe, bringing first-quality healthcare protocols and diagnostic assistance to everywhere with an internet connection, that will connect patients, patients's environments, clinicians and healthcare operators and institutions in an international fashion, regulated by new legal waves of civilisational technologisation (as can be seen in the Canadian case in Toronto, Vancouver and Quebec, in China and Singapore, or in the European cases with Estonia's programme for a digitalised nation, with the fruitful Swiss blockchain legal social projects in the Zug Crypto Valley, with Sweden's Node Pole in Stockholm, or in the UK in London), and controlled by adaptive standards informing clinicians of multiple drafts plausible options in their developing characterisation of pathological accounts. The question being, thus: how will respond nosographies to the risks, challenges and opportunities this new form of 'trusting' offers? Which are the measures that we, as societal intervenors and contributors, need to approach for evolving theory making and clinical practice in a neat, controllable (at least not to form a malfunctioning corruptive disequilibrium), serviceable, opener and globalised tool?

(8) *Platforms, Queries, Decentralisations: New Era for Nosographers*: Not claiming this new point as an answer, but as a collateral im-

portant topic, it is to mention that nosographies have these risks and opportunities just in the sense they are being created, designed, decided, morphed, cared upon: diagnostic facilitation and nosographical inflation, through its technologisation, are starting to be new 'forms of convention', of trust, of identification with a decision, and the big difference may strike in that this new form of making decisions comes with plural, alternative, provisional, globalised and interpersonal factors that were before just handled by personal, individual, historical convictions, and with much more probability, fallaciously biased monofield strategies.

The new forms of trusting conventionality will now provide of more space for debating, contrasting and enriching data through social and interconnected epistemic communities, accessible, professional and guided. Two values have the key in this process: Open Data Platforms and Policy Networking. Open data platforms can redistribute clinical knowledge through new types of nosographers that make probabilistic-frequentist analyses based on human work, research, case-reports and directions. Nosographers, in this sense, will deploy as the needed filter of massive information presented by a human query, information that needs be assessed and calibrated through decision on conventions from those to whom filtering will affect: patients, patients's ambiances, clinicians, institutions... Open data platforms, thus, need to work in relation with political, debatable, openly democratic (meaning, educated participatory trustworthy decision protocols), transparent and honest boundaries, where policies and policy-makers come to play in a scenario set for developing fruitful, beneficial and humane lines of evolution. Instead of running across the lines (minding the corruptive and thus socially demanded refurbishing of political, economical, financial, stabilising infrastructures underpinning societal endeavours), we need to arrive to 'new deals' appealing to so-

cial interests in the hands of clinical institutions (recovering the sense of cultural institutions for clinicians too, associations and patient communities), whose main goal should be to provide with compulsory and progressive agendas, in much need in mental healthcare for tomorrow's depiction of what is to be sufferable.

III — *On Future Work on  
Epidiagnostics Opened by the Present Thesis*

The present thesis on epidiagnostic assessment opens multiple research vectors, of which three major directions are to be depicted: (1) the introduction and enhancement of an Epidiagnostic Mindset for all stakeholders in healthcare, along the educational and divulgative actions showing the significance of developing a broad assisted evaluatory practice, which helps clinicians to better understand the role of multifactorial, prognostic and inflationary pathologisation of common current health problems. This especially affects to neuropsychiatric spaces, the selected interfield as case study (for it being one interfield where comorbidities and indetermination of pathology occurs more often), as to internal medicine (for overall diagnostic practices); (2) the introduction of Clinical Ergonomics in application to Clinical Assessment, and its impact in designing systems for epidiagnostic identification of pathological instantiations through Artificial Intelligence Assisted Diagnostics; and (3) the introduction of the study and development of Adaptive Nosographers building the new forms of trust and conventionality in decision making routines addressing selection, characterisation, clustering, contrast and identification of pathological traits and architectures as disposed in the previous pages.

The continuation of those three lines of research in immediate years will set the framework of my personal future research, in the hope that modern advancements in clinical interfields could build a better understanding

of pathology, experiences and healthcare interaction with those who suffer in pain and need of care.





~ The End ~

---


## Bibliographies: Sorted by Quarter.


QI .  297 — 300


---


QII . QII, §1  
 300 — 308

---


. QIII, §1  
 308 — 312


. QIII, §2  
 312 — 318


. QIII, §3  
 319 — 323


. QIII, §4  
 323 — 328


QIII . QIII, §5  
 329 — 335

. QIII, §6  
 335 — 345

. QIII, §7  
 346 — 352

. QIII, §8  
 353 — 360

. QIII, §9  
 361 — 363

. QIII, §10  
 364 — 369

## QI

---

### QI, §1-3

---

- Anjum, R, Copeland, S, Mumford, S, & Rocca, E (2015) CauseHealth: integrating philosophical perspectives into person centered healthcare. *European Journal for Person Centered Healthcare*, 3(4), 427-430.
- Aragona, M (2009) About and beyond comorbidity: Does the crisis of the DSM bring on a radical rethinking of descriptive psychopathology?. *PPP*, 16(1), 29-33.
- (2009b) The concept of mental disorder and the DSM-V. *Dial Phil Ment Neuro Sci*, 2:1-14.
- (2009c) The role of comorbidity in the crisis of the current psychiatric classification system. *PPP*, 16:1- 11.
- Borsboom, D., Cramer, A. O., Schmittmann, V. D., Epskamp, S., & Waldorp, L. J. (2011) The small world of psychopathology, *PLoS One*, 6(11), e27407.
- Cartwright, ND (1983) *How the Laws of Physics Lie*. Oxford: Clarendon Press.
- (1999) *The Dappled World: A Study of the Boundaries of Science*. Cambridge: Cambridge University Press.
- Cramer AOJ, Waldorp LJ, van der Maas HLJ, Borsboom D. (2010) Comorbidity: A network perspective. *Behav Brain Sci* 2010; 33:137-193.
- Crowley, K., & Jacobs, M. (2002) Islands of expertise and the development of family scientific literacy. G. Leinhardt, K. Crowley, and K. Knutson (eds) *Learning conversations in museums*, 333-356, Lawrence Erlbaum: Mahwah, NJ.
- Darden, L (2006) *Reasoning in Biological Discoveries*, Cambridge UP: Cambridge.
- Dupré, J (1981) Natural kinds and biological taxa. *Philosophical Review* 90: 66-90.
- Feger H. (2001) Classification: Conceptions in the social sciences. *International Encyclopedia of the Social & Behavioral Sciences*, 3:1966-1973.
- Fuller, S (1988) *Social Epistemology*, Bloomington: Indiana University Press.
- Galison, P (2004) Specific theory. *Critical Enquiry* 30, 2: 379-383.
- Galison, P & Stump, DJ (eds.) (1996) *The Disunity of Science: Boundaries, Contexts, and Power*. Stanford UP: Stanford.
- Giere, RN (1985a) Philosophy of Science Naturalized. *Philosophy of Science*. 52, 331-356.
- (1985b) Constructive Realism, P. Churchland & C. Clifford (eds.) *Images of Science*, 75-98, Chicago: Chicago UP
- (1999) *Science without Laws*. Chicago: Chicago UP.
- (2006a) *Scientific Perspectivism*. Chicago: Chicago UP.

- (2006b) Perspectival pluralism, Kellert, S; Longino, HE & Kenneth Waters, C (eds.) *Minnesota Studies in the Philosophy of Science*, Vol XIX, Scientific Pluralism: 26-41, Minnesota UP: London.
- Goffman, E (1968) *Stigma: Notes on the Management of Spoiled Identity*, Pelican: London.
- Goldberg, D (2011) The need for a special classification of mental disorders for general medical practice: towards ICD11, *Primary Care. European Psychiatry*, 26:53-56.
- Goldie, PL (2000) *The Emotions*, Oxford UP: Oxford.
- (2002) Emotion, personality and simulation, Goldie, PL (ed.) *Understanding Emotions: Mind and Morals*, 97-109. Ashgate P: Aldershot.
- (2003) Narrative and perspective; values and appropriate emotions, Hatzimoysis, A (ed.) *Philosophy and the Emotions*, 201-220, Cambridge UP: Cambridge.
- (2004) What people will do: personality and prediction, *Richmond Journal of Philosophy* 7, 1-9.
- Goldman, A (1987) Foundations of social epistemics, *Synthese*, 73: 109-144.
- (1999) *Knowledge in a social world*. Oxford: Oxford University Press.
- Hacking, I (1986) Making up people, Heller, T (ed.) *Reconstructing Individualism: Autonomy, Individuality in Self Investigation Thought*: 161-171, Stanford UP: Stanford.
- (1995) The looping effects of human kinds, Sperber, D & Premack, AJ (eds) *Causal Cognition*, 351-383, Oxford UP: Oxford.
- (2002) *Historical Ontology*, Harper U P: London
- Haraway, D J (1976) *Crystals, Fabrics, and Fields: Metaphors that Shape Embryos*. Yale UP: NH.
- (1991) *Simians, Cyborgs, and Women*, Routledge: NY.
- Harding, S (1991) *Whose Science? Whose Knowledge?* Cornell UP: NY.
- (1993) Rethinking standpoint epistemology: what is strong objectivity?, Alcof, L & Potter, E (eds.) *Feminist Epistemologies*, Routledge: London.
- Helmreich, S (2016) *Sounding the Limits of Life*, Princeton UP: Princeton.
- Hickey, S & Roberts, H (2011) Tarnished Gold: The Sickness of Evidence-based Medicine, *CreateSpace*.
- IDF, Interaction Design Foundation (2019) «OS and OA Literature», OnLine: 23-2-2019. Link: <https://www.interaction-design.org/literature>
- IEA, International Ergonomics Association (2019) «Definition and Domains of Ergonomics», OnLine: 23-2-2019. Link: <https://www.iea.cc/whats/index.html>
- Jakovljević M (2008) Integrating brave new psychiatry of the person, for the person, by the person and with the person: The postmodern turn, *Psychiatr Danub*, 20:2-5.
- Jakovljević, M & Ostojić, L (2013) Comorbidity and Multimorbidity in Medicine Today, *Medicina Academica Mostariensia*, 1, 8-28
- Keller, EF (1995) *Refiguring Life: Metaphors of Twentieth-Century Biology*, Columbia UP: NY.
- (2003a) *Making Sense of Life: Explaining Biological Development with Models, Metaphors, and Machines*, Harvard: Cambridge.
- (2003b) Models, simulation, and “computer experiments”, Radder, H (ed.) *The Philosophy of Scientific Experimentation*, 198-215, Pittsburg UP: Pittsburg.
- (2005) Ecosystems, organisms, and machines, *Bioscience* 55, 12: 1069-1074.
- Kitcher, P (1984) 1953 and All That: A Tale of Two Sciences, *Philosophical Review*, 93, 335-373.
- (1992) The Naturalists Return, *Philosophical Review*, 101, 53-114.
- (1993) *The Advancement of Science*, Oxford U P: Oxford.

- (2003) What kind of science should be done?, Lightman, A; Sarewitz, D & Dresser, C (eds.) *Living with the Genie*, 201-224, Island P: Washington.
- Klinkman, M & van Weel, C (2011) Prospects for person-centred diagnosis in general medicine, *Journal of Evaluation in Clinical Practice*, 17, 365–370
- Longino, HE (1990) *Science as social knowledge: Values and objectivity in scientific inquiry*. Princeton: Princeton University Press.
- (2000) Reply to P Kitcher, *Philosophy of Science* 69, 573-577.
- (2001) *The Fate of Knowledge*, Princeton UP: Princeton.
- (2006) Theoretical pluralism and the scientific study of behavior, Kellert, S; Longino, HE & Kenneth Waters, C (eds.) *Minnesota Studies in the Philosophy of Science*, vol XIX, Scientific Pluralism: 102-131, Minnesota UP: London.
- Maj M. (2005) ‘Psychiatric comorbidity’: an artifact of current diagnostic systems?, *Br J Psychiatry*, 186, 182-184.
- Merton, R. K. (1973) *Sociology of science*. Chicago: University of Chicago Press.
- Perdomo, I (2003) *Pragmatismo y Empirismo*. Acerca de W. James y Bas C. van Fraassen, *Laguna*, 13, 115-127.
- (2011) The characterisation of epistemology in Philip Kitcher, a critical reflection from new empiricism, *Scientific Realism and Democratic Society*, 113-138
- Rohde, M, & Shaffer, DW (2004) Us, ourselves, and we: Thoughts about social (self-) categorization, *Association for Computing Machinery (ACM) SigGROUP Bulletin* 24, 3, 19–24.
- Schwenk, TL (1999) The tyranny of names in mental health care, *Journal of the American Board of Family Practice* 12, 1, 99–101.
- Shaffer, DW (2004) Epistemic frames and islands of expertise: Learning from infusion experiences, Kafai, Y et al (eds) *Proceedings of the Sixth International Conference of the Learning Sciences*, 473-480, Erlbaum: Mahwah, NJ.
- (2006) Epistemic frames for epistemic games, *Computers & Education*, 46, 3, 223-234.
- (2007) Epistemic games to improve professional skills and values, *Organisation for Economic Co-operation and Development*. NP
- (2009) Wag the Kennel: Games, Frames, and the Problem of Assessment, R. Fertig (ed) *Handbook of Research on Effective Electronic Gaming in Education*, 577–592, Hershey, PA: IGI Global.
- Shiva, V (1995) *Democratizing Biology. Reinventing Biology from a Feminist, Ecological, and Third World Perspective*, Birke, L & Hubbard, R (eds) *Reinventing Biology*, Indiana: Indiana UP
- Thagard, P (1999) *How Scientists Explain Disease*, Princeton UP: NJ.
- van Fraassen, BC (1976) To save the phenomena, Boyd, P; Gasper, P & Trout, JD (eds.) (1992) *The Philosophy of Science*, 187-194, MIT: Cambridge.
- (1980) *The Scientific Image*, Oxford: Oxford UP.
- 1989. *Laws and Symmetry*, Oxford: Oxford UP.
- (1994) Interpretation of Science. Science as Interpretation, Hilgevoord, J (ed) *Physics and our View of the World*, 171ff, Harvard UP, Harvard.
- (2002) *The Empirical Stance*. New Haven: Yale UP
- van Praag, HM (1993) “Make-believes” in psychiatry or the perils of progress, Brunner/Mazel Publishers, NY.
- Weed, E & Rooney, E (2010) What’s the difference? The question of theory, *Differences* 21, 1: *Special Issue*.
- Weinberg, S (1993) *Dreams of a Final Theory*, Pantheon: NY.
- (2001) Can science explain everything? Anything?, *NY Rev Books*: 50.

Williams, L (2012) *Modeling, Building, Writing: A History of Nonlinear Dynamics and Complex Systems*, PhD Dissertation. Harvard UP.

## QII

---

### QII, §1

---

#### A

Alegria, AC (2011) Transgender identity and health care: Implications for psychosocial and physical evaluation, *Journal of the American Academy of Nurse Practitioners*, 23, issue 4, 175–182.

Álvarez, JM (2008) *La invención de las enfermedades mentales*. Gredos: Madrid.

Aragona, M (2009a) About and beyond comorbidity: Does the crisis of the DSM bring on a radical rethinking of descriptive psychopathology? *PPP* 2009c;16:29-33.

— (2009b) The concept of mental disorder and the DSM-V. *Dial Phil Ment Neuro Sci* 2009a;2:1-14.

— (2009c) The role of comorbidity in the crisis of the current psychiatric classification system. *PPP* 2009b;16:1- 11

Atkinson, S., Evans, B., Woods, A. and Kearns, R. (2015) ‘The Medical’ and ‘Health’ in a Critical Medical Humanities, *Journal of Medical Humanities*, 36(1), 71-81. <https://doi.org/10.1007/s10912-014-9314-4>

#### B

Bancroft, J (2008). Lust or Identity?, *Archives of Sexual Behavior*. 37 (3): 426–428. [doi:10.1007/s10508-008-9317-1](https://doi.org/10.1007/s10508-008-9317-1)

Bayer, R. (1981) *Homosexuality and American Psychiatry: The Politics of Diagnosis*. New York: Basic Books.

Beck, J & Stolterman, E (2016) Examining Practical, Everyday Theory Use in Design Research, *She Ji* 2, 2, 130

Beneduce, R (2013) Illusioni e violenza della diagnosi psichiatrica, *Aut Aut* 357: 187-212.

Bennett, MR, & Hacker PM, (2003) *Philosophical Foundations of Neuroscience*, Oxford: Basil Blackwell.

Berrios, G. E. (1984), Descriptive Psychopathology: Conceptual and Historical Aspects, *Psychological Medicine* 14: 303-313.

— (1994) Historiography of mental symptoms and diseases, *History of Psychiatry*, 5, 175-190.

— (1995) La historiografía de la psiquiatría clínica: estado presente, MA (1995), *Un siglo de psiquiatría en España*, 11-17. Extraeditorial, Madrid.

— (1996) *The History of Mental Symptoms. Descriptive psychopathology since the nineteenth century*. Cambridge UP: Cambridge.

Berrios, G. E. & Marková I.S. (2002) The concept of neuropsychiatry A historical overview, *Journal of Psychosomatic Research* 53, 629–638

Bland, M (2009) The tyranny of power: is there a better way to calculate sample size?, *British Medical Journal* 339: 1133-1135.

Bleakley, A. (2015). *Medical Humanities and Medical Education: How the Medical Humanities Can Shape Better Doctors*. London: Routledge.

Bleier, R (1984) *Feminist Approaches to Science*. NP: NY.

Bulbena Vilarrasa, A., Berrios, G. E., & Fernández de Larrinoa Palacios, P. (2003) *Medición clínica en psiquiatría y psicología*. Masson: Barcelona.

## C

Callard, F. & Fitzgerald, D. (2015) *Rethinking Interdisciplinarity across the Social Sciences and Neurosciences*. Basingstoke, Palgrave Macmillan. <https://doi.org/10.1057/9781137407962>

Cartwright, ND (1983) *How the Laws of Physics Lie*. Oxford: Clarendon Press.

— (1999) *The Dappled World: A Study of the Boundaries of Science*. Cambridge: Cambridge University Press.

— (2000) Against the completeness of science, M. W. F. Stone and J. Wolff (eds) *The Proper Ambition of Science*, London: Routledge.

Catanesi, R., & Troccoli, G. (2005) Dietro il velo, ovvero responsabilità professionale e contenzione fisica in psichiatria, *Lo psichiatra*, 1. NP

Chang, H (2012) *Is Water H<sub>2</sub>O? Evidence, Realism and Pluralism*, Springer: Dordrecht.

Charon, R. (2006) *Narrative Medicine: Honoring the Stories of Illness*. Oxford: Oxford University Press.

Christakis, N.A. (1997) The Ellipsis of Prognosis in Modern Medical Thought, *Social Science and Medicine* 44:301–15.

Churchland, P (2002) *Brain-wise: Studies in Neurophilosophy*, Cambridge, MA: MIT Press.

Cipriano, P. (2013) *La fabbrica della cura mentale. Diario di uno psichiatra riluttante*. Milan: Elèuthera.

Code, L (1983) Responsibility and the Epistemic Community: Women's Place. *Social Research* 50: 537–555.

— (1987) *Epistemic Responsibility*. Hanover: University Press of New England and Brown University Press.

— (2008) Thinking About Ecological Thinking. *Hypatia* 23 (1): 187–203. <https://doi.org/10.2307/25483158>.

Colina, F (2008) *Psiquiatria y cultura*, Álvarez, JM (2008) *La invención de las enfermedades mentales*. Gredos: Madrid.

Cowan WM, Kandel ER (2001) Prospects for neurology and psychiatry. *JAMA* 2001; 285:594–600

Craver, CF & Bechtel, W (2007) Top-down causation without top-down causes, *Biol. Philos.* 22: 547–663.

Cromby, J (2007) Integrating social science with neuroscience: Potentials and problems, *BioSocieties* 2: 149-169.

Crowley, K., & Jacobs, M. (2002) Islands of expertise and the development of family scientific literacy, *Learning conversations in museums*, G. Leinhardt, K. Crowley, and K. Knutson, Editors. (2002), Lawrence Erlbaum: Mahwah, NJ.

Cruikshank, J (2005) *Do Glaciers Listen? Local Knowledge, Colonial Encounters, and Social Imagination*, BCUP: Vancouver.

Cullen, W. (1800) *Nosology: Or, a Systematic Arrangement of Diseases*. Edinburgh: William Creech.

## D

Damoiseaux, JS & Greicius, MD (2009) Greater than the sum of its parts: a review of studies combining structural connectivity and resting-state functional connectivity, *Brain Struct Funct* 213: 525-533.

Darden, L (2006) Reasoning in Biological Discoveries: Essays on Mechanisms, Interfield Relations, and Anomaly Resolution Cambridge University Press: Cambridge

Darden, L., & Maull, N (1977) Interfield Theories, *Philosophy of Science* 44: 43–64.

Dodaro, G. (2011) Il problema della legittimità giuridica dell'uso della forza fisica o della contenzione meccanica nei confronti del paziente psichiatrico aggressivo o a rischio suicidario. *Rivista italiana di medicina legale*, (6), 1483-1518.

Dupré, J (1981). Natural Kinds and Biological Taxa, *Philosophical Review*, 90, 66-90.  
— (1993) *The Disorder of Things: Metaphysical Foundations of the Disunity of Science*. Cambridge, Mass.: Harvard UP.

## E

Edelman, N (2003) *Les métamorphoses de l'hystérique*. La Découverte, Paris.  
Eldredge, N (1985) *Unfinished Synthesis: Biological Hierarchies and Modern Evolutionary Thought*. Oxford UP: NY.  
Ellis, R (2017) Heritage and Stigma: Co-Producing and Communicating the Histories of Mental Health and Learning Disability. *Medical Humanities*, 43(2), 92–98. <https://doi.org/10.1136/medhum-2016-011083>  
Equaldex (2019) *Homosexuality rates up to 2019*. 6.April.2019 [<https://www.equaldex.com>]

## F

Faber, Knud. (1923) *Nosography in Modern Internal Medicine*. New York: Paul B. Hoeber.  
Fedigan, LM & Fedigan, L (1989) Gender and the Study of Primates, *Critical Reviews of gender and Anthropology*, 41-64, Am Anthropol As: Washington.  
Fehr, C & Plaisance, K (2010) Socially relevant philosophy of science: An introduction, *Synthese* 177, 301-316.  
Foster, S. L. & Funke, J. (2018) Feminist Encounters with the Medical Humanities. *Feminist Encounters: A Journal of Critical Studies in Culture and Politics*, 2(2), 14. <https://doi.org/10.20897/femenc/3882>  
Foucault, M (2003) *Le pouvoir psychiatrique. Cours au Collège de France. 1973-1974*. Gallimard: Paris.

Friedman, M (1998) On the sociology of scientific knowledge and its philosophical agenda, *SHPS*, 29: 239-271.

Fuller, S (1988) *Social Epistemology*, Bloomington: Indiana University Press.

## G

Galison, Peter. (1987) *How Experiments End*. Chicago: University of Chicago Press.  
— (1996) Computer simulation and the trading zone, Galison, P & Stump, DJ (eds.) *The Disunity of Science: Boundaries, Contexts, and Power*, 118-157, Stanford UP: Stanford.  
— (2003) *Einstein's Clocks, Poincaré's Maps: Empires of Time*, Norton: NY.  
— (2004) Specific theory, *Critical Enquiry* 30, 2: 379-383.  
— (2008) Ten problems in history and philosophy of science, *Isis* 99: 111-124.  
Galison, P & Stump, DJ (eds.) (1996) *The Disunity of Science: Boundaries, Contexts, and Power* Stanford UP: Stanford.  
Garrabé, J (1996) Epistemologie et histoire de la psychiatrie, *Confrontations Psychiatriques* 37: 285-334.  
Geller, P & Stockett (eds) (2006) *Feminist Anthropology: Past, Present and Future*, Pennsylvania UP: Philadelphia.  
Giere, RN (1985) Philosophy of Science Naturalized, *Philosophy of Science*. 52, 331-356.  
— (1985) Constructive Realism, P. Churchland & C. Clifford (eds.), *Images of Science*. 75-98. Chicago: Chicago UP.  
— (1988) *Explaining Science: A Cognitive Approach*. Chicago: University of Chicago Press.  
— (1999) *Science without Laws*. Chicago: University of Chicago Press.  
— (2006a) *Scientific Perspectivism*. Chicago: University of Chicago Press.  
— (2006b) Perspectival pluralism, Kellert, S; Longino, HE & Kenneth Waters, C (eds.)



- Minnesota Studies in the Philosophy of Science*, vol XIX, Scientific Pluralism: 26-41, Minnesota UP: London.
- Goffman, E (1968) *Stigma: notes on the management of spoiled identity*. Pelican: London.
- (1997) *The Goffman reader*. New York: Wiley-Blackwell.
- (2008) *Internados*. Amorrortu: Madrid.
- Goldman, A (1979) What Is Justified Belief?, G. Pappas (ed), *Justification and Knowledge*. Dordrecht: Reidel, 1-23.
- (1987) Foundations of social epistemics, *Synthese*, 73: 109-144.
- (1989) Epistemic Folkways and Justification and Scientific Epistemology, A. Goldman (ed), *Liaisons*. Cambridge, MA: MIT Press, 1992, 155-175.
- (1999) *Knowledge in a social world*. Oxford: Oxford University Press.
- Goldstein, J (2001) *Console and classify. The french psychiatric profession in the nineteenth century*. Chicago UP: Chicago.
- (2005) *The post-revolutionary self: Politics and psyche in France. 1750-1850*. Harvard UP: Cambridge.
- Greenhalgh, T. & Hurwitz, B. (1998) *Narrative-Based Medicine: Dialogue and Discourse in Clinical Practice*. London: BMJ Books.
- Grob, GN (1991) Origins of DSM-1: A Study in Appearance and Reality. *American Journal of Psychiatry* 148:421-31.
- H
- Hacking, I (1986) Making up people, Heller, T (ed.) (1986) *Reconstructing Individualism: Autonomy, Individuality in Self Investigation ought*, 161-171, Stanford UP: Stanford.
- (1994) Looping effects of human kinds, in Sperber, D, Premarck, D, & Premarck AJ (ed) (1994) *Causal cognition: a multidisciplinary approach*, 351-383. Clarendon: Oxford.
- (1995) *Rewriting the soul: Multiple personality and the sciences of memory*. Princeton UP: Princeton.
- (1998) *Mad Travellers. Reflections on the Reality of Transient Mental Illnesses*, Virginia UP: London.
- (2000) *The social construction of what?* MIT UP: Cambridge.
- (2002) *Historical Ontology*, Harper U P: London.
- Hammer, D. (1995) Epistemological considerations in teaching introductory physics. *Science, NP*.
- Hankinson Nelson, L (1993) Epistemological Communities, Linda Alcoff & Elizabeth (EDS.) (1993) *Potter Feminist Epistemologies*, 121-159. Routledge: NY.
- Haraway, DJ (1976) *Crystals, Fabrics, and Fields: Metaphors that Shape Embryos*. Yale UP: NH.
- (1989) *Primate visions. Gender, race and nature in the world of modern science*. Routledge: NY.
- (1991) *Simians, Cyborgs, and Women. The reinvention of nature* Routledge: NY.
- (1988) Situated Knowledges: The Science Question in Feminism and the Privilege of Partial Perspective. *Feminist Studies* 14 (3): 575-599.
- (2000) *How Like a Leaf: An Interview with Thyrza Nichols Goodeve*. Routledge: NY.
- (2014) *SF: String figures, multispecies muddles, staying with the trouble. Keynote Lecture, Knowings and Knots*, University of Alberta, Canada, March 24: [https:// www.youtube.com/watch?v=Z1uTVnhIHS8](https://www.youtube.com/watch?v=Z1uTVnhIHS8).
- (2016) *Staying with the trouble: Making kin in the Chthulucene*. Duke University Press.
- Harding, S (1991) *Whose Science? Whose Knowledge?* Cornell UP: NY.
- (1993) Rethinking standpoint epistemology: what is strong objectivity?, Alcof, L & Potter, E (eds.) *Feminist Epistemologies*, Routledge: London.

- (1998) *Is Science Multicultural? Postcolonialism, Feminisms and Epistemologies*. Bloomington: Indiana University Press.
- (2008) *Borderlands Epistemologies*, Jaggar, MA (2008) *Just Methods: An Interdisciplinary Feminist Reader*. 331–341. Boulder, CO: Paradigm Publishers.
- Harding, S & Hintikka, MB (eds.) (2003) *Discovering Reality: Feminist Perspectives on Epistemology, Metaphysics, Methodology and Philosophy of Science*. Springer Netherlands: Dordrecht.
- Hawkins, DM (2004) The problem of overfitting, *Journal of Chemical Information and Computer Science* 44 (1): 1-12.
- Heckman, JJ (1979) Sample selection bias as a specification error, *Econometrica* 47 (1): 153-162.
- Hekman, S (2010) *The Material of Knowledge: Feminist Disclosures*. Bloomington, IN: Indiana University Press.
- Helmreich, S (2006) The signature of life: Designing the astrobiological imagination, *Grey Room* 23, 4: 66-95.
- (2007) ‘Life is a Verb’: Inflections of Artificial Life in Cultural Context, *Artificial Life* 13, 2: 189-201.
- (2016) *Sounding the Limits of Life*, Princeton UP: Princeton.
- Helmreich, S & Roosth, S (2016) Life forms: a keyword entry, Helmreich, S (2016) *Sounding the Limits of Life*, 19-34, Princeton UP: Princeton.
- Hickey, DS, Hickey, A & Noriega, LA (2012) The failure of evidence-based medicine?, *European Journal for Person Centered Healthcare* 1, 1: 69-79
- Hofer, BK & Pintrich, PR (eds.) (2002) *Personal epistemology: The psychology of beliefs about knowledge and knowing*. Mahwah, NJ: Erlbaum.
- Howgate, S & Stern Shapiro, B (2006) *David Hockney Portraits* (catalogue). National Portrait Gallery: London.
- Huertas, R (2001) Historia de la psiquiatría. ¿Por qué? ¿Para qué? Tradiciones históricas y nuevas tendencias, *Frenia* 1.1: 9-36.
- (2003) Cuerpo visto, cuerpo sentido: de la anatomía a la clínica psiquiátrica, *Revista de la Asociación española de Neuropsiquiatría* 23. 88: 111-126.
- (2011) On the social construction of madness. Ian Hacking and the cultural history of psychiatry, *Rev. Asoc. Esp. Neuropsiq.* 31. 111: 437-456. doi: 10.4321/S0211-57352011000300004
- (2012) *Historia Cultural de la Psiquiatría*. Catarata: Madrid.
- I
- Intemann, K (2010) Feminist Empiricism and Standpoint Theory: Where Are We Now? *Hypatia* 25 (4): 778–796.
- J
- Jordanova, L (1995) The social construction of medical knowledge, *Social history of medicine* 8: 361-382.
- K
- Keller, EF (1995) *Refiguring Life: Metaphors of Twentieth-Century Biology*, Columbia UP: NY.
- (2003a) *Making Sense of Life: Explaining Biological Development with Models, Metaphors, and Machines*, Harvard: Cambridge.
- (2003b) Models, simulation, and “computer experiments”, Radder, H (ed.) *The Philosophy of Scientific Experimentation*, 198-215, Pittsburg UP: Pittsburg.
- (2005) Ecosystems, organisms, and machines, *Bioscience* 55, 12: 1069-1074.

- Kirk, S.A., & H. Kutchins (1992) *The Selling of DSM: The Rhetoric of Science in Psychiatry*. New York: Aldine DeGruyter.
- Kitcher, P (1984) 1953 and All That: A Tale of Two Sciences, *Philosophical Review*, 93, 335-373.
- (1992) The Naturalists Return, *Philosophical Review*, 101, 53-114.
- (1993) *The Advancement of Science*, Oxford UP: Oxford.
- (2003) What kind of science should be done?, Lightman, A; Sarewitz, D & Dresser, C (eds.) (2003) *Living with the Genie*, 201-224, Island P: Washington.
- (2004) Evolutionary theory and the social uses of biology, *Biology and Philosophy* 19, 1-15.
- Kitcher, P & Salmon, W (eds) (1989) *Scientific Explanation*. Minneapolis: University of Minnesota.
- Kölbel, M (2002) *Truth Without Objectivity*. London: Routledge.
- (2008). “True” as ambiguous, *Philosophy and Phenomenological Research*, 77: 359–384.
- L
- Latour, B (1987) *Science in Action*. Open UP: Stanford.
- (2011) *La Esperanza de Pandora*, Gedisa: BCN.
- Lerer, S (2003) *Error and the Academic Self: The Scholarly Imagination, Medieval to Modern*. Columbia UP: NY.
- Longino, HE (1990) *Science as social knowledge: Values and objectivity in scientific inquiry*. Princeton: Princeton University Press.
- (1993) Subjects, Power and Knowledge: Description and Prescription in Feminist Philosophies of Science. Alcoff, L & Potter, E (eds.) (1993) *Feminist Epistemologies*, London: Routledge.
- (1996) Cognitive and Non-Cognitive Values in Science, Feminism, L. H. Nelson & J. Nelson, Science, and the Philosophy of Science, 39–58. Dordrecht: Kluwer.
- (2000) Reply to P Kitcher, *Philosophy of Science* 69, 573-577.
- (2001) *The Fate of Knowledge*, Princeton UP: Princeton.
- (2006) Theoretical pluralism and the scientific study of behavior, Kellert, S; Longino, HE & Kenneth Waters, C (eds.) (2006) *Minnesota Studies in the Philosophy of Science*, vol XIX, Scientific Pluralism: 102-131, Minnesota UP: London.
- M
- MacCormack, C & Strathern, M (eds) (1980) *Nature, Culture and Gender*, Cambridge UP: Cambridge.
- MacFarlane, J (2005) Making sense of relative truth. *Proceedings of the Aristotelian Society*, 105: 321–339.
- (2007) Relativism and disagreement. *Philosophical Studies*, 132: 17–31.
- (2014) *Assessment sensitivity: Relative Truth and its Applications*. Oxford: Oxford University Press.
- Machamer, P & Sytsma, J (2002) Philosophy and the Brain Sciences, *Iris* 1, 2, 353-374.
- McCauley, RN (2009) Time is of the essence: explanatory pluralism and accommodating theories about long-term processes, *Philos. Psychol.* 22: 611–635.
- McCauley, RN & Bechtel, W (2001) Explanatory pluralism and the heuristic identity theory, *Theory Psychol.* 11: 736–760.
- Merton, R. K. (1973) *Sociology of science*. Chicago: University of Chicago Press.
- Minard, M (2013) La validità delle diagnosi psichiatriche. Dalla battaglia degli omosessuali alla lotta dei veterani, *Aut Aut* 357: 113-126.

- Mitchell, S. (2002) Integrative Pluralism, *Biology and Philosophy* 17: 55–70.
- (2003) *Biological Complexity and Integrative Pluralism*. Cambridge: Cambridge UP.
- Mitchell, WJT (2004) Medium Theory, *Critical Inquiry* 30, 2: 324-335.
- Morgan, M & Morrison, M (eds) (1999) *Models as Mediators*, Cambridge: Cambridge UP.
- Morton, T (2013) *Hyperobjects. Philosophy and Ecology after the End of the World*, Minneapolis: Minnesota UP.
- N
- Niiniluoto, I (1984) *Is Science Progressive?*, Riedel: Dordrecht.
- Novello, M. (2013) Il risolvibile nodo della contenzione fisica nelle pratiche dei servizi di salute mentale. *Rivista Italiana di Medicina Legale (e del Diritto in campo sanitario)*, 1, 236-44.
- O
- P
- Perdomo, I (2003) Pragmatismo y Empirismo. Acerca de W. James y Bas C. van Fraassen, *Laguna*, 13, 115-127.
- (2011) The characterisation of epistemology in Philip Kitcher, a critical reflection from new empiricism, *Scientific Realism and Democratic Society*, 113-138
- Poggenpohl, S. H. (2009a). Time for change: Building a design discipline, in S. Poggenpohl & K. Sato (Eds.), *Design integrations. Research and collaboration*. 3–22. Bristol and Chicago: Intellect.
- (2009b) Practicing collaborative action in design, S. Poggenpohl & K. Sato (Eds.), *Design integrations. Research and collaboration*. 3–22. Bristol and Chicago: Intellect.
- (2015) Communities of Practice in Design Research”, *She Ji* 1, 48
- Poggenpohl, S., & Sato, K. (Eds.) (2009) *Design integrations. Research and collaboration*. Bristol and Chicago: Intellect.
- Popper, K. (2014) *Conjectures and refutations: The growth of scientific knowledge*. Routledge: London.
- Q
- R
- Racine, E & Illes, J (2009) Emergence at the crossroads of philosophy, neurotechnology and the enhancement debate, Bickle, J (ed.) *Philosophy of Neuroscience*: 431-453. Oxford UP: NY.
- Raishaun Jones, T (2018) *Developing and testing a K-12 engineering epistemic frame to uncover engineering in the interactions of a high school summer session*. (Unpublished PhD dissertation). Purdue University.
- Raman, R (2011) Evidence-based medicine and patient-centered care: cross-disciplinary challenges and healthcare information technology enabled solutions, *International Journal of Person Centered Medicine* 1 (2): 279-294.
- Redish, E. F. (2004) A theoretical framework for physics education research: Modeling student thinking, *arXiv preprint physics/0411149*.
- Reger, J (ed) (2005) *Different Wavelengths: Studies of the Contemporary Women’s Movements*, Routledge: NY.
- Rohde, M., & D. W. Shaffer (2004) Us, ourselves, and we: Thoughts about social (self-) categorization. *Association for Computing Machinery (ACM) SigGROUP Bulletin* 24 (3): 19–24
- Rolin, Kristina. 2011. Contextualism in Feminist Epistemology and Philosophy of Science, *Feminist Epistemology and Philosophy*

- of Science: Power in Knowledge*, ed. Heidi E. Grasswick, 25–44. New York, NY: Springer.
- Rose, N (2006) *The politics of Life Itself: Bio-medicine, Power, and Subjectivity in the Twenty-First Century*. Princeton UP: Princeton.
- Rosen, G (1968) *Madness in society. Chapters in the historical sociology of mental illness*. Routledge KP: London.
- Rosenberg, C.E. (1977) The Therapeutic Revolution: Medicine, Meaning, and Social Change in Nineteenth-Century America, *Perspectives in Biology and Medicine* 20:485–506.
- (1987) *The Care of Strangers: The Rise of America's Hospital System*. New York: Basic Books.
- (1989) Disease in history: Frames and framers, *Milbank Quarterly* 67, 1: 1-15.
- (1992) *Explaining Epidemics and Other Studies in the History of Medicine*. Cambridge: Cambridge University Press.
- (2002) The Tyranny of Diagnosis: Specific Entities and Individual Experience, *Milbank Quarterly* 80, 2: 237-260.
- Rosenberg, CE & Goldberg, J (ed) (1991) *Framing disease. Studies in cultural history*. Rutgers UP: New Brunswick.
- S
- Sato, K. (2009) Perspectives on design research, S. Poggenpohl & K. Sato (Eds.), *Design integrations. Research and collaboration*, 25–48. Intellect: Chicago.
- Schank, R. C. (1990) *Tell me a story: A new look at real and artificial memory*. Charles Scribner's Sons. London.
- Schommer-Aikins, M. (2002) An evolving theoretical framework for an epistemological belief system, B. K. Hofer & P. R. Pintrich (Eds.), *Personal epistemology: The psychology of beliefs about knowledge and knowing*, 103–118. Mahwah, NJ: Erlbaum.
- Shaffer, DW (2004) Epistemic frames and islands of expertise: Learning from infusion experiences, *Proceedings of the Sixth International Conference of the Learning Sciences*, 473-480 Y. Kafai, et al., Editors. 2004, Erlbaum: Mahwah, NJ.
- (2005) Epistemic Games, *Innovate: Journal of Online Education*: Vol. 1 : Iss. 6,2. Available at: <https://nsuworks.nova.edu/innovate/vol1/iss6/2>
- (2006) Epistemic frames for epistemic games, *Computers & education*, 46(3), 223-234.
- (2007) Epistemic games to improve professional skills and values. *Organisation for Economic Co-operation and Development*. NP
- (2009) Wag the Kennel: Games, Frames, and the Problem of Assessment, R. Fertig (Ed.), *Handbook of Research on Effective Electronic Gaming in Education*, 577–592. Hershey, PA: IGI Global.
- Shaffer, DW, Collier, W, & Ruis, AR (2016) A tutorial on epistemic network analysis: Analyzing the structure of connections in cognitive, social and interaction data, *JLA* 3.3: 9-45.
- Solomon, M. (2001) *Social Empiricism*. Cambridge: MIT Press, MA.
- Solomon, M & Richardson, A (2005) A critical context for Longino's critical contextual empiricism, *Studies in History and Philosophy of Science* 36: 211-222.
- Stump, D (1992) Naturalized Philosophy of Science with a Plurality of Methods, *Philosophy of Science* 59: 456–60.
- T
- Thagard, P (1999) *How Scientists Explain Disease*. Princeton UP: NJ.
- Tuana, N (2001) Material Locations: An Interactionist Alternative to Realism/Social Constructivism, *Engendering Rationalities*, ed. Nancy Tuana and Sandra Morgen. Albany, NY: SUNY Press.

Tuhiwai Smith, L (ed) (2012) *Decolonizing Methodologies: Research and Indigenous Peoples*. 2nd ed. London: Zed Books.

U

V

van Fraassen, BC (1976) To save the phenomena, Boyd, P; Gasper, P & Trout, JD (eds.) (1992) *The Philosophy of Science*, 187-194, MIT: Cambridge.

—(1980) *The Scientific Image*. Oxford UP: Oxford

—(1989) *Laws and Symmetry*. Oxford UP: Oxford

—(1994) Interpretation of Science; Science as Interpretation, J. Hildevoord (ed.) *Physics and our view of the world*, 169-187. Cambridge UP: Cambridge.

—(1997) Structure and Perspective: Philosophical Perplexity and Paradox, M.L. Dalla Chiara (eds.) *Logic and Scientific Methods*, 511-530, Kluwer Academic Publishers, Netherlands.

—(2002) *The Empirical Stance*. Yale UP: New Haven

—(2008) Scientific Representation: Paradoxes of Perspective. Oxford UP, NY

W

Walsh, B & Gillett, G (2011) A post-structuralist view of evidence-based medicine (EBM): what EBM contributes to philosophy, *International Journal of Person Centred Medicine* 1 (2) 223-231.

Weed, E & Rooney, E (2010) What's the difference? The question of theory, *Differences* 21, 1: Special Issue.

Weinberg, S (1993) *Dreams of a Final Theory*, Pantheon: NY.

—(2001) Can science explain everything? Anything?, *NY Rev Books*: 50.

Wenger, E (1999) *Communities of practice: learning, meaning, and identity*. Cambridge UP: Cambridge.

Williams, L (2012) *Modeling, Building, Writing: A History of Nonlinear Dynamics and Complex Systems*, PhD Dissertation. Harvard UP

World Economic Forum (2019) WeForum. 6.April.2019 [https://www.weforum.org/agenda/2018/06/lgbti-rights-around-the-world-in-2018/].

---

### QIII

---

#### QIII, §1

---

A

Allen, RC (1999) *David Hartley on human nature*. State University of NY Press: NY.

Agrawal, A (ed) (2005) *In search of Vedic Harappan Relationship*, N. Delhi, Aryan Books Intern.

B

Basbaum, A (2012) (Online) Specific vs Patterning Theory: Continuing the Debate, in *Pain Research Forum* [accessed 30/06/18, 13:42] https://www.painresearchforum.org/forums/discussion/7347-specificity-versus-patterning-theory-continuing-debate

Bell C, & Shaw A (1868) Reprint of the "Idea of a New Anatomy of the Brain," with Letters, &c. *J Anat Physiol* 3: 147-182.

Berrios, GE, Marková, IS (2002) The concept of neuropsychiatry. A historical overview, *Journal of Psychosomatic Research* 53, 629-638

- Bertalanffy, L (von) (1950a) The theory of open systems in physics and biology, *Science* 111: 23-29.
- (1950b) An outline of general system theory, *British Journal of Philosophy of Science* 1: 139-164.
- (1955) An essay on the relativity of categories, *Philosophy of Science* 22: 243-263.
- Bollack, J (1965-69) *Empédocle*, Minuit: Paris
- Burrow T (1975) The early Aryans, Basham A. (ed) *A Cultural History of India*, NP: Oxford UP, Oxford.

## C

- Chang, H (2012) *Is Water H2O? Evidence, Realism and Pluralism*, Springer: Dordrecht.
- Cobb, M (2002) Exorcizing the animal spirits, *Nature Reviews Neuroscience* 3: 395-400.
- Coleman, W (1977) *Biology in the Nineteenth Century: Problems of Form, Function and Transformation*. Cambridge UP: Cambridge.
- Cruikshank, J (2005) *Do Glaciers Listen? Local Knowledge, Colonial Encounters, and Social Imagination*, BCUP: Vancouver.

## D

- Dales, G (1966) The Decline of the Harappans, *Scientific American* 241 (92-99).
- Descartes, R (1662) *De Homine Figuris, Lugduni Batavorum* (Apud Petrum Leffen & Franciscum Moyardum), Leiden.
- Darwin, E & Darwin, RW (1794) *Zoonomia; or, The Laws of Organic Life*. J. Johnson. London.
- Davis, K. D., & Moayedi, M. (2013) Central mechanisms of pain revealed through functional and structural MRI, *J. Neuroimmune Pharmacol.* 8, 518–534. doi: 10.1007/s11481-012-9386-8

- Dodds, E (1962) *The Greeks and the Irrational*, UCP: Oxford

- Dupré, J (1993) *The Disorder of Things: Metaphysical Foundations of the Disunity of Science*. Harvard UP: Cambridge.

## E

- Erb WH (1895) Krankheiten der peripherischen cerebrospinalen Nerven, *Amer. J. Psychol.*, 7: 109

## F

- Frankfort, H, Wilson Thokild Jacobsen, JA, Irwi, WA (1946) *The intellectual adventure of ancient man*, Chicago UP: Chicago.

## G

## H

- Hacking, I (2002) *Historical Ontology*, Harper U P: London.
- Haigh E (1984) Xavier Bichat and the medical theory of the eighteenth century, *Wellcome Institute for the History of Medicine*, (Suppl 4, NP).
- Hall, TS (ed) (1951) *A Source Book in Animal Biology*. McGraw–Hill: NY
- Haraway, DJ (1976) *Crystals, Fabrics, and Fields: Metaphors that Shape Embryos*. Yale UP: NH.
- Hasenpflug, R (2006) *The Inscriptions of the Indus Civilization*, Books on Demand, Ciano.
- Helmreich, S (2016) *Sounding the Limits of Life*, Princeton UP: Princeton.
- Helmreich, S & Roosth, S (2010) Life Forms: A Keyword Entry, *Representations* 112: 27-53.

Huffman, C (2017) (On Line) Alcmaeon, *Stanford Encyclopedia of Philosophy*. At <https://plato.stanford.edu/entries/alcmaeon/> (11-7-2018)

I

J

Jackson, SW (1970) Force and kindred notions in eighteenth century neurophysiological and medical psychology, *Bull Hist Med*; 44:397– 410, 539 – 554.

Jacobsen K (1999) *Prakṛti in Samkhya-yoga: Material Principle, Religious Experience, Ethical Implications*. Peter Lang. NS.

Jaynes, J (1990) The problem of animate motion in seventeenth century, *JHI* 31: 219-234.

Joost-Gaugier, CL (2006) *Measuring Heaven: Pythagoras and his Influence on Thought and Art in Antiquity and the Middle Ages, Ithaca*. Cornell UP: NY.

K

Keller, EF (1995) *Refiguring Life: Metaphors of Twentieth-Century Biology*, Columbia UP: NY.

— (2005) Ecosystems, organisms, and machines, *Bioscience* 55, 12: 1069-1074.

Kingsley, P (1994) Empedocles and his interpreters: the four element doxography, *Phronesis* 39: 235-54.

— (1995) Notes on air: some questions of meaning in Empedocles and Anaxagoras, *CQ* 45: 26-9.

— (2008) *Filosofía Antigua. Empédocles y la Tradición Pitagórica*, Atalanta: BCN

Kirk, GS, Raven, JE & Schofield, M (2003) *The Presocratic Philosophers*. Cambridge UP: Cambridge.

Kivisild T1, Rootsi S, Metspalu M, Mastana S, Kaldma K, Parik J, Metspalu E, Adojaan M, Tolk HV, Stepanov V, Gölge M, Usanga E, Papiha SS, Cinnioglu C, King R, Cavalli-Sforza L, Underhill PA, Villems R. *Am J Hum Genet*. (2003) The genetic heritage of the earliest settlers persists both in Indian tribal and caste populations, *Feb Epub*;72(2):313-32.

Knuuttila, S (2004) *Emotions in Ancient and Medieval Philosophy*. Oxford UP: Oxford.

Koch, C & Laurent, G (1999) Complexity and the nervous system. *Science*: 284:96–98

L

Levitt, SH (2003) The Dating of the Indian Tradition, *Anthropos* vol 98: 341-59.

Lloyd, G (1975) Alcmeon and the early history of dissection, *Sudhoffs Archiv*, 59: 113–47 = Lloyd, 1991: 164–193.

Long, AA, & Sedley, DN (1987), *The Hellenistic Philosophers, I–II*. Cambridge UP: Cambridge

M

Martin, J (2002) The Integration of Neurology, Psychiatry, and Neuroscience in the 21st Century, *Am J Psychiatry* 159:5

Massa, N (1536) *Liber introductorius anatomiae, sed dissectionis corporis humanis*. NP: Venice.

Meulenbeld, G (1999-2002) *A History of Indian Medical Literature*, Egber Forsten: Groningen.

Müller, J (1835–1840) *Handbuch der Physiologie des Menschen für Vorlesungen* (two volumes translated into English), Baly, W *Elements of Physiology*. Taylor & Walton: London.

Mylius, K (2015) *Historia de la Literatura India Antigua*, Trotta: Madrid.



## N

Nemesius (de Emesa) *De natura hominis*, ed. Morani, M (1987) Teubner: Leipzig.

Norman, J (ed.) (1991) *Morton's Medical Bibliography no. 574*. Also: Hook & Norman, The Haskell F. (1991) *Norman Library of Science and Medicine*, no. 627. NP.

## O

Oester YT, Fudema JJ. 1969 Historical notes on electromyography. *AAEE Bulletin* 15:79-80.

## P

Pearce, J (2005) The Law of Specific Nerve Energies and Sensory Spots, *Eur Neurol*; 54:115–117 DOI: 10.1159/000088647

Pritchard, J (ed) (1969) *Ancient near eastern texts Relating to the Old testament*, Princeton UP: Princeton

Pubols, BH (1959) Jan Swammerdam and the history of reflex action. *Am. J. Psychol.* 72, 131–135 (1959).

## Q

## R

Reddy, WM (2001) *The Navigation of Feeling: A Framework for the History of Emotions*, Cambridge UP: Cambridge.

Reich, W (2010) *Análisis del carácter*, Paidós Surcos 5: Madrid.

## S

Scheer, M (2012) Are emotions a kind of practice (and is that what makes them have his-

tory)? A Bourdieuan approach to understanding emotion, *History and theory* 51: pg. 193-220.

Sherrington, CS. (1903) Qualitative difference of spinal reflex corresponding with qualitative difference of cutaneous stimulus. *J Physiol* 30: 39 – 46.

— (1906) Observations on the scratch-reflex in the spinal dog. *J Physiol* 34: 1–50.

Schiff, J.M. (1858) Lehrbuch der Physiologie des Menschen I: Muskel und Nervenphysiologie. *Lahr M. Schauenburg*, 234: 253-255.

Solmsen, F (1961) Greek Philosophy and the Discovery of Nerves, *Museum Helveticum*, 18: 150–97.

Smith, CUM (1987) David Hartley's Newtonian Neuropsychology, *Journal of the History of the Behavioral Sciences*, 23: 123–36.

Steckerl, F, (1958) The Fragments of Praxagoras of Cos and his School, *Philosophia Antiqua*, 8:10–22.

Swammerdam, J (1758) *The Book of Nature (Biblia Naturæ) or the History of Insects*, CG Seyffert, London.

## T

## U

Underhill PA, Myres NM, Rootsi S, Metspalu M, Zhivotovsky LA, King RJ, Lin AA, Chow CE, Semino O, Battaglia V, Kutuev I, Järve M, Chaubey G, Ayub Q, Mohyuddin A, Mehdi SQ, Sengupta S, Rogaev EI, Khusnutdinova EK, Pshenichnov A, Balanovsky O, Balanovska E, Jeran N, Augustin DH, Baldovic M, Herrera RJ, Thangaraj K, Singh V, Singh L, Majumder P, et al (2010) Separating the post-Glacial coancestry of European and Asian Y chromosomes within haplogroup R1a1, *Eur J Hum Genet*, 18:479–484.

## V

von Frey (1894) Beitrage zur Physiologie des Smerzsinnens. *Ber. Verhndl. konig. sachs. Ges. Wiss.* 46: 185-188, 1894.

von Staden, H (2000) Body, Soul, and Nerves: Epicurus, Herophilus, Erasistratus, the Stoics, and Galen, *Wright and Potter*, 87–96.

## W

Wheeler, LR (1939) *Vitalism: its history and validity*. Whitherby: London.

Williams, L (2012) *Modeling, Building, Writing: A History of Nonlinear Dynamics and Complex Systems*. PhD Dissertation. Harvard UP

## X

## Y

Yolton, JW (1983) *Thinking matter. Materialism in eighteenth-century Britain*. University of Minnesota Press: Minneapolis.

## Z

Zhmud, L (2014) Sixth-, fifth-, and fourth-century Pythagoreans, C. A. Huffman, (ed.), *A History of Pythagoreanism*, 97–102, Cambridge UP: Cambridge.

---

 QIII, §2
 

---

## A

Allen, NJ & Barres, BA (2009) Neuroscience: glia — more than just brain glue, *Nature* 457: 675-677.

Akil, H, Mayer, DJ, & Liebeskind, J. C. (1972) Comparison chez le rat entre l’analgésie induite par stimulation de la substance grise péri-aqueducale et l’analgésie morphinique, *CR Acad. Sci.(Paris)*, 274, 3603-3605.

Apkarian AV, Bushnell MC Treede RD & Zubieta JK (2005) Human brain mechanisms of pain perception and regulation in health and disease, *Eur J Pain*, 9: 463–484.

## B

Basbaum, A (2012) (Online) Specific vs Patterning Theory: Continuing the Debate, *Pain Research Forum* [accessed 30/06/18, 13:42] <https://www.painresearchforum.org/forums/discussion/7347-specificity-versus-patterning-theory-continuing-debate>

Baumgärtner U1, Iannetti GD, Zambreanu L, Stoeter P, Treede RD, Tracey I (2010) Multiple somatotypic representations of heat and mechanical pain in the uperculo-insular cortex: a high-resolution fMRI study, *Journal of Neurophysiology* 104: 2863-72.

Berrios, G.E., I.S. Marková (2002) The concept of neuropsychiatry. A historical overview, *Journal of Psychosomatic Research* 53: 629–638.

Bell C, Shaw A (1868) Reprint of the “Idea of a New Anatomy of the Brain,” with Letters, &c. *J Anat Physiol* 3: 147–182.

Bernard C & Magendie F (1856) *Leçon d’ouverture du Cours de Médecine du Collège de France*. Baillière, Paris.

Bessou P, Perl ER. (1969) Response of cuta-

neous sensory units with unmyelinated fibers to noxious stimuli, *J Neurophysiol* 32: 1025–1043.

Blix, M (1883): *Uppsala Läkareföreningars Förhandlingar*, vol 18, plate VI.

Boccard, S. G., Pereira, E. A., Moir, L., Van Hartvelt, T. J., Kringelbach, M. L., FitzGerald, J. J., et al. (2014). Deep brain stimulation of the anterior cingulate cortex: targeting the affective component of chronic pain. *Neuroreport* 25, 83–88. doi: 10.1097/WNR.0000000000000039

Boring EG (1942) *Sensation and Perception in the History of Experimental Psychology*. D. Appleton-Century: London.

Braz, J, Solorzano, C, Wang, X., and Basbaum, A.I. (2014) Transmitting pain and itch messages: a contemporary view of the spinal cord circuits that generate gate control, *Neuron* 82, 522–536.

Brooks J, Tracey I (2005) From nociception to pain perception: imaging the spinal and supraspinal pathways, *J Anat* 207, 19–33.

Burgess PR, Perl ER. Myelinated afferent fibres responding specifically to noxious stimulation of the skin. *J Physiol* 190: 541–562, 1967.

## C

Cartwright, ND (1983) *How the Laws of Physics Lie*. Oxford: Clarendon Press.

Caterina MJ, Schumacher MA, Tominaga M, et al. (1997) The capsaicin receptor: a heat-activated ion channel in the pain pathway, *Nature* 389:816–824.

Carr, F.B., & Zachariou, V. (2014) Nociception and pain: lessons from optogenetics. *Front. Behav. Neurosci.* 8, 69.

Christensen, AJ, Shrivats M. Iyer, Amaury François, Saurabh Vyas, Charu Ramakrishnan, Sam Vesuna, Karl Deisseroth, Gregory Scherrer & Scott L. Delp (2016) In Vivo Interrogation of Spinal Mechanosensory Circuits. *Cell Reports* 17, 1699–1710: <http://dx.doi.org/10.1016/j.celrep.2016.10.010>

Claudel, RM (2006) Memory in astrocytes. A hypothesis, *Theor Biol Med Model* 3: 2.

Cobb, M (2002) Exorcizing the animal spirits, *Nature Reviews Neuroscience* 3: 395–400.

Cowan, WM & Kandel, ER (2001) Prospects for neurology and psychiatry. *JAMA*; 285:594–600

Koch, C & Laurent, G (1999) Complexity and the nervous system. *Science*; 284:96–98

## D

Dallenbach, KM (1939) Pain: history and present status. *Am J Psychol* 52: 331–347.

Damoiseaux, JS & Greicius, MD (2009) Greater than the sum of its parts: a review of studies combining structural connectivity and resting-state functional connectivity, *Brain Struct Funct* 213: 525–533.

Darden, L (2006) *Reasoning in Biological Discoveries: Essays on Mechanisms, Interfield Relations, and Anomaly Resolution*. Cambridge UP: Cambridge

Duan, B, Longzhen Cheng, Steeve Bourane, Olivier Britz, Christopher Padilla, Lidia Garcia-Campmany, Michael Krashes, Wendy Knowlton, Tomoko Velasquez, Xiangyu Ren, Sarah E. Ross, Bradford B. Lowell, Yun Wang, Martyn Goulding, and Qiufu Ma (2014) Identification of Spinal Circuits Transmitting and Gating Mechanical Pain, *Cell* 159, 1417–1432

Davis, KD & Moayed, M (2013) Central mechanisms of pain revealed through functional and structural, *MRI. J. Neuroimmune Pharmacol.* 8, 518–534. doi: 10.1007/s11481-012-9386-8

## E

Erb WH (1895) Krankheiten der peripherischen cerebrospinalen Nerven. *Amer. J. Psychol.*, 7: 109.

- Erlanger J, Gasser HS & Bishop GH (1924) The compound nature of the action current of nerve as disclosed by the cathode ray oscillograph. *Am J Physiol*;70:624-666.
- Erlanger J, Gasser HS (1930) The action potential in fibers of slow conduction in spinal roots and somatic nerves. *Am J Physiol*;92:43-82.
- F
- Farmer MA, Baliki MN, Apkarian AV (2012) A dynamic network perspective of chronic pain. *Neurosci Lett*, 520: 197–203.
- Fields HL, Heinricher MM, Mason P (1991) Neurotransmitters in nociceptive modulatory circuits. *Annu Rev Neurosci* 14:219-245.
- Fuchs PN, Peng YB, Boyette-Davis JA & Uehlski ML (2014) The anterior cingulate cortex and pain processing. *Front. Integr. Neurosci.* 8:35. doi: 10.3389/fnint.2014.00035
- G
- Galison, P (1996) Computer simulation and the trading zone, Galison, P & Stump, DJ (eds.) *The Disunity of Science: Boundaries, Contexts, and Power*, 118-157, Stanford UP: Stanford.
- (2004) Specific theory, *Critical Enquiry* 30, 2: 379-383.
- (2008) Ten problems in history and philosophy of science, *Isis* 99: 111-124.
- Gao, YJ, Ren, WH, Zhang, YQ, & Zhao, ZQ (2004). Contributions of the anterior cingulate cortex and amygdala to pain- and fear-conditioned place avoidance in rats. *Pain* 110, 343–353. doi: 10.1016/j.pain.2004.04.030
- Gasser HS. The classification of nerve fibers. *Ohio J Sci* 1941;41:145-159.
- Gasser HS, Erlanger J (1927) The role played by the sizes of the constituent fibers of a nerve-trunk in determining the form of its action potential wave. *Am J Physiol*;80:522-547.
- Gell-Mann, M (1995) *Complexity*. Wiley: NY.
- Gibson HE, Edwards JG, Page RS, Van Hook MJ, Kauer JA (2008) TRPV1 channels mediate long-term depression at synapses on hippocampal interneurons, *Neuron*. 57 (5): 746–59. doi:10.1016/j.neuron.2007.12.027. PMC 2698707 . PMID 18341994.
- Giere, R (1999) *Science without Laws*. Chicago UP: Chicago.
- Goldscheider, A (1884) Neue Tzachen uber die Hautsinnesnerven. *Arch. Anat. Physiol. (Physiol Abth, Suppl Bd)*, 1110, 1885 (*Gesammelte Abhandlungen*), 1: 197, 1898.
- H
- Häbler, HJ, Jänig, W, & Koltzenburg, M (1990) Activation of unmyelinated afferent fibres by mechanical stimuli and inflammation of the urinary bladder in the cat, *The Journal of Physiology*, 425, 545–562.
- Han, L., Ma, C., Liu, Q., Weng, H.-J., Cui, Y., Tang, Z., Kim, Y., Nie, H., Qu, L., Patel, K.N., et al. (2012) A subpopulation of nociceptors specifically linked to itch, *Nat. Neurosci.* 16, 174–182. doi:10.1038/nn.3289
- Haraway, D (1991) *Simians, Cyborgs, and Women*, Routledge: NY.
- Hardy J.D, Wolff H.D., Godell H. (1952) *Pain Sensations and Reactions*. Williams & Wilkins: Baltimore.
- Hauck M, Domnick C, Lorenz J, Gerloff C, Engel AK (2015) Top-down and bottom-up modulation of pain-induced oscillations. *Front Hum Neurosci*, 9: 375.
- Head H (1920) *Studies in Neurology*. Oxford UP: London.
- (1992) An address on certain aspects of pain, *BMJ*: 1, 1–5.
- (1923–24) The conception of nervous and mental energy II. ('Vigilance'; a physiolo-

gical state of the nervous system, *Br. J. Psychol. Gen. Sect.*, 14, 126–147.)

Head, H & Rivers, W (1908) A Human Experiment in Nerve Division, *Brain*. 31 (3): 323–450. doi:10.1093/brain/31.3.323.

Helmreich, S (2016) *Sounding the Limits of Life*, Princeton UP: Princeton.

Henry MS, Gendron L, Tremblay ME, Drolet G (2017) Enkephalins: Endogenous Analgesics with an Emerging Role in Stress Resilience, *Neural Plasticity* 1546125. doi:10.1155/2017/1546125. PMC 5525068 . PMID 28781901.

## I

Iannetti, G. D., Salomons, T. V., Moayedi, M., Mourauz, A., and Davis, K. D. (2013) Beyond metaphor: contrasting mechanisms of social and physical pain, *Trends Cog. Sci.* 17, 371–378. doi: 10.1016/j.tics.2013.06.002

Iqbal, SA, Wallach, JD, Khoury, MJ, Schully, SD & Io- annidis, JP (2016) Reproducible research practices and transparency across the biomedical literature, *PLoS Biology* 14: e1002333.

## J

Jia, RR, Temugin, B & Nedergaardb, M (2013) Glia and pain: Is chronic pain a gliopathy?, *Pain* 154(1): S10–S28. doi:10.1016/j.pain.2013.06.022.

## K

Keller, EF (2003) *Making Sense of Life: Explaining Biological Development with Models, Metaphors, and Machines*, Harvard: Cambridge.

Kettenmann, H & Kirchhoff, F & Verkhratsky, A (2013) Microglia: New roles for the synaptic stripper, *Neuron* 77: 10-18.

Kiernan, J & Rajakumar, N (eds.) (2014) *Barr's 'The Human Nervous System' 10th Edition*, Phil: LW&W.

Kim, HS, Seto-Ohshima, A, Nishiyama, H & Itoharu, S (2011), Normal delay eyeblink in conditioningin mice devoid of astrocytic S100B, *Neurosci Lett* 489: 148-153.

## L

LaMotte, R.H., Shimada, S.G., Green, B.G. & Zelterman, D (2009) Pruritic and nociceptive sensations and dysesthesias from a spicule of cowhage, *J. Neurophysiol.* 101, 1430–1443.

LeBars, D, Dickenson, AH & Besson, JM (1979) Diffusenoxiousinhibitorycontrol-s(DNIC)II Lack of effect on non-convergent neurones, supraspinal involvement and theoretical implications, *Pain*;6(3):305–27.

Lele PP, Sinclair DC, Weddell G (1954) The reaction time to touch. *J Physiol* 123: 187–203.

Li, X.-Y., Ko, H.-G., Chen, T., Descalzi, G., Koga, K., Wang, H., et al. (2010) Alleviating neuropathic pain hypersensitivity by inhibiting PKM $\zeta$  in the anterior cingulate cortex. *Science* 330, 1400–1404. doi: 10.1126/science.1191792

Liu, Q & Dong, X (2015) The role of the Mrgpr receptor family in itch, *Handb Exp Pharmacol*, 226, 71–88.

Liu, Q, Hao-Jui Weng, Kush N. Patel1, Zongxiang Tang, Haihua Bai1, Martin Steinhoff, & Xinzhong Dong (2011) The distinct roles of two GPCRs, MrgprC11 and PAR2, in itch and hyperalgesia, *Science Signaling*, 4, no. 181, 45.

Livingston WK (1943) *Pain Mechanisms*. New York, Mcmillan, .

Lloyd DPC (1943) Neuron patterns controlling transmission of ipsilateral hind limb reflexes, *J Neurophysiol*;6:293-315.

Lu, C, Tao Yang, Huan Zhao, Ming ZhanG, Fancheng Meng, Hao Fu, Yingli Xie, Hui

Xu (2016) Insular Cortex is Critical for the Perception, Modulation, and Chronification of Pain, *Neurosci. Bull.* 32(2):191–201.

## M

Manzano, GM, Lydia M.P. Giuliano2, João A.M. (2008) A brief historical note on the classification of nerve fibers, *Nóbrega Arq Neuropsiquiatr*;66(1):117-119.

Mar, L., Yang, F.C., & Ma, Q. (2012) Genetic marking and characterization of Tac2-expressing neurons in the central and peripheral nervous system, *Mol. Brain* 5, 3.

Marshall, H.R. Pleasure, pain and emotion, *Psychol. Res.*, 2: 57-64, 1895.

Martin, J (2002) The Integration of Neurology, Psychiatry, and Neuroscience in the 21st Century, *Am J Psychiatry*, 159:5

Melzack, R (1961) The perception of pain, *Sci Am* 204:197-210.

Melzack, R & Wall, P.D (1962) On the nature of cutaneous sensory mechanisms. *Brain*, 85: 331-356.

— (1965) Pain mechanisms: a new theory. *Science*, 150: 971-979.

Melzack, R, & Casey, KL (1968) Sensory, motivational and central control determinants of pain, Kenshalo D.R. (ed.) *The Skin Senses*, 423-439. Springfield, Illinois, Charles C. Thomas Publisher.

Messlinger, K (1996) Functional morphology of nociceptive and other fine sensory endings (free nerve endings) in different tissues; in Kumazawa T, Kruger L, Mizumura K (eds): *The Polymodal Receptor: A Gateway to Pathological Pain*, 273– 298. Amsterdam, Elsevier.

Millan, MJ (1999) The induction of pain: an integrative review, *Progr Neurobiol* 57, 1–164.

Milne, RJ & Gamble GD (1990): Behavioural modification of bulbospinal serotonergic inhibition and morphine analgesia. *Brain Res*, 521:167-174.

Moayedi, M & Davis, K (2013) Theories of pain: from specificity to gate control, *J Neurophysiol* 109: 5-12.

Morton, T (2013) *Hyperobjects. Philosophy and Ecology after the End of the World*, Minnesota UP: Minneapolis.

Müller, J (1838-1843) *Handbuch der Physiologie des Menschen für Vorlesungen*. Coblenz, J. Hölscher, 1835–1840 (two volumes translated into English); in Baly W: *Elements of Physiology*. London, Taylor & Walton.

Murinson BB1, Griffin JW (2004) C-fiber structure varies with location in peripheral nerve, *J Neuropathol Exp Neurol.* 63(3):246-54.

## N

Nafe, JP. (1929) A quantitative theory of feeling. *J Gen Psychol* 2: 199–211.

—(1934) The pressure, pain, and temperature senses, Murchison C.A. (ed.) *Handbook of general, experimental Psychology*, Worcester, Clark UP: MA.

Naunyn, B (1889) Ueber die Auslösung von Schmerzempfindung durch Summation sich zeitlich folgender sensibler Erregungen, *Naunyn-Schmiedeberg's Archives of Pharmacology*. 25 (3–4): 272–305. doi:10.1007/BF01833969.

Nishiyama, H et al (2002) Glial protein S100B modulates long-term neuronal synaptic plasticity, *Proc Natl Acad Sci USA* 99: 4037-42.

Noordenbos, W (1959) *Pain*, Elsevier: Amsterdam.

## O

Oester, YT, Fudema JJ (1969) Historical notes on electromyography. *AAEE Bulletin* 15:79-80.

Ochoa, J & Torebjörk, E (1989) Sensations evoked by intraneural microstimulation of C nociceptor fibres in human skin nerves, *The Journal of Physiology*, 415, 583–599.

Ochs, SA (2004) *History of Nerve Functions: from Animal Spirits to Molecular Mechanisms*. Cambridge UP: Cambridge.

Oh, U, Hwang SW & Kim D (1996) Capsaicin activates a nonselective cation channel in cultured neonatal rat dorsal root ganglion neurons, *J Neurosci*; 16:1659 – 1667.

## P

Pearce, J (2005) The Law of Specific Nerve Energies and Sensory Spots, *Eur Neurol*;54:115–117 DOI: 10.1159/000088647

Peltz, El, Seifert F, DeCol R, Dörfler A, Schwab S, Maihöfner C (2011) Functional connectivity of the human insular cortex during noxious and innocuous thermal stimulation, *Neuroimage* 54:1324-35.

Pereira, EAC, Paranathala, M, Hyam, JA, Green, AL, & Aziz, TZ (2013) Anterior cingulotomy improves malignant mesothelioma pain and dyspnoea, *Br. J. Neurosurg.* doi: 10.3109/02688697.2013.857006.

Perl, ER, Kruger L (1996) Nociception and pain: evolution of concepts and observations, Kruger L. *Pain and Touch* 180–212, CA Academic: San Diego.

Pert CB, Snowman, AM, Snider S.H (1974) Localization of opiate receptor binding in synaptic membranes in the rat brain, *Brain Res.*, 70: 184-188.

Peters JH, McDougall SJ, Fawley JA, Smith SM, Andresen MC (2010) Primary afferent activation of thermosensitive TRPV1 triggers asynchronous glutamate release at central neurons, *Neuron*. 65 (5): 657–69. doi:10.1016/j.neuron.2010.02.017. PMC 2837850 . PMID 20223201.

## Q

## R

Rey, R (1995) *The History of Pain*. Cambridge, Harvard UP: MA.

Reynolds, DV (1969) Surgery in the rat during electrical analgesia induced by focal electrical stimulation. *Science*, 164: 444-445.

Rexed, B (1952) The cytoarchitectonic organization of the spinal cord in the cat, *JCN* 96, 3: 415-495.

## S

Schiff, JM (1858) *Lehrbuch der Physiologie des Menschen I: Muskel und Nervenphysiologie*. Lahr M. Schauenburg, 234: 253-255.

Shamliyan, T, Kane, R.L. & Jansen, S. (2010) Quality of systematic reviews of observational nontherapeutic studies, *Preventing Chronic Disease* 7 (6): A133.

Shapiro, LA, Bialowas-McGoey, LA & Whitaker-Azmitia, PM (2010) Effects of S100B on serotonergic plasticity and neuroinflammation in the hippocampus in Down syndrome and Alzheimer's disease: studies in an S100B overexpressing mouse model, *Cardiovasc Psychiatry Neurol*: 153657.

Sherrington, CS. (1903) Qualitative difference of spinal reflex corresponding with qualitative difference of cutaneous stimulus. *J Physiol* 30: 39 – 46.

— (1906) Observations on the scratch-reflex in the spinal dog. *J Physiol* 34: 1–50.

Sherrington CS. *The Integrative Action of the Nervous System*. Cambridge, UK: Cambridge University Press, 1947.

Sherwood, CC, Stimpson, CD & Raghanti, MA et al (2006) Evolution of increased glia-neuron ratios in frontal cortex, *Proc Natl Acad Sci USA* 103: 13606-13611.

Slezak, M & Pfrieder, FW & Soltys, Z (2006) Synaptic plasticity, astrocytes and morphological homeostasis, *Journal of Physiology* 99 (Paris): 84-91.

Sneddon, LU, V.A. Braithwaite, M.J. Gentle (2003) Do fish have nociceptors: evidence for the evolution of a vertebrate sensory system, *Proc. R. Soc. Lond.*, B 270:1115–1122.

Sneddon, L (2004) Evolution of nocicep-

- tion in vertebrates: comparative analysis of lower vertebrates, *Brain Research Reviews* 46: 123–130. doi:10.1016/j.brainres-rev.2004.07.007
- Sinclair DC (1955) Cutaneous sensation and the doctrine of specific nerve energies. *Brain*;78: 584–614.
- Song, J, Dehai Xian, Lingyu Yang, Xia Xiong, Rui Lai & Jianqiao Zhong (2018) Pruritus: Progress toward Pathogenesis and Treatment, *BioMed Research International* 1-12. <https://doi.org/10.1155/2018/9625936>
- Starr, ChJ, Lumy Sawaki, George F. Wittenberg, Jonathan H. Burdette, Yoshitetsu Oshiro, Alexandre S. Quevedo, & Robert C. Coghill (2009) Roles of the Insular Cortex in the Modulation of Pain: Insights from Brain Lesions, *J Neurosci* 4; 29(9): 2684–2694. doi:10.1523/JNEUROSCI.5173-08.2009.
- Strong, C.A. The psychology of pain. *Psychol. Rev.*, 2: 329-327, 1895.
- Strughold, H (1924) Über die Dichte und Schwellen der Schmerzpunkte der Epidermis in den verschiedenen Körperregionen. *Z Biol*;80: 367–380.
- Sun, S, Qian Xu, Changxiong Guo, Yun Guan,2 Qin Liu, & Xinzhong Dong (2017) Leaky Gate Model: Intensity-Dependent Coding of Pain and Itch in the Spinal Cord, *Neuron* 93, 840–853, <http://dx.doi.org/10.1016/j.neuron.2017.01.012>
- T
- Thagard, P (2005) *Mind: Introduction to Cognitive Science, 2nd ed.* MIT: Cambridge.
- (2010) *The Brain and the Meaning of Life.* Princeton UP: NJ.
- Torebjörk, HE, Hallin, RG (1970) C-fibre units recorded from human sensory nerve fascicles in situ. *Acta Soc Med Upsal*;75:81–84.
- U
- V
- Venkatachalam, K & Montell, C (2007) TRP Channels. *Annu Rev Biochem*;76:387–417.
- von Frey, M (1894) Beiträge zur Physiologie des Schmerzsinners. *Ber. Verhndl. konig. sachs. Ges. Wiss.* 46: 185-188.
- (1896) Untersuchungen über die Sinnesfunktionen der menschlichen Haut. Erste Abhandlung. *Abhandlungen der mathematisch-physischen Klasse derBer. Verhndl. konig. sachs. Ges. Wiss*; 23:208–217.
- W
- Wall, PD (1960) Cord cells responding to touch, damage and temperature skin, *J Neurophysiol* 23: 197-210.
- (1990) Obituary William Noordenbos, *Pain* 42: 265-261
- (1979) On the relation of injury to pain. The John J. Bonica lecture. *Pain* 6:253–264.
- Weddell, G, Sinclair DC, Feindel WH (1948) An anatomical basis for alterations in quality of pain sensibility. *J Neurophysiol*;11:99–109.
- Weddell, G. Somesthesia in chemical senses. *Ann. Rev. Psychol.*, 6: 119-136, 1955.
- Weinberg, S (1993) *Dreams of a Final Theory*, Pantheon: NY.
- Williams, L (2012) *Modeling, Building, Writing: A History of Nonlinear Dynamics and Complex Systems*, PhD Dissertation. Harvard UP.
- Y
- Yizhar, O, Fenno, L.E., Davidson, T.J., Mogri, M & Deisseroth, K. (2011). Optogenetics in neural systems. *Neuron* 71, 9–34.
- Yuan, W, Dan, L., Netra, R., Shaohui, M., Chenwang, J & Ming, Z. (2013) A pharmacofMRI study on pain networks induced by electrical stimulation after sumatriptan injection. *Exp. Brain Res.* 226, 15–24. doi: 10.1007/s00221-013-3405-8



A

B

- Basbaum, A (2012) (Online) Specific vs Patterning Theory: Continuing the Debate, *Pain Research Forum* [accessed 30/06/18, 13:42] <https://www.painresearchforum.org/forums/discussion/7347-specificity-versus-patterning-theory-continuing-debate>
- Bechtel, W & Richardson, RC (1993) *Discovering Complexity*. Princeton UP: Princeton.
- Bennett, MR & Hacker, PM (2003) *Philosophical Foundations of Neuroscience*, Basil Blackwell: Oxford.
- Bergson, H (1911) *Creative Evolution*. Holt: NY.
- Berrios, GE, & Marková, IS (2002) The concept of neuropsychiatry A historical overview, *Journal of Psychosomatic Research* 53: 629–638
- Bertalanffy, L (von) (1950a) The theory of open systems in physics and biology, *Science* 111: 23-29.
- (1950b) An outline of general system theory, *British Journal of Philosophy of Science* 1: 139-164.
- (1955) An essay on the relativity of categories, *Philosophy of Science* 22: 243-263.
- (1966) General system theory and psychiatry, Arieti, S (ed) *American Handbook of Psychiatry*, 3. Basic Books: NY.
- Boccard, SG, Pereira, E. A., Moir, L., Van Hartvelt, T. J., Kringelbach, M. L., FitzGerald, J. J., et al (2014) Deep brain stimulation of the anterior cingulate cortex: targeting the affective component of chronic pain. *Neuroreport* 25, 83– 88. doi: 10.1097/WNR.0000000000000039
- Boddice, R (2012) (On Line) Species of compassion: aesthetics, anaesthetics, and pain in

the physiological laboratory, *Interdisciplinary Studies in the Long Nineteenth Century* 15: <http://doi.org/10.16995/ntn.628> [consulted in 13.2.2015].

- Boring, EG (1942) *Sensation and Perception in the History of Experimental Psychology*, D. Appleton-Century: London.
- Bourke, J (2014) *The story of pain, from prayer to painkillers*, Oxford UP: NY.
- Bureman, L (2013) Synecdoche: The Art of Getting Eyeballs, *The Write Practice*. 2 January 2019.
- Burke, Kenneth (1941) Four Master Tropes, *The Kenyon Review* 3 (4): 426. JSTOR 4332286.

C

- Cartwright, ND (1999) *The Dappled World: A Study of the Boundaries of Science*. Cambridge: Cambridge University Press.
- Churchland, P (2002) *Brain-wise: Studies in Neurophilosophy*, MIT UP: Cambridge.
- Craver, CF & Bechtel, W (2007) Top-down causation without top-down causes, *Biol. Philos.* 22: 547–663.
- Corlett, PR; Taylor, JR; Wang, XJ; Fletcher, PC & Krystal, JH (2010) Toward a neurobiology of delusions, *Prog Neurobiol* 92(3):345–369. DOI:10.1016/j.pneurobio.2010.06.007.
- Cowan WM & Kandel ER (2001) Prospects for neurology and psychiatry. *JAMA* 2001; 285:594–600

D

- Dallenbach, KM (1939) Pain: history and present status. *Am J Psychol* 52: 331–347.
- Damoiseaux, JS & Greicius, MD (2009) Greater than the sum of its parts: a review of studies combining structural connectivity and resting-state functional connectivity, *Brain Struct Funct* 213: 525-533.
- Darden, L (2006) *Reasoning in Biological Discoveries: Essays on Mechanisms, Interfield Relations, and Anomaly Resolution*. Cambridge University Press: Cambridge.

- Darden, L., & N. Maull (1977) Interfield Theories, *Philosophy of Science* 44: 43–64.
- Duncan S, Barrett LF (2007) Affect is a form of cognition: a neurobiological analysis. *Cognition and Emotion* 21, 1184–1211.
- Dupré, J (1981) Natural Kinds and Biological Taxa, *Philosophical Review* 90, 66-90.
- (1993) *The Disorder of Things: Metaphysical Foundations of the Disunity of Science*. Cambridge: HUP.
- E
- Eldredge, N (1985) *Unfinished Synthesis: Biological Hierarchies and Modern Evolutionary Thought*. Oxford UP: NY.
- Enelow, David (2011) The Four Master Tropes, *Head-Royce School*. [22-03-2019] Online at: <http://faculty.headroyce.org/~denelow/English%2011/rhetoric/Mastertropes.html>
- F
- Fedigan, LM & Fedigan, L (1989) Gender and the Study of Primates, *Critical Reviews of gender and Anthropology*, 41-64.
- Fehr, C & Plaisance, K (2010) Socially relevant philosophy of science: An introduction, *Synthese* 177, 301-316.
- Fuchs PN, Peng YB, Boyette-Davis JA and Uehlski ML (2014) The anterior cingulate cortex and pain processing. *Front. Integr. Neurosci.* 8:35. doi: 10.3389/ fnint.2014.00035
- G
- Galison, P. (1987). *How Experiments End*. Chicago: University of Chicago Press.
- (1996) Computer simulation and the trading zone, Galison, P & Stump, DJ (eds.) *The Disunity of Science: Boundaries, Contexts, and Power*, 118-157, Stanford UP: Stanford.
- (2003) *Einstein's Clocks, Poincaré's Maps: Empires of Time*, Norton: NY.
- (2004) Specific theory, *Critical Enquiry* 30, 2: 379-383.
- (2008) Ten problems in history and philosophy of science, *Isis* 99: 111-124.
- Galison, P & Stump, DJ (eds.) (1996) *The Disunity of Science: Boundaries, Contexts, and Power*, Stanford UP: Stanford.
- Gao, YJ, Ren, W. H., Zhang, Y. Q., and Zhao, ZQ (2004) Contributions of the anterior cingulate cortex and amygdala to pain- and fear-conditioned place avoidance in rats. *Pain* 110, 343–353. doi: 10.1016/j.pain.2004.04.030
- Gell-Mann, M (1995) *Complexity*. Wiley: NY.
- Giere, RN (1988) *Explaining Science: A Cognitive Approach*. Chicago UP: Chicago.
- (1999) *Science without Laws*. Chicago: University of Chicago Press.
- (2006a) *Scientific Perspectivism*, Chicago UP: Chicago.
- (2006b) Perspectival pluralism, Kellert, S; Longino, HE & Kenneth Waters, C (eds.) *Minnesota Studies in the Philosophy of Science*, vol XIX, Scientific Pluralism: 26-41, Minnesota UP: London.
- H
- Hacking, I (1986) Making up people, Heller, T (ed.) (1986) *Reconstructing Individualism: Autonomy, Individuality in Self Investigation ought*, 161-171, Stanford UP: Stanford.
- (1998) *Mad Travellers. Reflections on the Reality of Transient Mental Illnesses*, Virginia UP: London.
- (2002) *Historical Ontology*, Harper U P: London.
- Han, L, Ma, C., Liu, Q., Weng, H.-J., Cui, Y., Tang, Z., Kim, Y., Nie, H., Qu, L., Patel, K.N., et al(2012). A subpopulation of nociceptors specifically linked to itch. *Nat. Neurosci.* 16, 174–182. doi:10.1038/nn.3289

- Haraway, D J (1976) *Crystals, Fabrics, and Fields: Metaphors that Shape Embryos*. Yale UP: NH.
- Harding, S (1991) *Whose Science? Whose Knowledge?*, Cornell UP: NY.
- (1993) Rethinking standpoint epistemology: what is strong objectivity?, Alcof, L & Potter, E (eds.) *Feminist Epistemologies*, Routledge: London.
- Helmreich, S (2016) *Sounding the Limits of Life*, Princeton UP: Princeton.
- Heylighen, F (2000) Evolutionary transitions: how do levels of complexity emerge?, *Complexity* 6: 53–57.
- I
- J
- K
- Adam P. Kardon, Erika Polgár, Junichi Hachisuka, Lindsey M. Snyder, et al (2014) Dynorphin Acts as a Neuromodulator to Inhibit Itch in the Dorsal Horn of the Spinal Cord, *Neuron* 82, 573–586
- Keller, EF (1995) *Refiguring Life: Metaphors of Twentieth-Century Biology*, Columbia UP: NY.
- (2003a) *Making Sense of Life: Explaining Biological Development with Models, Metaphors, and Machines*, Harvard: Cambridge.
- (2003b) Models, simulation, and “computer experiments”, Radder, H (ed.) *The Philosophy of Scientific Experimentation*, 198-215, Pittsburg UP: Pittsburg.
- (2005) Ecosystems, organisms, and machines, *Bioscience* 55, 12: 1069-1074.
- Kitcher, P (1993) *The Advancement of Science*, Oxford U P: Oxford.
- (2003) What kind of science should be done?, Lightman, A; Sarewitz, D & Dresser, C (eds.) (2003) *Living with the Genie*, 201-224, Island P: Washington.
- (2004) Evolutionary theory and the social uses of biology, *Biology and Philosophy* 19, pg. 1-15.
- Kitcher, P & Salmon, W (eds) (1989) *Scientific Explanation*. Minnesota UP: Minneapolis.
- Koch, C & Laurent G (1999) Complexity and the nervous system. *Science*; 284:96–98
- L
- Lane, D (2006) Hierarchy, complexity, society, Pumaine, D (ed) *Hierarchy in Natural and Social Sciences*, 81–119. Springer: Berlin.
- Longino, HE (1990). *Science as social knowledge: Values and objectivity in scientific inquiry*. Princeton UP: Princeton.
- (1996) Cognitive and Non-Cognitive Values in Science, *Feminism, Science, and the Philosophy of Science*, ed. L. H. Nelson and J. Nelson, 39–58. Dordrecht: Kluwer.
- (2001) *The Fate of Knowledge*, Princeton UP: Princeton.
- (2006) Theoretical pluralism and the scientific study of behavior, Kellert, S; Longino, HE & Kenneth Waters, C (eds.) *Minnesota Studies in the Philosophy of Science*, vol XIX, Scientific Pluralism: 102-131, Minnesota UP: London.
- M
- Machamer, P & Sytsma, J (2002) Philosophy and the Brain Sciences, *Iris* I, 2, 353-374
- Martin, J (2002) The Integration of Neurology, Psychiatry, and Neuroscience in the 21st Century, *Am J Psychiatry* 159:5.
- Mayr, E (1982) *The Growth of Biological Thought*. Harvard UP: Cambridge.
- McCauley, RN (2009) Time is of the essence: explanatory pluralism and accommodating theories about long-term processes, *Philos. Psychol.* 22: 611–635.
- McCauley, RN & Bechtel, W (2001) Expla-

natory pluralism and the heuristic identity theory, *Theory Psychol.* 11: 736–760.

McShea, DW (2001) The hierarchical structure of organisms: a scale and documentation of a trend in the maximum, *Paleobiology* 27: 405–423.

Melzack R. & Casey K.L (1968) Sensory, motivational and central control determinants of pain. In: Kenshalo D.R. (ed.), *The Skin Senses, Springfield, Illinois, Charles C. Thomas Publisher*, 423-439.

Mitchell, SD (2003) *Biological complexity and integrative pluralism*. Cambridge UP: Cambridge.

Mitchell, WJT (2004) Medium Theory, *Critical Inquiry* 30, 2: 324-335.

Moayed, M & Davis, K (2013) Theories of pain: from specificity to gate control, *J Neurophysiol* 109: 5-12.

## N

## O

## P

Pavé, A (2006) Biological and ecological systems hierarchical organization: natural mechanisms and human driven processes' role in the emergence of living systems' organisation levels and properties, Pumain, D (ed) *Hierarchy in Natural and Social Sciences*: 39–70. Springer: Dordrecht.

Pereira, E. A. C., Paranathala, M., Hyam, J. A., Green, A. L., and Aziz, T. Z. (2013) Anterior cingulotomy improves malignant mesothelioma pain and dyspnoea. *Br. J. Neurosurg.* doi: 10.3109/02688697.2013.857006. [Epub ahead of print].

## Q

## R

Racine, E & Illes, J (2009) Emergence at the crossroads of philosophy, neurotechnology and the enhancement debate, Bickle, J (ed.) *Philosophy of Neuroscience*: 431-453. Oxford UP: NY.

## S

Sherrington, CS. (1903) Qualitative difference of spinal reflex corresponding with qualitative difference of cutaneous stimulus. *J Physiol* 30: 39 – 46, 1903.

—(1906) Observations on the scratch-reflex in the spinal dog. *J Physiol* 34: 1–50, 1906.

Stump, D (1992) Naturalized Philosophy of Science with a Plurality of Methods, *Philosophy of Science* 59: 456–60.

Sun, Shuohao, Qian Xu, Changxiong Guo, Yun Guan, Qin Liu, & Xinzhong Dong (2017) Leaky Gate Model: Intensity-Dependent Coding of Pain and Itch in the Spinal Cord, *Neuron* 93, 840–853 <http://dx.doi.org/10.1016/j.neuron.2017.01.012>

## T

Thagard, P (1999) *How Scientists Explain Disease*. Princeton UP: NJ.

— (2005) *Mind: Introduction to Cognitive Science, 2nd ed.* MIT: Cambridge.

— (2010) *The Brain and the Meaning of Life*. Princeton UP: NJ.

— (2012) Mapping minds across cultures, Sun, R (ed.) *Grounding Social Sciences in Cognitive Sciences*: 35–62. MIT: Cambridge.

Tracey, I (2005) Nociceptive processing in the human brain. *Curr. Opin Neurobiol.* 15, 478–487.

## U

## V

- van Fraassen, BC (1976) To save the phenomena, Boyd, P; Gasper, P & Trout, JD (eds.) (1992) *The Phillosophy of Science*, 187-194, MIT: Cambridge.
- (1980) *The Scientific Image*. Oxford UP: Oxford
- (1989) *Laws and Symmetry*. Oxford UP: Oxford
- (1994) Interpretation of Science; Science as Interpretation, J. Hildevoord (ed.) *Physics and our view of the world*, 169-187. Cambridge UP: Cambridge.
- (1997) Structure and Perspective: Philosophical Perplexity and Paradox, M.L. Dalla Chiara (eds.) *Logic and Scientific Methods*, 511-530, Kluwer Academic Publishers, Netherlands.
- (2002) *The Empirical Stance*. Yale UP: New Haven
- (2008) *Scientific Representation: Paradoxes of Perspective*. Oxford UP, NY

## W

- Wall, PD: On the relation of injury to pain, The John J. Bonica lecture. *Pain* 6:253–264, 1979.
- Williams, L (2012) *Modeling, Building, Writing: A History of Nonlinear Dynamics and Complex Systems*, PhD Dissertation. Harvard UP

## X

## Y

## Z

- Zylstra, U (1992) Living things as hierarchically organized structures, *Synthese* 91: 111–133.

## QIII, §4

## A

- Abbas, AB & Lichtman A.H. (2009) Innate Immunity, *Basic Immunology. Functions and disorders of the immune system*, Els. Saunders.
- Abraira, VE & Ginty, DD (2013) The sensory neurons of touch. *Neuron* 79, 618–639.
- Apkarian AV (2008) Pain perception in relation to emotional learning. *Curr Opin Neurobiol*; 18: 464–8.
- Avitan, L., Pujic, Z., Mölter, J., Van De Poll, M., Sun, B., Teng, H., Amor, R., Scott, E.K., Goodhill, G.J. (2017) Spontaneous Activity in the Zebrafish Tectum Reorganizes over Development and Is Influenced by Visual Experience. *Current biology : CB*. 27(16):2407-2419.e4.

## B

- Baffy G1, Loscalzo J (2014) Complexity and network dynamics in physiological adaptation: an integrated view, *Physiol Behav*. 28;131:49-56. doi: 10.1016/j.physbeh.2014.04.018. Epub 2014 Apr 18.
- Baldeweg T, Spence S, Hirsch SR, Gruzelier J. PMID (1998) Gamma-band electroencephalographic oscillations in a patient with somatic hallucinations. *Lancet* 22;352(9128):620-1. DOI: 10.1016/S0140-6736(05)79575-1
- Bateson, P (1992) Assessment of pain in animals, *Anim. Behav.* 42 827 – 839.
- Behrendt RP (2003) Hallucinations: synchronisation of thalamocortical gamma oscillations underconstrained by sensory input, *Conscious Cogn* 12(3):413-51
- Berrios, GE & Marková, IS (2002) The concept of neuropsychiatry A historical overview, *Journal of Psychosomatic Research* 53 629–638

Bermejo, P., López, M., Larraya, I., Chamorro, J., Cobo, J. L., Ordóñez, S., & Vega, J. A. (2017) Innervation of the Human Cavum Conchae and Auditory Canal: Anatomical Basis for Transcutaneous Auricular Nerve Stimulation. *BioMed research international* 2017, 7830919.

Braz, J., Solorzano, C., Wang, X., and Basbaum, A.I. (2014) Transmitting pain and itch messages: a contemporary view of the spinal cord circuits that generate gate control. *Neuron* 82, 522–536.

Butti, C, Sherwood, CC, Hakeem, AY, Allman, JM, Hof, PR (2009) Total number and volume of Von Economo neurons in the cerebral cortex of cetaceans, *The Journal of comparative neurology* 515 (2): 243-59. PMID 19412956. doi:10.1002/cne.22055.

## C

Carr, FB & Zachariou, V (2014) Nociception and pain: lessons from opto- genetics. *Front. Behav. Neurosci.* 8, 69.

Chaudhry SR, Kum B. Biochemistry, Endorphin (2019). *StatPearls* [Internet]. *Treasure Island* (FL): StatPearls Publishing; 2019

Chen, J., Huang, J., Wei, Y.Y., Sun, X.X., Wang, W., Bai, L., Wang, Y.Y., Kaneko, T., Li, Y.Q., and Wu, S.X. (2014) Birth-date dependent arrangement of spinal enkephalinergic neurons: evidence from the pre-proenkephalin-green fluorescent protein transgenic mice, *Neuroscience* 260, 47–58.

Christensen, AJ, Shrivats M. Iyer, Amaury François, Saurabh Vyas, Charu Ramakrishnan, Sam Vesuna, Karl Deisseroth, Gregory Scherrer & Scott L. Delp (2016) In Vivo Interrogation of Spinal Mechanosensory Circuits. *Cell Reports* 17, 1699–1710 <http://dx.doi.org/10.1016/j.celrep.2016.10.010>

Craig, AD (2002) How do you feel? Interoception: The sense of the physiological condition of the body. *Nat Rev Neurosci*;3:655.

Cruce, W.L.R., Stuesse, SL & Northcutt, RC (1999) Brainstem neurons with descending projections to the spinal cord of two elasmobranch fishes: thornback guitarfish, *Platyhinoidis triseriata*, and horn shark, *Heterodontus francisci*, *J. Comp. Neurol.* 403 534 – 560.

## D

Duan, B, Longzhen Cheng, Steeve Bourane, Olivier Britz, Christopher Padilla, Lidia Garcia-Campmany, Michael Krashes, Wendy Knowlton, Tomoko Velasquez, Xiangyu Ren, Sarah E. Ross, Bradford B. Lowell, Yun Wang, Martyn Goulding & Qiufu Ma (2014) Identification of Spinal Circuits Transmitting and Gating Mechanical Pain, *Cell* 159, 1417–1432

Dworkin, BR (1993) Learning and physiological regulation. ChicagoUP: Chicago.

## E

## F

Fajardo, Escobar, M.I.; Buriticá, E.; Arteaga, G.; Umbarila, J.; Casanova, M.F.; Pimienta, H. (2008) Von Economo neurons are present in the dorsolateral (dysgranular) prefrontal cortex of humans, *Neuroscience Letters* 435 (3): 215-218. PMID 18355958. doi:10.1016/j.neulet.2008.02.048.

Fields HL (2006) A motivation-decision model of pain: the role of opioids. *Proceedings of the 11th world congress on pain, IASP*: 449–59.

François, A., Low, S. A., Sypek, E. I., Christensen, A. J., Sotoudeh, C., Beier, K. T., ... & Delp, S. L. (2017) A brainstem-spinal cord inhibitory circuit for mechanical pain modulation by GABA and enkephalins. *Neuron*, 93(4), 822-839.

Freneau, R.T.J., Jr., Voglmaier, S., Seal, R.P.,

and Edwards, R.H. (2004) VGLUTs define subsets of excitatory neurons and suggest novel roles for glutamate. *Trends Neurosci.* 27, 98–103.

## G

Gentle, MJ (1992) Pain in birds, *Anim. Welf.* 1; 235 – 247.

Giere, R (2006a) *Scientific Perspectivism*. Chicago UP: Chicago.

— (2006b) Perspectival pluralism, Kellert, S; Longino, HE & Kenneth Waters, C (eds.) *Minnesota Studies in the Philosophy of Science*, vol XIX, Scientific Pluralism: 26–41, Minnesota UP: London.

Gu ZH, Wang B, Kou ZZ, Bai Y, Chen T, Dong YL, Li H, Li YQ (2017) Endomorphins: Promising Endogenous Opioid Peptides for the Development of Novel Analgesics. *Neurosignals*;25(1):98-116.

## H

Harlan, R.E., Shivers, B.D., Romano, G.J., Howells, R.D., and Pfaff, D.W. (1987) Localization of preproenkephalin mRNA in the rat brain and spinal cord by in situ hybridization. *J. Comp. Neurol.* 258, 159–184.

Hashmi, JA, Marwan N. Baliki, Lejian Huang, Alex T. Baria, Souraya Torbey, Kristina M. Hermann, Thomas J. Schnitzer & A. Vania Apkarian (2013) Shape shifting pain: chronification of back pain shifts brain representation from nociceptive to emotional circuits, *Brain* 136; 2751–2768 doi:10.1093/brain/awt211

Heap LA, Vanwalleghem GC, Thompson AW, Favre-Bulle I, Rubinsztein-Dunlop H, Scott EK (2018) Hypothalamic Projections to the Optic Tectum in Larval Zebrafish, *Front Neuroanat* 11:135. <https://www.frontiersin.org/article/10.3389/fnana.2017.00135>.

Henry MS, Gendron L, Tremblay ME, Drolet G (2017) Enkephalins: Endogenous Analgesics with an Emerging Role in Stress Resilience, *Neural Plasticity*: 1546125. doi:10.1155/2017/1546125. PMC 5525068 PMID 28781901.

## I

## J

Jin Y, Kong J (2016) Transcutaneous Vagus Nerve Stimulation: A Promising Method for Treatment of Autism Spectrum Disorders. *Front Neurosci* 10:609.

## K

Karatsoreos IN, McEwen BS (2011) Psychobiological allostasis: resistance, resilience and vulnerability, *Trends Cogn Sci.* 2011 Dec; 15(12):576-84.

Kisseleva T, Brenner DA (2008) Mechanisms of fibrogenesis, *Exp Biol Med* 233(2):109–22. doi: 10.3181/0707-MR-190.

Kobayashi S, Okazawa M, Hori A, Matsuura K, Hosokawa H (2006) Paradigm shift in sensory system - Animals do not have sensors. *Journal of Thermal Biology.* ;31(1–2):19–23. doi: 10.1016/J.jtherbio.2005.11.011.

Komi, Daniel Elieh Ali; Rambasek, Todd; Wöhrle, Stefan (2017) Mastocytosis: from a Molecular Point of View, *Clin Rev Allergy Immunol* 54 (3): 397–411.

Krashes, M.J., Shah, B.P., Madara, J.C., Olson, D.P., Strohlic, D.E., Garfield, A.S., Vong, L., Pei, H., Watabe-Uchida, M., Uchida, N., et al. (2014) An excitatory paraventricular nucleus to AgRP neuron circuit that drives hunger. *Nature* 507, 238–242.

## L

Lindquist KA, Wager TD, Kober H, Bliss-Moreau E, Barrett LF (2012) The brain basis of emotion: a meta-analytic review. *Behav Brain Sci*; 35: 121–43.

Liu, T., Li, J., Liu, H., Wang, X., Fan, F., Zhang, P., Tu, Y., and Zhang, Y. (2015) The coexistence of VGluT2 and neurotensin or leu-enkephalin in the medullary dorsal horn: a confocal and electron microscopic immunohistochemical study in the rat. *Neurosci. Lett.* 584, 390–394.

Lynn, B (1994) The fibre composition of cutaneous nerves and the classification and response properties of cutaneous afferents, with particular reference to nociception, *Pain Rev.* 1 172 – 183.

## M

Mar, L., Yang, F.C., & Ma, Q. (2012). Genetic marking and characterization of Tac2-expressing neurons in the central and peripheral nervous system. *Mol. Brain* 5, 3.

Marmigère, F, Andreas Montelius, Michael Wegner, Yoram Groner, Louis F Reichardt & Patrik Ernfors (2006) The Runx1/AML1 transcription factor selectively regulates development and survival of TrkA nociceptive sensory neurons, *Nature Neuroscience* 9, 180–187.

Marshall R, Taylor I, Lahr C, Abell TL, Espinoza I, Gupta NK, Gomez CR (2015) Bioelectrical Stimulation for the Reduction of Inflammation in Inflammatory Bowel Disease. *Clin Med Insights Gastroenterol* 8:55-9.

Melzack, R (1961) The perception of pain, *Sci Am* 204:197-210.

Melzack, R & Wall, PD (1962) On the nature of cutaneous sensory mechanisms. *Brain*, 85: 331-356.

—(1965) Pain mechanisms: a new theory. *Science*, 150: 971-979.

Murinson BB1, Griffin JW.J (2004) C-fiber structure varies with location in peripheral nerve, *Neuropathol Exp Neurol* 63(3):246-54.

## N

## O

Orr JM, Weissman DH (2009) Anterior cingulate cortex makes 2 contributions to minimizing distraction. *Cereb Cortex* 2:703–11.

## P

Patel, T, Alana Jackman, Frank L Rice, Jan Kucera, William D Snider (2000) Development of Sensory Neurons in the Absence of NGF/TrkA Signaling In Vivo, *Neuron* 25, Issue 2, p345–357. [https://doi.org/10.1016/S0896-6273\(00\)80899-5](https://doi.org/10.1016/S0896-6273(00)80899-5)

Peters, A, McEwen BS (2012) Introduction for the allostatic load special issue, *Physiol Behav* 12; 106(1):1-4.

Pezard L & Nandrino JL. (2001) Dynamic paradigm in psychopathology: “chaos theory”, from physics to psychiatry, *Encephale* 27(3):260-8.

Posner MI, DiGirolamo GJ (2000) Attention in cognitive neuroscience, Gazzaniga MS, (ed.) *New cognitive neurosciences*, 623–631, 2nd ed. MIT Press: Cambridge.

## Q

## R

Ramsay, DS & Woods, CS (2014) Clarifying the Roles of Homeostasis and Allostasis in Physiological Regulation, *Psychol Rev* 121(2): 225–247. doi: 10.1037/a0035942

Ranft, K; Dobrowolny, H; Krell, D; Bielau, H;



Bogerts, B; Bernstein, HG (2010) Evidence for structural abnormalities of the human habenular complex in affective disorders but not in schizophrenia, *Psychol. Med.* 40 (4): 557–67. doi:10.1017/S0033291709990821. PMID 19671211.

Rong P, Liu J, Wang L, Liu R, Fang J, Zhao J, Zhao Y, Wang H, Vangel M, Sun S, Ben H, Park J, Li S, Meng H, Zhu B, Kong J (2016) Effect of transcutaneous auricular vagus nerve stimulation on major depressive disorder: A nonrandomized controlled pilot study, *J Affect Disord.* 195():172-9.

Rossi, J., Balthasar, N., Olson, D., Scott, M., Berglund, E., Lee, C.E., Choi, M.J., Lauzon, D., Lowell, B.B., & Elmquist, J.K. (2011) Melanocortin-4 receptors expressed by cholinergic neurons regulate energy balance and glucose homeostasis. *Cell Metab.* 13, 195–204.

Roy M, Shohamy D, Wager TD (2012) Ventromedial prefrontal-subcortical systems and the generation of affective meaning. *Trends Cogn Sci*; 16: 147–56.

## S

Saito N, Shirai Y (2002) Protein kinase C gamma (PKC gamma): function of neuron specific isotype, *J Biochem* 132(5):683-7.

Sardell, T.C., Polgár, E., Garzillo, F., Furuta, T., Kaneko, T., Watanabe, M., & Todd, A.J. (2011) Dynorphin is expressed primarily by GABAergic neurons that contain galanin in the rat dorsal horn. *Mol. Pain* 7, 76.

Schreiter, A., Gore, C., Labuz, D., Fournie-Zaluski, M.C., Roques, B.P., Stein, C., and Machelska, H. (2012) Pain inhibition by blocking leukocytic and neuronal opioid peptidases in peripheral inflamed tissue. *FASEB J.* 26, 5161–5171.

Serafini, G; Howland, RH; Rovedi, F; Girardi, P; Amore, M ( 2017) The Role of Ketamine in Treatment-Resistant Depression: A Systematic Review, *Current Neuropharmacology.* 12 (5): 444–461. doi:10.2174/157015

9X12666140619204251. ISSN 1570-159X. PMC 4243034. Archived from the original on 19 April 2017.

Sneddon, LU, Braithwaite, VA, & Gentle, MJ (2003), Do fish have nociceptors: evidence for the evolution of a vertebrate sensory system, *Proc. R. Soc. Lond.*, B 270: 1115–1122.

Sneddon, L (2004) Evolution of nociception in vertebrates: comparative analysis of lower vertebrates, *Brain Research Reviews* 46 (2004) 123–130. doi:10.1016/j.brainres-rev.2004.07.007

Snow, PJ, Renshaw, GMC & Hamlin KE (1996) Localization of enkephalin immunoreactivity in the spinal cord of the long-tailed ray *Himantura fai*, *J. Comp. Neurol.* 367: 264 – 273.

Sporns O, Chialvo DR, Kaiser M, Hilgetag CC (2004) Organization, development and function of complex brain networks. *Trends Cogn Sci*; 8: 418–25.

Sterling P (2004) Principles of Allostasis: Optimal Design, Predictive Regulation, Pathophysiology, and Rational Therapeutics, Schulkin J (ed.) *Allostasis, homeostasis and the costs of physiological adaptation*, 17–64: Cambridge UP: NY.

Straube, A, Ellrich J, Eren O, Blum B, Ruscheweyh R (2015) Treatment of chronic migraine with transcutaneous stimulation of the auricular branch of the vagal nerve (auricular t-VNS): a randomized, monocentric clinical trial, *J Headache Pain* 16:543.

Shuohao Sun, Qian Xu, Changxiong Guo, Yun Guan, Qin Liu, & Xinzhong Dong (2017) Leaky Gate Model: Intensity-Dependent Coding of Pain and Itch in the Spinal Cord, *Neuron* 93, 840–85. <http://dx.doi.org/10.1016/j.neuron.2017.01.012>

## T

Todd, AJ (2002) Anatomy of primary afferents and projection neurones in the rat spinal dorsal horn with particular emphasis on substance P and the neurokinin 1 receptor. *Exp. Physiol.* 87, 245–249.

—(2011) Dynorphin is expressed primarily by GABAergic neurons that contain galanin in the rat dorsal horn. *Mol. Pain* 7, 76.

## U

## V

Valet M, Sprenger T, Boecker H, Willloch F, Rummeny E, Conrad B, Erhard P, Tolle TR. (2004) Distraction modulates connectivity of the cingulo-frontal cortex and the mid-brain during pain—an fMRI analysis. *Pain* 109:399–408.

Villemure, C & Bushnell, MC (2002) Cognitive modulation of pain: how do attention and emotion influence pain processing? *Pain* 95:195–9.

van Fraassen, BC (1994) Interpretation of Science; Science as Interpretation, J. Hildevoord (ed.) *Physics and our view of the world*, 169-187. Cambridge UP: Cambridge.

— (1997) Structure and Perspective: Philosophical Perplexity and Paradox, M.L. Dalla Chiara (eds.) *Logic and Scientific Methods*, 511-530, Kluwer Academic Publishers, Netherlands.

— (2002) *The Empirical Stance*. Yale UP: New Haven

— (2008) *Scientific Representation: Paradoxes of Perspective*. Oxford UP, NY

## W

Wall, PD (1960) Cord cells responding to touch, damage and temperature skin, *J Neurophysiol* 23: 197-210.

— (1979) On the relation of injury to pain. The John J. Bonica lecture. *Pain* 6:253–264.

Weinberg, S (2001) *Can science explain everything? Anything?*, NY Rev Books: 50.

Weise D, Adamidis M, Pizzolato F, Rumpf JJ, Fricke C, Classen (2015) Assessment of brainstem function with auricular branch of vagus nerve stimulation in Parkinson's disease, *JPLoS One*. 2015; 10(4):e0120786.

Willenbring, S & Stevens,, CW (1996) Thermal, mechanical and chemical peripheral sensation in amphibians: opioid and adrenergic effects, *Life Sci*. 58:125 – 133.

## X

## Y

Yasaka, T., Tiong, S.Y., Hughes, D.I., Ridde-ll, J.S., & Todd, A.J. (2010) Populations of inhibitory and excitatory interneurons in lamina II of the adult rat spinal dorsal horn revealed by a combined electrophysiological and anatomical approach. *Pain* 151, 475–488.

Yizhar, O., Fenno, L.E., Davidson, T.J., Mogri, M., and Deisseroth, K. (2011). Optogenetics in neural systems. *Neuron* 71, 9–34.

## Z

A

- Allen, L. B., Tsao, J. C. I., Seidman, L. C., Ehrenreich-May, J., & Zeltzer, L. K. (2012) A Unified, Transdiagnostic Treatment for Adolescents With Chronic Pain and Comorbid Anxiety and Depression. *Cognitive and Behavioral Practice*, 19(1), 56-67. doi:10.1016/j.cbpra.2011.04.007
- Angold A, Costello EJ, Erkanli A (1999) Comorbidity. *J Child Psychol Psychiatry* 40(1):57-87.
- Anjum, RL, Samantha Copeland, Stephen Mumford & Elena Rocca (2015) CauseHealth: integrating philosophical perspectives into personcentered healthcare, *European Journal for Person Centered Healthcare* 3 Issue 4 pp 427-430
- Aragona, M (2009a) About and beyond comorbidity: Does the crisis of the DSM bring on a radical rethinking of descriptive psychopathology? *PPP*;16:29-33.
- (2009b) The concept of mental disorder and the DSM- V. *Dial Phil Ment Neuro Sci* 2:1-14.
- (2009c) The role of comorbidity in the crisis of the current psychiatric classification system. *PPP*16:1- 11.
- Asmundson, G. J., & Katz, J. (2009) Understanding the co-occurrence of anxiety disorders and chronic pain: state-of-the-art. *Depression and anxiety*, 26(10), 888-901. doi:10.1002/da.20600

B

- Ballerini, A (1997) *La Diagnose in Psiquiatria*, La Nuova Italia Scientifica: Rome.
- Barsevick, AM (2007) The elusive concept of the symptom cluster. *Oncology Nursing Forum*; 34:971-980.

- Bechtel, W & Richardson, RC (1993) *Discovering Complexity*, Princeton UP: Princeton.
- Booth, A (2006) Brimful of STARLITE: toward standards for reporting literature searches. *J Med Libr Assoc.* 94(4):421-9, e205.
- Borsboom D, Cramer AOJ, Schmittmann VD, Epskamp S, Waldorp LJ (2011) The small world of psychopathology. *PLoS ONE*;6: 1-11.
- Boyd, JH & Burke, JD (1984): Exclusion criteria of DSM-III: a study of co-occurrence of hierarchy-free syndromes. *Arch Gen Psychiatry*; 41:983-989.
- Breivik, H., Collett, B., Ventafridda, V., Cohen, R., & Gallacher, D. (2006) Survey of chronic pain in Europe: Prevalence, impact on daily life, and treatment. *European Journal of Pain*, 10(4), 287-333. doi:10.1016/j.ejpain. 06.009
- Bullis, J. R., Fortune, M. R., Farchione, T. J., & Barlow, D. H. (2014) A preliminary investigation of the long-term outcome of the Unified Protocol for Transdiagnostic Treatment of Emotional Disorders, *Comprehensive psychiatry*, 55(8), 1920-1927. doi:10.1016/j.comppsy.2014.07.016
- Burke, A. L., Mathias, J. L., & Denson, L. A. (2015) Psychological functioning of people living with chronic pain: A meta-analytic review. *British Journal of Clinical Psychology*, 54(3), 345-360.
- Busch V, Haas J, Cronlein T, Pieh C, Geisler P, Hajak G, Eichhammer P (2012) Sleep deprivation in chronic somatoform pain-effects on mood and pain regulation. *Psychiatry Res* 195:134-43.

C

- Cardeña, A (2018) Perspectivas sobre el Diagnóstico Neuropsiquiátrico Personalizado como Práctica Científica, *Actas del IV Congreso Iberoamericano de Filosofía de la Ciencia y la Tecnología*, CIFICyT 2017: Universidad de Salamanca.

Collishaw, S. (2015) Annual research review: secular trends in child and adolescent mental health. *Journal of Child Psychology and Psychiatry*, 56(3), 370-393.

Cowan WM, Kandel ER (2001): Prospects for neurology and psychiatry. *JAMA* 2001; 285:594–600

Cox, B. J., Fleet, C., & Stein, M. B. (2004) Self-criticism and social phobia in the US national comorbidity survey. *Journal of Affective Disorders*, 82(2), 227-234.

Craig, J. (2008) Complex diseases: research and applications. *Nature Education* 1, 184.

Cramer AOJ, Waldorp LJ, van der Maas HLJ, Borsboom D. Comorbidity: A network perspective. *Behav Brain Sci* 2010; 33:137-193.

## D

Darden, L (2006) *Reasoning in Biological Discoveries*, Cambridge UP: Cambridge.

de Groot V, Beckerman H, Lankhorst GJ & Bouter LM: How to measure comorbidity: a critical review of available method. *Journal of Clinical Epidemiology* 2003; 56:221-229.

Dodd MJ, Miaskowski C, Paul S (2001) Symptom clusters and their effect on the functional status of patients with cancer, *Oncology Nursing Forum* 28:465–470.

Dupré, J (1981) Natural kinds and biological taxa, *Philosophical Review* 90: 66-90.

## E

Eriksen, T.E., Kerry, R., Mumford, S., Lie, S.A.N. & Anjum, R.L. (2013) At the border of medical reasoning: the aetiological and ontological challenges of medically unexplained symptoms, *Philosophy, Ethics and Humanities in Medicine* 8, 1-11.

## F

Feger, H (2001) Classification: Conceptions in the social sciences. *International Encyclopedia of the Social & Behavioral Sciences* 3:1966-1973.

Feighner, J; Eli Robins, Samuel B. Guze, Eobert A. Woodruff Jr, George Winokur & Rodrigo Mum (1972) Diagnostic Criteria for Psychiatric Research, *Gen Psychiat* 26: 57-63

Feinstein, AR (1967) *Clinical Judgment*. Huntington, NY: Robert E. Krieger.

— (1970) The pre-therapeutic classification of comorbidity in chronic disease, *Journal of Chronic Diseases* 1970; 23:455-468.

Finan PH, Goodin BR, Smith MT (2013) The association of sleep and pain: an update and a path forward. *J Pain*;14:1539–52.

Fishbain DA (2007) The psychiatric and psychological evaluation of the chronic pain patient: an algorithmic approach, Slippman CW (ed.) *Interventional spine: an algorithmic approach*, 105–112. Philadelphia, Elsevier.

Fishbain DA, Bruns D, Disorbio J, et al (2010) Exploration of the illness uncertainty concept in acute and chronic pain patients vs community patients, *Pain* 11:658–689.

Fishbain D1, Gao JR, Lewis J, Bruns D, Meyer LJ, Disorbio JM (2014) Examination of symptom clusters in acute and chronic pain patients. *Pain Physician* 17(3):E349-57.

Forgeron, P. A., King, S., Stinson, J. N., McGrath, P. J., MacDonald, A. J., & Chambers, C. T. (2010) Social functioning and peer relationships in children and adolescents with chronic pain: A systematic review. *Pain Research and Management*, 15(1), 27-41.

## G

Gaebel W, Zielasek J (2011) Experience with ICD-10 in Europe and scientific eviden-

- ce for new aspects of ICD-11 from German-language publications. *Eur Psychiatry*;26:6- 10.
- Gadernann, A. M., Alonso, J., Vilagut, G., Zaslavsky, A. M., & Kessler, R. C. (2012) Comorbidity and disease burden in the national comorbidity survey replication (NCS-R). *Depression and anxiety*, 29(9), 797-806. doi:10.1002/da.21924
- Goffman, E (1968) *Stigma: Notes on the Management of Spoiled Identity*, Pelican: London.
- Goldberg, D (2011) The need for a special classification of mental disorders for general medical practice: towards ICD11 – Primary Care. *European Psychiatry*: 26:53-56.
- Gustafsson, M., Ekholm, J., & Ohman, A. (2004) From shame to respect: musculoskeletal pain patients' experience of a rehabilitation programme, a qualitative study. *Journal of Rehabilitation Medicine*, 36(3), 97-103.
- Grenon P, Smith B, Goldberg L (2004) Biodynamic ontology: applying BFO in the biomedical domain. *Stud Health Technol Inform*, 102:20–38.
- Grumbach, K (2003) Chronic illness, comorbidities, and the need for medical generalism. *Annals of Family medicine*; 1:4-7.
- H
- Hacking, I (1986) Making up people, Heller, T (ed.) (1986) *Reconstructing Individualism: Autonomy, Individuality in Self Investigation Thought*: 161-171, Stanford UP: Stanford.
- (1995) The looping effects of human kinds, Sperber, D & Premack, AJ (eds) *Causal Cognition*, 351-383, Oxford UP: Oxford.
- (2002) *Historical Ontology*, Harper U P: London
- Haraway, DJ (1976) *Crystals, Frabrics, and Fields: Metaphors that Shape Embryos*, Yale UP: New Haven
- Hauser W, Schmutzer G, Brahler E, Glaesmer H. A (2009) cluster within the continuum of biopsychosocial distress can be labeled “fibromyalgia syndrome”- evidence from a representative German population survey. *Journal of Rheumatology* 36:2806-2812.
- Helmreich, S (2016) *Sounding the Limits of Life*, Princeton UP: Princeton.
- Heningerl, GR (1990) A biologic perspective on comorbidity of major depressive disorder and panic disorder, Maser JD, Cloninger CR. (eds) *Comorbidity of Mood and Anxiety Disorders*, 381-401. American Psychiatric Press, Washington DC.
- Heylighen, F (2000) Evolutionary transitions: how do levels of complexity emerge?, *Complexity* 6: 53–57.
- Hickey, S & Roberts, H (2011) *Tarnished Gold: The Sickness of Evidence-based Medicine*, CreateSpace, NP.
- Hoehndorf R, Kelso J, Herré H (2009) The ontology of biological sequences. *BMC Bioinformatics* 18;10:377.
- I
- Iqbal, SA, Wallach, JD, Khoury, MJ, Schully, SD & Io- annidis, JP (2016) Reproducible research practices and transparency across the biomedical literature, *PLoS Biology* 14: e1002333.
- J
- Jakovljević, M (2008) Integrating brave new psychiatry of the person, for the person, by the person and with the person: The postmodern turn. *Psychiatr Danub* 20:2-5.
- Jakovljević, M & Ostojčić, L (2013) Comorbidity and multimorbidity in medicine today, *Medicina Academica Mostariensia* 1,1,18-28
- Jakovljević, M & Crnčević (2012) Comorbidity as an epistemological challenge to modern psychiatry *DIAL PHIL MENT NEURO SCI* 2012; 5(1): 1-13

Johansson, I; Smith, B; Munn, K; Tsikolia, N; Elsner, K; Ernst, D; & Siebert, D (2005) Functional anatomy: a taxonomic proposal, *Acta Biotheoretica* 53(3): 153–166.

## K

Kaplan, MH, Feinstein AR (1974) The importance of classifying initial co-morbidity in evaluating the outcome of diabetes mellitus. *J Chronic Dis* 27(7-8):387-404.

Kaplan RM, Ong M (2007) Rationale and public health implications of changing CHD risk factor definitions, *Annu Rev Public Health* 28:321-344.

Kato K, Sullivan PF, Evengard B, Pedersen NL. (2006) Chronic widespread pain and its comorbidities: A population-based study. *Archives of Internal Medicine* 166:1659-1654.

Kessels, Roy P. C.; Kortrijk, Hans E.; Wester, Arie J.; Nys, Gudrun M. S. (2008) Confabulation behavior and false memories in Korsakoff's syndrome: Role of source memory and executive functioning, *Psychiatry and Clinical Neurosciences*. 62 (2): 220–5. doi:10.1111/j.1440-1819.2008.01758.x. PMID 18412846.

Klabunde CN, Potosky AL, Legler JM, Warren JL (2000) Development of a comorbidity index using physician claims data. *J Clin Epidemiol* 53(12):1258-1267.

Klinkman, M & van Weel, C (2011) Prospects for person-centred diagnosis in general medicine, *Journal of Evaluation in Clinical Practice* 17: 365–370

Koch, C & Laurent G (1999) Complexity and the nervous system. *Science*; 284:96–98

Krueger RE, Markon KE (2006) Reinterpreting comorbidity: A model based approach to understanding and classifying psychopathology. *Ann Rev Clin Psychol* 2:111-33

## L

Lallukka T, Overland S, Haaramo P, Saastamoinen P, Bjorvatn B, Sivertsen B (2014) The joint contribution of pain and insomnia to sickness absence and disability retirement: a register-linkage study among Norwegian and Finnish employees. *Eur J Pain* 18:883–92.

Lavori PW (1990) Double diagnosis: The role of the prior odds on each disorder. In: Maser JD, Cloninger CR. (eds) *Comorbidity of Mood and Anxiety Disorders*, 681-692. American Psychiatric Press, Washington DC.

Lilienfeld, SO & Marino, L (1999) Essentialism revisited: Evolutionary theory and the concept of mental disorder, *Journal of Abnormal Psychology* 108: 400-411.

Linton, SJ (2013) A Transdiagnostic Approach to Pain and Emotion, *Journal of Applied Biobehavioral Research* 18(2), 82-103. doi:10.1111/jabr.12007

## M

MacMahon, JA; Phillips, DL; Robinson, JV & Schimpf, DJ (1978) Levels of biological organization: an organism-centered approach, *Bioscience* 28: 700–704.

Maj, M (2005) Psychiatric comorbidity: an artifact of current diagnostic systems? *Br J Psychiatry*;186:182-184.

Mansell, W., Harvey, A., Watkins, E., & Shafan, R. (2009) Conceptual foundations of the transdiagnostic approach to CBT. *Journal of Cognitive Psychotherapy* 23(1), 6-19.

Martin, J (2002) The Integration of Neurology, Psychiatry, and Neuroscience in the 21st Century, *Am J Psychiatry* 159:5

Masuya, H & Mizoguchi, R (2012) An Ontology of Gene, *Proceedings of the 3rd International Conference on Biomedical Ontology*: 897-903.

McWilliams LA, Goodwin RD, Cox BJ (2004) Depression and anxiety associated with three pain conditions: results from a nationally representative sample, *Pain* 111:77–83.

- Mezzich JE & Salloum IM (2008) Clinical complexity and person-centered integrative diagnosis. *World Psychiatry*; 7:1-2.
- Monti JM, Monti D (2007) The involvement of dopamine in the modulation of sleep and waking. *Sleep Med Rev*;11:113–33.
- Morton, T (2013) *Hyperobjects. Philosophy and Ecology after the End of the World*, Minnesota UP: Minneapolis.
- Mumford, S & Anjum, RL (2011) *Getting Causes from Powers*. Oxford UP: Oxford.
- Murberg, T. A., & Bru, E. (2004) School-related stress and psychosomatic symptoms among Norwegian adolescents. *School psychology international*, 25(3), 317-332.
- Musalek, M & Schebenbogen, O (2008) From categorical to dimensional diagnostics: deficiency-oriented vs person-centered diagnostics, *Eur Arch Psychiatry Clin Neurosci* 258:18–21.
- N
- O
- O'Brien, E. M., Atchison, J. W., Gremillion, H. A., Waxenberg, L. B., & Robinson, M. E. (2008) Somatic focus/awareness: Relationship to negative affect and pain in chronic pain patients, *European Journal of Pain* 12(1), 104-115. doi:10.1016/j.ejpain.2007.04.001
- O'Brien EM, Waxenberg LB, Atchison JW, Gremillion HA, Staud RM, McCrae CS, Robinson ME (2010) Negative mood mediates the effect of poor sleep on pain among chronic pain patients. *Clin J pain* 26:310–19.
- Oschman, J (2003) *Energetic Medicine in Therapeutics and Human Performance*. Butterworth-Heinemann, ElsevierScience.
- P
- Piccirillo JF, Feinstein AR (1996) Clinical symptoms and comorbidity: significance for the prognostic classification of cancer. *Cancer* 77(5):834-842.
- Q
- R
- Ritchie C (2007) Health care quality and multimorbidity: the jury is still out, *Med Care* 45(6):477-479.
- Roehrs T, Hyde M, Blaisdell B, Greenwald M, Roth T (2006) Sleep loss and REM sleep loss are hyperalgesic. *Sleep* 29:145–51.
- S
- Sawicka M, Osuchowska A, Waniek J, Kosznik K, Meder J (2009) The phenomenon of dual diagnosis in the light of attachment theory - a case study. *Arch Psychiatr Psychother* 4:57-64.
- Schaefer I, von Leitner EC, Schoen G, Koller D, Hansen H, Kolonko T, Kaduszkiewicz H, Wegscheider K, Glaeske G, van den Busche H (2010) Multimorbidity patterns in the elderly: A new approach of disease clustering identifies complex interrelations between chronic conditions. *PLoS One*; 5:1-10. e15941.
- Schuh-Hofer S, Wodarski R, Pfau DB, Caspani O, Magerl W, Kennedy JD, Treede RD (2013) One night of total sleep deprivation promotes a state of generalized hyperalgesia: a surrogate pain model to study the relationship of insomnia and pain, *Pain* 154:1613–21.
- Schulz, S; Brochhausen, M; Hoehndorf, R (2011) Higgs Bosons, Mars Missions, and Unicorn Delusions: How to Deal with Terms of Dubious Reference in Scientific Ontologies, *Proceedings of the 2nd International Conference on Biomedical Ontology* 183-189.
- Schwenk, TL (1999) The tyranny of names in mental health care, *Journal of the American Board of Family Practice* 12 (1): 99–101.
- Shamliyan, T, Kane, R.L. & Jansen, S. (2010) «Quality of systematic reviews of observational nontherapeutic studies, *Preventing Chronic Disease* 7 (6): A133.

Starfield, B (2006) Threads and yarns: Weaving the tapestry of comorbidity. *Annals of Family Medicine* 4:101-103.

Strakowski SM, Keck PE Jr, McElroy SL, Lonczak HS, West SA (1995) Chronology of comorbid and principal syndromes in first-episode psychosis. *Compr Psychiatry* 36:106-112.

Sutherland, R., & Morley, S. (2008) Self-pain enmeshment: future possible selves, socio-tropy, autonomy and adjustment to chronic pain, *Pain* 137(2), 366-377.

## T

Taylor AW, Price K, Gill TK, Adams R, Pilkington R, Carrangis N, Shi Z & Wilson D (2010) Multimorbidity – not just an older person’s issue. Result from an Australian biomedical study. *BMC Public Health* 10:718. <http://www.biomedcentral.com/1471-2458/10/718>

Tegethoff, M., Belardi, A., Stalujanis, E., & Meinschmidt, G. (2015) Comorbidity of mental disorders and chronic pain: chronology of onset in adolescents of a national representative cohort. *The Journal of Pain*, 16(10), 1054-1064.

Thagard, P (1999) *How Scientists Explain Disease*. Princeton UP: NJ.

Thomson, Allan D.; Cook, Christopher C. H.; Guerrini, Irene; Sheedy, Donna; Harper, Clive; Marshall, E. Jane (2008) Wernicke encephalopathy revisited: Translation of the case history section of the original manuscript by Carl Wernicke ‘Lehrbuch der Gehirnkrankheiten für Aerzte und Studierende’ (1881) with a commentary, *Alcohol and Alcoholism*. 43 (2): 174–9. doi:10.1093/alcalc/agm144. PMID 18056751.

## U

## V

Valderas JM, Starfield B, Sibbald B, Salisbury C & Roland M (2009) Defining comorbidity: Implications for understanding health and health services, *Ann Fam Med* 7:357-363.

van Praag HM (1993) “*Make-believes*” in *psychiatry or the perils of progress*. Brunner/Mazel Publishers: NY.

## W

Wong, W. S., Lam, H. M. J., Chen, P. P., Chow, Y. F., Wong, S., Lim, H. S, Fielding, R. (2015) The Fear-Avoidance Model of Chronic Pain: Assessing the Role of Neuroticism and Negative Affect in Pain Catastrophizing Using Structural Equation Modeling, *International Journal of Behavioral Medicine*, 22(1), 118-131. doi:10.1007/s12529-014-9413-7

Wurm, M (2018) *Understanding Comorbid Pain and Emotions: A transdiagnostic approach*. PhD Dissertation, Örebro University, Sweden.

## X

## Y

Yamagata, Y; Kou, H; Kozaki, K; Imai, T; Ohe, K & Mizoguchi, R (2013) Ontological model of abnormal states and its application in the medical domain, *4th International Conference on Biomedical Ontology* 28–33. ICBO2013: Montreal.

## Z



A

Aloisi AM, Berlincioni V, Torta R, et al. (2016) The role of gender, psycho-social factors and anthropological-cultural dimensions on pain in neurorehabilitation. Evidence and recommendations from the Italian Consensus Conference on Pain in Neurorehabilitation. *Eur J Phys Rehabil Med* 52(5):730–40.

Asmundson GJ, Coons MJ, Taylor S, Katz J (2002) PTSD and the experience of pain: research and clinical implications of shared vulnerability and mutual maintenance models. *Can J Psychiatry* 47(10):930–937.

Asmundson, G. J., & Katz, J. (2009). Understanding the co-occurrence of anxiety disorders and chronic pain: state-of-the-art. *Depression and anxiety*, 26(10), 888-901. doi:10.1002/da.20600

B

Baake, V.; Reijntjes, R. H. A. M.; Dumas, E. M.; Thompson, J. C.; Roos, R. A. C.; Roos, R. A. C (2017) Cognitive decline in Huntington’s disease expansion gene carriers. *Cortex*; 95: 51–62, doi:10.1016/j.cortex.2017.07.017.

Bair MJ, Robinson RL, Katon W, et al (2003): Depression and pain comorbidity: a literature review, *Archives of Internal Medicine* 163:2433–2445.

Bair, M. J., Poleshuck, E. L., Wu, J., Krebs, E. K., Damush, T. M., Tu, W., & Kroenke, K. (2013) Anxiety but Not Social Stressors Predict 12- Month Depression and Pain Severity. *The clinical Journal of Pain*, 29(2), 95-101. doi:10.1097/AJP.0b013e3182652ee9

Baudino, B., D’agata, F., Caroppo, P., Castellano, G., Cauda, S., Manfredi, M., et al. (2012) The chemotherapy long-term effect on cognitive functions and brain metabolism in lymphoma patients. *Q. J. Nucl. Med. Mol. Imaging* 56, 559–568.

Beiske AG, Loge JH, Ronningen A, Svensson E (2009) Pain in Parkinson’s disease: Prevalence and characteristics, *Pain* 141: 173–7.

Berridge KC, Robinson TE (2003) Parsing reward. *Trends Neurosci* 26:507–513.

Block BM, Wu CL. (2001) Pain and sleep. *Int J Pain Med Palliat Care* 1:56–61.

Blum K, Chen AL, Chen TJ, Braverman ER, Reinking J, Blum SH, Cassel K, Downs BW, Waite RL, Williams L, Prihoda TJ, Kerner MM, Palomo T, Comings DE, Tung H, Rhoades P, Oscar-Berman M (2008) Activation instead of blocking mesolimbic dopaminergic reward circuitry is a preferred modality in the long term treatment of reward deficiency syndrome (RDS), *Theor Biol Med Model* 5:24

Boly M, Coleman MR, Davis MH, Hampshire A, Bor D, Moonen G, et al. (2007) When thoughts become action: an fMRI paradigm to study volitional brain activity in non-communicative brain injured patients. *Neuroimage* 36: 979–92.

Bondy, B., Baghai, T. C., Minov, C., Schüle, C., Schwarz, M. J., Zwanzger, P., et al. (2003) Substance P serum levels are increased in major depression: preliminary results. *Biol. Psychiatry* 53, 538–542. doi: 10.1016/s0006-3223(02)01544-5

Booij, L., Van der Does, A. J. W., & Riedel, W. J. (2003) Monoamine depletion in psychiatric and healthy populations, *Mol. Psychiatry* 8, 951–973. doi: 10. 1038/sj.mp.4001423

Borsook D, Becerra L, Carlezon WA Jr, et al. (2007) Reward-aversion circuitry in analgesia and pain: implications for psychiatric disorders. *Eur J Pain*. 11(1):7–20.

Boscarino JA, Rukstalis M, Hoffman SN, et al (2010) Risk factors for drug dependence among out-patients on opioid therapy in a large US health-care system. *Addiction* 105(10):1776–1782.

Bourke, J (2003) Fear and Anxiety: Writing about Emotion in Modern History, *History Workshop Journal*, 55,1,1:111–133, https://doi.org/10.1093/hwj/55.1.111

- Breivik, H., Collett, B., Ventafridda, V., Cohen, R., & Gallacher, D. (2006) Survey of chronic pain in Europe: Prevalence, impact on daily life, and treatment. *European Journal of Pain*, 10(4), 287-333. doi:10.1016/j.ejpain.2005.06.009
- Brochet B, Deloire MS, Ouallet JC, et al (2009) Pain and quality of life in the early stages after multiple sclerosis diagnosis: a 2-year longitudinal study, *Clin J Pain*. 25(3):211–7.
- Bruehl S, Chung OY, Burns JW (2006) Anger expression and pain: an overview of findings and possible mechanisms. *J. Behav. Med*;29:593–606.
- Bruehl S, Burns JW, Chung OY, Quartana P. (2008) Anger management style and emotional reactivity to noxious stimuli among chronic pain patients and healthy controls: the role of endogenous opioids, *Health Psychol* 27:204–214.
- Bullis, J. R., Fortune, M. R., Farchione, T. J., & Barlow, D. H. (2014) A preliminary investigation of the long-term outcome of the Unified Protocol for Transdiagnostic Treatment of Emotional Disorders, *Comprehensive psychiatry*, 55(8), 1920-1927. doi:10.1016/j.comppsy.2014.07.016
- Burke, A. L., Mathias, J. L., & Denson, L. A. (2015) Psychological functioning of people living with chronic pain: A meta-analytic review. *British Journal of Clinical Psychology*, 54(3), 345-360.
- Busch V, Haas J, Cronlein T, Pieh C, Geisler P, Hajak G, Eichhammer P (2012) Sleep deprivation in chronic somatoform pain-effects on mood and pain regulation. *Psychiatry Res* 195:134–43.
- C
- Carballedo, A., Scheuerecker, J., Meisenzahl, E., Schoepf, V., Bokde, A., Möller, H. J., et al. (2011) Functional connectivity of emotional processing in depression. *J. Affect. Disord.* 134, 272–279. doi: 10.1016/j.jad.2011.06.021
- Cerimele JM, Chan YF, Chwastiak LA, Unutzer J (2014) Pain in primary care patients with bipolar disorder. *Gen Hosp Psychiatry* 36(2):228.
- Chapman, C. R., Tuckett, R. P., and Song, C. W. (2008) Pain and stress in a systems perspective: reciprocal neural, endocrine and immune interactions. *J. Pain* 9, 122–145. doi: 10.1016/j.jpain.2007.09.006
- Cheatle, MD (2011) Depression, chronic pain, and suicide by overdose: on the edge. *Pain Med.* 12, 2:S43–S48.
- Cheng, S.-T., T. Kwok, & L. C. W. Lam (2012) Neuropsychiatric symptom clusters of Alzheimer's disease in Hong Kong Chinese: prevalence and confirmatory factor analysis of the Neuropsychiatric Inventory, *International Psychogeriatrics* 24, 9: 1465–1473.
- Chou, K. L. (2007) Reciprocal relationship between pain and depression in older adults: evidence from the English longitudinal study of ageing. *J. Affect. Disord.* 102, 115–123. doi: 10.1016/j.jad.2006.12.013
- Clark, JD (2007) Opioid self-administration: a better way to evaluate analgesics in animal models? *Anesthesiology* 106(2):208–209.
- Cohen, JY, Haesler S, Vong L, Lowell BB, Uchida, N (2012) Neuron type-specific signals for reward and punishment in the ventral tegmental area. *Nature* 482(7383):85–8.
- Cole L, Farrell M, Duff E, Barber J, Egan G, Gibson S (2006) Pain sensitivity and fMRI pain-related brain activity in Alzheimer's disease, *Brain* 129(pt 11):2957–2965.
- Cook DB, Lange G, Ciccone DS, Liu WC, Steffener J, Natelson BH (2004) Functional imaging of pain in patients with primary fibromyalgia. *The Journal Of Rheumatology* 31:364–378.
- Cox BJ, McWilliams L (2002) Mood and anxiety disorders in relation to chronic pain: evidence from the National Comorbidity Study. *Pain Res Manag* 7A:11A.
- Cox, B. J., Fleet, C., & Stein, M. B. (2004) Self-criticism and social phobia in the US national comorbidity survey. *Journal of Affective Disorders*, 82(2), 227-234.

## D

de Felice M, Porreca F (2009) Opiate-induced persistent pronociceptive trigeminal neural adaptations: potential relevance to opiate-induced medication overuse headache. *Cephalalgia*. Dec; 29(12):1277–1284.

de Peuter S, Van Diest I, Vansteenwegen D, Van den Bergh O, Vlaeyen JW (2011) Understanding fear of pain in chronic pain: interoceptive fear conditioning as a novel approach. *Eur J Pain* 15:889–894.

Dickerson BC, Goncharova I, Sullivan MP, et al (2001) MRI-derived entorhinal hippocampal atrophy in incipient and very mild Alzheimer's disease. *Neurobiol Aging* 22(5):747–754.

Duan, B, Longzhen Cheng, Steeve Bourane, Olivier Britz, Christopher Padilla, Lidia Garcia-Campmany, Michael Krashes, Wendy Knowlton, Tomoko Velasquez, Xiangyu Ren, Sarah E. Ross, Bradford B. Lowell, Wang, Martyn Goulding, & Qiufu Mal (2014) Identification of Spinal Circuits Transmitting and Gating Mechanical Pain, *Cell* 159, 1417–1432

## E

Eaton, D.K.; Kann, L.; Jinchon, S.; Shanklin, S.; Ross, J.; Hawkins, J.; Harris, W.A.; Lowry, R.; McManus, T.; Chyen, D. (2008) Youth risk behavior surveillance—United States, 2007. *MMWR Surveill. Summ.* 57, 1–131.

Elman I, Karlsgodt KH, Gastfriend DR, Charbis CF, Breiter HC. Cocaine-primed craving and its relationship to depressive symptomatology in individuals with cocaine dependence. *J Psychopharmacol.* 2002; 16:163–167.

Elman, I, Jon-Kar Zubieta, & David Borsook (2011) The Missing “P” in Psychiatric Training: Why is it Important to Teach Pain to

Psychiatrists? *Arch Gen Psychiatry.* 2011 January ; 68(1): 12–20. doi:10.1001/archgenpsychiatry.2010.174.

Engel CC Jr, Engel AL, Campbell SJ, McFall ME, Russo J, Katon WJ (1993) Posttraumatic stress disorders symptoms and pre-combat sexual and physical abuse in Desert Storm veterans. *J Nerv Ment Dis* 181:683–8.

Engel CC, Liu X, McCarthy BD, Miller RF, Ursano R (2000) Relationship of physical symptoms to posttraumatic stress disorder among veterans seeking care for Gulf War-related health concerns. *Psychosom Med* 62:739–45.

## F

Fairhurst M, Wiech K, Dunckley P, Tracey I (2007) Anticipatory brainstem activity predicts neural processing of pain in humans. *Pain* 128: 101–110.

Farmer, M. A., Baliki, M. N., and Apkarian, A. V. (2012) A dynamic network perspective of chronic pain. *Neurosci. Lett.* 520, 197–203. doi: 10.1016/j.neulet. 2012.05.001

Finan PH, Goodin BR, Smith MT (2013) The association of sleep and pain: an update and a path forward. *J Pain* 14:1539–52.

Fiore NT & Austin PJ (2016) Are the emergence of affective disturbances in neuropathic pain states contingent on supraspinal neuroinflammation? *Brain Behav Immun* 56:397–411

Fishbain DA, Goldberg M, Meagher BR, et al (1986) Male and female chronic pain patients categorized by DSM-III psychiatric diagnostic criteria, *Pain* 26:181–197.

Fishbain, DA (2007) The psychiatric and psychological evaluation of the chronic pain patient: an algorithmic approach, Slippman CW (ed.) *Interventional spine: an algorithmic approach*, 105–112. Philadelphia, Elsevier.

Fishbain, DA, Cole B, Lewis JE, Gao J, Rosomoff RS. (2009) Do opioids induce hyperal-

- gesia in humans? An evidence-based structured review. *Pain Med.* 10(5):829–839.
- Fishbain DA, Bruns D, Disorbio J, et al (2010) Exploration of the illness uncertainty concept in acute and chronic pain patients vs community patients, *Pain* 11:658–689.
- Flaten MA, Aslaksen PM, Lyby PS, Bjørkedal E (2011) The relation of emotions to placebo responses. *Philos Trans R Soc Lond, B, Biol Sci* 366: 1818–1827.
- Finnerup NB, Attal N, Haroutounian S, et al (2015) Pharmacotherapy for neuropathic pain in adults: a systematic review and meta-analysis. *Lancet Neurol.* 14(2):162–73.
- Folstein MF, Robinson R, Folstein S, McHugh PR. (1985) Depression and neurological disorders. New treatment opportunities for elderly depressed patients. *J Affect Disord* 19 (Suppl 1): S11–4.
- Ford, B (2010) Pain in Parkinson's disease. *Mov Disord* 25 (Suppl 1): S98–103.
- Forgeron, P. A., King, S., Stinson, J. N., McGrath, P. J., MacDonald, A. J., & Chambers, C. T. (2010) Social functioning and peer relationships in children and adolescents with chronic pain: A systematic review. *Pain Research and Management* 15(1), 27-41.
- Frodl, T., Schaub, A., Banac, S., Charypar, M., Jäger, M., Kümmler, P., et al (2006) Reduced hippocampal volume correlates with executive dysfunctioning in major depression. *J. Psychiatry Neurosci.* 31, 316–323.
- G
- Gadermann, A. M., Alonso, J., Vilagut, G., Zaslavsky, A. M., & Kessler, R. C. (2012) Comorbidity and disease burden in the national comorbidity survey replication (NCS-R). *Depression and anxiety*, 29(9), 797-806. doi:10.1002/da. 21924
- George O, Koob GF. (2010) Individual Differences in Prefrontal Cortex Function and the Transition from Drug Use to Drug Dependence. *Neurosci Biobehav Rev.* NP.
- Gibson S, Voukelatos X, Ames D, Flicker L, Helme RD (2001) An examination of pain perception and cerebral event-related potentials following carbon dioxide laser stimulation in patients with Alzheimer's disease and aged-matched control volunteers, *Pain Res Manag.* 6(3):126–132.
- Giladi N, McMahon D, Przedborski S, et al (1992) Motor blocks in Parkinson's disease, *Neurology* 42:333 – 339.
- Goldenberg, DL (2010) Pain/Depression dyad: a key to a better understanding and treatment of functional somatic syndromes. *Am J Med* 123(8):675–682.
- Goldie, PL (2000) *The Emotions*, Oxford UP: Oxford.
- (2002a) Emotions, Feelings and Intentionality, *Phenomenology and the Cognitive Sciences* 1: 235-254.
- (2002b) Emotion, personality and simulation, Goldie, PL (ed.) (2002) *Understanding Emotions: Mind and Morals*, 97-109. Ashgate P: Aldershot.
- (2003) Narrative and perspective; values and appropriate emotions, Hatzimoysis, A (ed.) (2003) *Philosophy and the Emotions*, 201-220, Cambridge UP: Cambridge.
- (2004) What people will do: personality and prediction, *Richmond Journal of Philosophy* 7: 1-9.
- Gauntlett-Gilbert J, Eccleston C (2007) Disability in adolescents with chronic pain: Patterns and predictors across different domains of functioning, *Pain* 131:132–41.
- Gracely RH, Petzke F, Wolf JM, Clauw DJ. (2002) Functional magnetic resonance imaging evidence of augmented pain processing in fibromyalgia. *Arthritis Rheum.* 46:1333–1343.
- Graybiel AM, Rauch SL (2000) Toward a neurobiology of obsessive-compulsive disorder, *Neuron.* 28:343–7
- Greicius MD, Krasnow B, Reiss AL, Menon V. (2003) Functional connectivity in the resting brain: a network analysis of the default mode hypothesis. *Proc Natl Acad Sci USA* 100: 253–8.

Großschädl F, Freidl W, Rásky E, Burkert N, Muckenhuber J, et al. (2014) A 35-Year Trend Analysis for Back Pain in Austria: The Role of Obesity. *PLoS ONE* 9(9): e107436. doi:10.1371/journal.pone.0107436

Gunderson, J. G. (2006). Descriptive and longitudinal observations on the relationship of borderline personality disorder and bipolar disorder. *American Journal of Psychiatry*, 163, 1173-1178.

## H

Habiger, Torstein F.,<sup>1</sup> Elisabeth Flo,<sup>1</sup> Wilco P. Achterberg,<sup>2</sup> and Bettina S. Husebo (2016) The Interactive Relationship between Pain, Psychosis, and Agitation in People with Dementia: Results from a Cluster-Randomised Clinical Trial, Hindawi Publishing Corporation, *Behavioural Neurology* 2016, ID 7036415, 8 pages <http://dx.doi.org/10.1155/2016/7036415>

Hamilton NA, Pressman M, Lillis T, Atchley R, Karlson C, Stevens N. (2012) Evaluating evidence for the role of sleep in fibromyalgia: a test of the sleep and pain diathesis model. *Cognit Ther Res* 36:806–14.

Hamilton, J. L., Stange, J. P., Abramson, L. Y., & Alloy, L. B. (2015) Stress and the development of cognitive vulnerabilities to depression explain sex differences in depressive symptoms during adolescence. *Clinical Psychological Science*, 3(5), 702-714.

Hauser W, Thieme K, Turk DC. (2010) Guidelines on the management of fibromyalgia syndrome—a systematic review. *Eur J Pain*. 14(1):5–10.

Heberlein I, Ludin HP, Scholz J, et al. Personality, depression, and premorbid lifestyle in twin pairs discordant for Parkinson's disease. *J Neurol Neurosurg Psychiatry* 1998;64:262 – 266.

Holley, AL, E.F. Law, C. Zhou, L. Murphy, G. Clarke, & T.M (2013) Palermo, Reciprocal Longitudinal Associations between Pain and Depressive Symptoms in Adolescents, *Eur J Pain*. 17(7): 1058–1067. doi:10.1002/j.1532-2149.2012.00272.x.

Holman AJ, Myers RR. (2005) A randomized, double-blind, placebo-controlled trial of pramipexole, a dopamine agonist, in patients with fibromyalgia receiving concomitant medications, *Arthritis Rheum* 52: 2495–505.

Hölscher, C. (1999) Stress impairs performance in spatial water maze learning tasks. *Behav. Brain Res.* 100, 225–235. doi: 10.1016/s0166-4328(98)00134-x

## I

Ilgen MA, Zivin K, Austin KL, Bohnert AS, Czymek EK, Valenstein M, Kilbourne AM (2010) Severe pain predicts greater likelihood of subsequent suicide. *Suicide Life Threat Behav* 40:597–608.

## J

Jamison RN, Ross EL, Michna E, Chen LQ, Holcomb C, Wasan AD (2010) Substance misuse treatment for high-risk chronic pain patients on opioid therapy: A randomized trial. *Pain*. 23. NP.

Janssen, SA (2002) Negative affect and sensitization to pain. *Scand. J. Psychol* 2002;43:131–137.

Jokinen, J., Nordström, A-L., and Nordström, P (2009) CSF 5-HIAA and DST non-suppression—orthogonal biologic risk factors for suicide in male mood disorder inpatients. *Psychiatry Res.* 165, 96–102. doi: 10.1016/j.psychres.2007.10.007

Julien N, Goffaux P, Arsenault P, Marchand S. (2005) Widespread pain in fibromyalgia is related to a deficit of endogenous pain inhibition. *Pain* 114:295.

## K

Kamping, S., Bomba, I. C., Kanske, P., Diesch, E., and Flor, H. (2013). Deficient modulation of pain by a positive emotional context in fibromyalgia patients. *Pain* 154, 1846–1855. doi: 10.1016/j.pain.2013.06.003

- Katon W, Sullivan MD (1990) Depression and chronic medical illness. *J Clin Psychiatry* 51 (6):3-11.
- Kashikar-Zuck S, Lynch AM, Slater S, Graham TB, Swain NF, Noll RB (2008) Family factors, emotional functioning, and functional impairment in juvenile fibromyalgia syndrome. *Arthritis Rheum.* 59:1392–8.
- Koike AK, Unutzer J, Wells KB (2002) Improving the care for depression in patients with comorbid medical illness. *Am J Psychiatry* 159(10):1738–1745.
- Koyama T, Kato K, Mikami A (2000) During pain-avoidance neurons activated in the macaque anterior cingulate and caudate. *Neurosci Lett*; 283: 17–20.
- Krebs EE, Lurie JD, Fanciullo G, et al (2010) Predictors of long-term opioid use among patients with painful lumbar spine conditions, *Journal of Pain* 11:44–52.
- Kroenke K, Jackson JL, Chamberlin J (1997) Depressive and anxiety disorders in patients presenting with physical complaints: clinical predictors and outcome. *Am J Med* 103:339- 347.
- Krullewitch H, London MR, Skakel VJ, Lundstedt GJ, Thomason H, Brummel-Smith K (2000) Assessment of pain in cognitively impaired older adults: a comparison of pain assessment tools and their use by non-professional caregivers, *J Am Geriatr Soc* 48: 1607–11.
- L
- Lallukka T, Overland S, Haaramo P, Saastamoinen P, Bjorvatn B, Sivertsen B (2014) The joint contribution of pain and insomnia to sickness absence and disability retirement: a register-linkage study among Norwegian and Finnish employees, *Eur J Pain* 18:883–92.
- Law, S.; Liu, P (2008) Suicide in China: Unique demographic patterns and relationship to depressive disorder. *Curr. Psychiatry Rep.* 10, 80–86.
- Lee, R. S. C., Hermens, D. F., Porter, M. A., and Redoblado-Hodge, M. A. (2012) A meta-analysis of cognitive deficits in first-episode major depressive disorder. *J. Affect. Disord.* 140, 113–124. doi: 10.1016/j.jad.2011.10.023
- Leite-Almeida H, Almeida-Torres L, Mesquita AR, Pertovaara A, Sousa N, Cerqueira JJ, Almeida A (2009) The impact of age on emotional and cognitive behaviours triggered by experimental neuropathy in rats, *Pain* 144:57–65.
- Lemogne, C., Delaveau, P., Freton, M., Guionnet, S., and Fossati, P. (2012) Medial prefrontal cortex and the self in major depression. *J. Affect. Disord.* 136, e1–e11. doi: 10.1016/j.jad.2010.11.034
- Lin EH, Katon W, Von Korff M, Tang L, Williams JW Jr, Kroenke K, Hunkeler E, Harpole L, Hegel M, Arean P, Hoffing M, Della Penna R, Langston C, Unutzer J (2002) Effect of improving depression care on pain and functional outcomes among older adults with arthritis: a randomized controlled trial. *JAMA* 2003, 290(18):2428–2429.
- Linehan MM. (2008) Suicide intervention research: a field in desperate need of development. *Suicide Life Threat Behav.* 2008; 38:483–485.
- Logan DE, Simons LE, Kaczynski KJ.(2009) School functioning in adolescents with chronic pain: the role of depressive symptoms in school impairment, *J Pediatr Psychol* 34:882–92.
- Lohle M, Storch A, Reichmann H (2009) Beyond tremor and rigidity: non-motor features of Parkinson's disease. *J Neural Transm* 116: 1483–92.
- Love TM, Stohler CS, Zubieta JK (2009) Positron emission tomography measures of endogenous opioid neurotransmission and impulsiveness traits in humans. *Arch Gen Psychiatry* 66(10): 1124–1134.
- Lumley MA, Cohen JL, Borszcz GS, Cano A, Radcliffe AM, Porter LS, Schubiner H, Keefe FJ. Pain and emotion: a biopsychosocial review of recent research. *J Clin Psychol.* 2011; 67:942–968. [PubMed: 21647882]

## M

- MacDonald, C.J. et al. (2011) Hippocampal 'time cells' bridge the gap in memory for discontinuous events. *Neuron* 71, 737–749.
- Macoveanu J, Knorr U, Skimminge A, et al. (2014) Altered reward processing in the orbitofrontal cortex and hippocampus in healthy first-degree relatives of patients with depression. *Psychol Med* 44:1183–95.
- Marchetti, I., Koster, E. H. W., Sonuga-Barke, E. J., and De Raedt, R. (2012) The default mode network and recurrent depression: a neurobiological model of cognitive risk factors. *Neuropsychol. Rev.* 22, 229–251. doi: 10.1007/s11065-012-9199-9
- Marsden, W. N. (2013) Synaptic plasticity in depression: molecular, cellular and functional correlates. *Prog. Neuropsychopharmacol. Biol. Psychiatry* 43, 168–184. doi: 10.1016/j.pnpbp.2012.12.012
- Martin TJ, Kim SA, Buechler NL, Porreca F, Eisenach JC (2007) Opioid self-administration in the nerve-injured rat: relevance of antiallodynic effects to drug consumption and effects of intrathecal analgesics. *Anesthesiology* 106(2):312–322.
- Matell MS, Meck WH (2004) Cortico-striatal circuits and interval timing: coincidence detection of oscillatory processes. *Brain Res Cogn Brain Res* 21(2):139-70.
- Mayeux R, Stern Y, Rosen J, et al. (1981) Depression, intellectual impairment and Parkinson disease. *Neurology* 31(6): 645–650.
- McWilliams LA, Goodwin RD, Cox BJ (2004) Depression and anxiety associated with three pain conditions: results from a nationally representative sample, *Pain* 111(1–2):77–83.
- Miaskowski, IJ, C, Cooper B, Levine JD, Dunn L, West C, Dodd M, Dhruva A, Paul SM, Baggott C, Cataldo J, Langford D, Schmidt B, Aouizerat BE (2012) Association between pro- and anti-inflammatory cytokine genes and a symptom cluster of pain, fatigue, sleep disturbance, and depression. *Cytokine*, 58(3):437–447.
- Monleón, S., Vinader-Caerols, C., Arenas, M. C., and Parra, A. (2008) Antidepressant drugs and memory: insights from *animal studies*. *Eur. Neuropsychopharmacol.* 18, 235–248. doi: 10.1016/j.euroneuro.2007.07.001
- Monti JM, Monti D (2007) The involvement of dopamine in the modulation of sleep and waking. *Sleep Med Rev* 11:113–33.
- Monroe, TB, John C. Gore, Li Min Chen, Lorraine C. Mion, & Ronald L. Cowan (2012) Pain in People With Alzheimer Disease: Potential Applications for Psychophysical and Neurophysiological Research, *J Geriatr Psychiatry Neurol* 25(4): 240–255. doi:10.1177/0891988712466457.
- Moriarty O, McGuire BE, Finn DP (2011) The effect of pain on cognitive function: a review of clinical and preclinical research. *Prog Neurobiol* 93: 385–404.
- Morris, M (1991) Delusional infestation. *Br. J. Psychiatry* 1991: 83–87.
- Moseley G, Brhyn L, Ilowiecki M, Solstad K, Hodges P (2003) The threat of predictable and unpredictable pain: Differential effects on central nervous system processing?, *Australian J Physiotherapy* 49: 263–267.
- Murberg, T. A., & Bru, E. (2004). School-related stress and psychosomatic symptoms among Norwegian adolescents. *School psychology international*, 25(3), 317-332.
- Murray CB, Murphy LK, Palermo TM, Clarke GM (2012) Brief report: Pain and sleep-wake disturbances in adolescents with depressive disorders. *J Clin Child Adolesc Psychol* 41:482–90.
- Murrough, J. W., Iacoviello, B., Neumeister, A., Charney, D. S., and Iosifescu, D. V. (2011) Cognitive dysfunction in depression: neurocircuitry and new therapeutic strategies. *Neurobiol. Learn. Mem.* 96, 553–563. doi: 10.1016/j.nlm. 2011.06.006

## N

- Nair-Roberts RG, Chatelain-Badie SD, Benson E, White-Cooper H, Bolam JP, Ungless MA. (2008) Stereological estimates of dopaminergic, GABAergic and glutamatergic neurons in the ventral tegmental area, sub-

- stantia nigra and retrorubral field in the rat. *Neuroscience* 152(4):1024–31.
- Napadow V, LaCount L, Park K, As-Sanie S, Clauw DJ, Harris RE (2010) Intrinsic brain connectivity in fibromyalgia is associated with chronic pain intensity. *Arthritis Rheum* 62: 2545–55.
- Nasrullah. M (2018) Huntington’s Disease: Understanding the Pathophysiology Through the Huntingtin Gene, *NJM*; 05(01).
- Nekovarova1, Tereza, Anna Yamamotova, Karel Vales, Ales Stuchlik1, Jitka Fricova, & Richard Rokyta (2014) Common mechanisms of pain and depression: are antidepressants also analgesics? *Frontiers in Behavioral Neuroscience* 8, 99 doi: 10.3389/fnbeh.2014.00099
- Neylan, TC (2003) Neurodegenerative Disorders. *J. Neuropsychiatry Clin. Neurosci.* 15:108–108, doi:10.1176/jnp.15.1.108.
- Nicholl, Barbara, Daniel Mackay, Breda Cullen, Daniel J Martin, Zia Ul-Haq, Frances S Mair, Jonathan Evans, Andrew M McIntosh, John Gallagher, Beverly Roberts, Ian J Deary, Jill P Pell & Daniel J Smith (2014) Chronic multisite pain in major depression and bipolar disorder: cross-sectional study of 149,611 participants in UK Biobank, *BMC Psychiatry* 0(2014)14:35 ,doi 10.1186/s12888-014-0350-4
- Nicholson, B & Verma, S (2004) Comorbidities in Chronic Neuropathic Pain, *Pain Medicine* 5, S1.
- Nock, M.K (2009) Why do people hurt themselves? New insights into the nature and functions of self-injury. *Curr. Dir. Psychol. Sci* 18, 78–83.
- Nock MK, Green JG, Hwang I, McLaughlin KA, Sampson NA, Zaslavsky AM, Kessler RC (2013) Prevalence, correlates, and treatment of lifetime suicidal behavior among adolescents: results from the National Comorbidity Survey Replication Adolescent Supplement. *JAMA Psychiatry* 70:300–310.
- Nolen-Hoeksema, S (2000) The role of rumination in depressive disorders and mixed anxiety/depressive symptoms. *J. Abnorm. Psychol.* 109, 504–511. doi: 10.1037//0021-843x.109.3.504
- O
- O’Brien, E. M., Atchison, J. W., Gremillion, H. A., Waxenberg, L. B., & Robinson, M. E. (2008) Somatic focus/awareness: Relationship to negative affect and pain in chronic pain patients. *European Journal of Pain*, 12(1), 104–115. doi:10.1016/j.ejpain.2007.04.001
- Okada-Ogawa A, Porreca F, Meng ID (2009) Sustained morphine-induced sensitization and loss of diffuse noxious inhibitory controls in dura-sensitive medullary dorsal horn neurons. *J Neurosci.* 16; 29(50):15828–15835.
- Okifuji A, Turk DC, Marcus DA (1999) Comparison of generalized and localized hyperalgesia in patients with recurrent headache and fibromyalgia. *Psychosom Med* 61:771.
- Otis JD, Keane TM, Kerns RD (2003) An examination of the relationship between chronic pain and post- traumatic stress disorder. *J Rehabil Res Dev* 40:397–405.
- P
- Palermo TM, Wilson AC, Peters M, Lewandowski A, Somhegyi H (2009) Randomized controlled trial of an Internet-delivered family cognitive-behavioral therapy intervention for children and adolescents with chronic pain, *Pain* 146:205–13.
- Patten SB (2001) Long-term medical conditions and major depression in a Canadian population study at waves 1 and 2, *J Affect Disord.* 63:35- 41.
- Paulsen JS (2011) Cognitive impairment in Huntington disease: diagnosis and treatment. *Curr Neurol Neurosci Rep.* 11(5):474–83.



- Paulson GW, Dadmehr N (1991) Is there a pre-morbid personality typical for Parkinson's disease? *Neurology* 41(S2): 73–76.
- Pavic L, Gregurek R, Petrovic R, et al (2003) Alterations in brain activation in posttraumatic stress disorder patients with severe hyperarousal symptoms and impulsive aggressiveness. *Eur Arch Psychiatry Clin Neurosci.* 253(2):80–83.
- Perrotta A, Sandrini G, Serrao M, Buscone S, Tassorelli C, Tinazzi M, et al (2010) Facilitated temporal summation of pain at spinal level in Parkinson's disease. *Mov Disord* 26: 442–8.
- Peyron R, Laurent B, García-Larrea L (2000) Functional imaging of brain responses to pain. A review and meta-analysis, *Neurophysiol. Clin* 30:263–288.
- Pickering G, Eschaliier A, Dubray C (2000) Pain and Alzheimer's disease. *Gerontology*; 46: 235–41.
- Ploghaus A, Narain C, Beckmann CF, Clare S, Bantick S, et al (2001) Exacerbation of pain by anxiety is associated with activity in a hippocampal network. *J Neurosci* 21: 9896–9903.
- Popoli, M., Yan, Z., McEwen, B. S., and Sarnacora, G. (2011). The stressed synapse: the impact of stress and glucocorticoids on glutamate transmission. *Nat. Rev. Neurosci.* 13, 22–37. doi: 10.1038/nrn3138
- Price DD, Verne GN, Schwartz JM (2006) Plasticity in brain processing and modulation of pain. *Prog Brain Res.* 157:333–352.
- Ploghaus A, Narain C, Beckmann CF, Clare S, Bantick S, et al (2001) Exacerbation of pain by anxiety is associated with activity in a hippocampal network. *J Neurosci* 21: 9896–9903.
- Raymond, L. A.; André, V. M.; Cepeda, C.; Gladding, C. M.; Milnerwood, A. J.; Levine, M. S (2011) Pathophysiology of Huntington's disease: timedependent alterations in synaptic and receptor function. *Neuroscience* 198: 252–73, doi:10.1016/j.neuroscience.2011.08.052.
- Reading SA, Dziorny AD, Peroutka LA, Schreiber M, Gourley LM, Yallapragada V, et al (2004) Functional brain changes in presymptomatic Huntington's disease. *Ann Neurol* 55(6):879-83.
- Remick RA, Blasberg B, Campos PE, Miles JE. (1983) Psychiatric disorder associated with atypical facial pain, *Can J Psychiatry* 28:178–181.
- Ro T, Farne A, Johnson RM, Wedeen V, Chu Z, Wang ZJ, et al (2007) Feeling sounds after a thalamic lesion. *Ann Neurol* 62: 433241.
- Roehrs T, Hyde M, Blaisdell B, Greenwald M, Roth T (2006) Sleep loss and REM sleep loss are hyperalgesic, *Sleep* 29:145–51.
- Rokyta, R., Haklova, O., and Yamamotova, A. (2009) Assessment of chronic benign and cancer pain using blood plasma biomarkers. *Neuroendocrinol. Lett.* 30, 637– 642.
- Roose, S.P., Glassman, A.H., Walsh, B.T. et al (1983) Depression, delusions, and suicide. *Am J Psychiatry* 140 (9): 1159–1162.
- Ross CA, Tabrizi SJ (2011) Huntington's disease: from molecular pathogenesis to clinical treatment, *Lancet Neurol* 10: 83–98.
- Russell, S.T., Joyner, K. (2001) Adolescent sexual orientation and suicide risk: Evidence from a National study, *Am. J. Public Health* 91, 1276–1281.
- Q
- R
- Radat F, Margot-Duclot A, Attal N (2013) Psychiatric co-morbidities in patients with chronic peripheral neuropathic pain: a multicentre cohort study. *Eur J Pain* 17(10):1547–57.
- S
- Sandi, C (2011) Glucocorticoids act on glutamatergic pathways to affect memory processes. *Trends Neurosci.* 34, 165–176. doi: 10.1016/j.tins.2011.01.006
- Schaefer I, von Leitner EC, Schoen G, Koller D, Hansen H, Kolonko T, Kaduszkiewicz

- H, Wegscheider K, Glaeske G, van den Busche H (2010) Multimorbidity patterns in the elderly: A new approach of disease clustering identifies complex interrelations between chronic conditions. *PLoS One*; 5:1-10. e15941.
- Selbæk, G & K. Engedal (2012) Stability of the factor structure of the Neuropsychiatric Inventory in a 31-month follow-up study of a large sample of nursing-home patients with dementia, *International Psychogeriatrics* 24,1:62–73.
- Selbæk, K. Engedal, J, Benth, & S. Bergh (2014) The course of neuropsychiatric symptoms in nursing-home patients with dementia over a 53-month follow-up period, *International Psychogeriatrics* 26,1: 81–91.
- Scott DJ, Heitzeg MM, Koeppe RA, Stohler CS, Zubieta JK (2006) Variations in the human pain stress experience mediated by ventral and dorsal basal ganglia dopamine activity. *J Neurosci* 26: 10789–95.
- Sharp TJ, Harvey AG (2001) Chronic pain and posttraumatic stress disorder: mutual maintenance? *Clin Psychol Rev.* 21(6):857–877.
- Shimura H, Hattori N, Kubo S, et al (2000) Familial parkinson disease gene product, parkin, is a ubiquitin-protein ligase, *Nat Genet* 25:302 – 305.
- Shurman J, Koob GF, Gutstein HB (2010) Opioids, pain, the brain, and hyperkatifeia: a framework for the rational use of opioids for pain. *Pain Med.* 11(7):1092–1098.
- Silva, R., Mesquita, A. R., Bessa, J., Sousa, J. C., Sotiropoulos, I., Leão, P., et al (2008) Lithium blocks stress-induced changes in depressive-like behavior and hippocampal cell fate: the role of glycogen-synthase-kinase-3beta, *Neuroscience* 152, 656–669. doi: 10.1016/j.neuroscience.2007.12.026
- Simons, L. E., Elman, I., and Borsook, D. (2014) Psychological processing in chronic pain: a neural systems approach. *Neurosci. Biobehav. Rev.* doi: 10.1016/j.neurosci.2013.12.006.
- Børge Sivertsen, Tea Lallukka, Keith J Petrief, AnnaSteingrimsdóttir, Audun Stubh-augh, Christopher Sivert Nielsen (2015) Sleep and pain sensitivity in adults, *Pain* 156:1433–1439 dx.doi.org/10.1097/j.pain.0000000000000131
- Smith MT, Perlis ML, Smith MS, Giles DE, Carmody TP (2000) Sleep quality and presleep arousal in chronic pain, *J Behav Med* 23:1–13.
- Starfield B (2006) Threads and yarns: Weaving the tapestry of comorbidity. *Annals of Family Medicine* 4:101-103.
- Staud R, Robinson ME, Price DD (2005) Isometric exercise has opposite effects on central pain mechanisms in fibromyalgia patients compared to normal controls, *Pain* 118:176–184.
- Svanborg, P., & Åsberg, M. (2001) A comparison between the Beck Depression Inventory (BDI) and the self-rating version of the Montgomery Åsberg Depression Rating Scale (MADRS). *Journal of Affective Disorders*, 64(2), 203-216.
- T
- Takahashi, Y (2001) Depression and Suicide, *JMAJ* 44(8): 359–363, 2001
- (2011) Neuroeconomics of suicide. *Neuro Endocrinol Lett* 32:400–404.
- Tandberg E, Larsen JP, Aarsland D, et al (1996) The occurrence of depression in Parkinson's disease. A community-based study. *Arch Neurol* 53:175–179.
- Tegethoff, M., Belardi, A., Stalujanis, E., & Meinschmidt, G. (2015) Comorbidity of mental disorders and chronic pain: chronology of onset in adolescents of a national representative cohort, *The Journal of Pain* 16(10), 1054-1064.
- Tekin S, Mega MS, Masterman DM, et al (2001) Orbitofrontal and anterior cingulate cortex neurofibrillary tangle burden is associated with agitation in Alzheimer disease. *Ann Neurol.* 49(3):355–361.
- Todes CJ, Lees AJ. (1985) The pre-morbid personality of patients with Parkinson's disease, *J Neurol Neurosurg Psychiatry* 48: 97 – 100.

- Torta, R. G., and Munari, J. (2010) Symptom cluster: depression and pain. *Surg. Oncol.* 19, 155–159. doi: 10.1016/j.suronc.2009.11.007
- Torta, R, Ieraci, V, & Zizzi, F (2017) Review of the Emotional Aspects of Neuropathic Pain: From Comorbidity to Co-Pathogenesis, *Pain Ther* 6,1 :S11–S17 doi 10.1007/s40122-017-0088-z
- Tracey I, Ploghaus A, Gati JS, Clare S, Smith S, et al (2002) Imaging attentional modulation of pain in the periaqueductal gray in humans. *J Neurosci* 22: 2748–2752.
- U
- V
- Valet M, Sprenger T, Boecker H, Willoch F, Rummeny E, et al. (2004) Distraction modulates connectivity of the cingulo-frontal cortex and the midbrain during pain—an fMRI analysis. *Pain* 109: 399–408.
- van Orden KA, Witte TK, Cukrowicz KC, Braithwaite SR, Selby EA, Joiner TE Jr. (2010) The interpersonal theory of suicide. *Psychol Rev.* 117:575–600.
- W
- Wagner AW, Wolfe J, Rotnitsky A, Proctor SP, Erickson DJ (2000) An investigation of the impact of posttraumatic stress disorder on physical health. *J Trauma Stress* 13:41–55.
- Walker AK, Kavelaars A, Heijnen CJ, Dantzer R (2014) Neuroinflammation and comorbidity of pain and depression. *Pharmacol Rev.* 66(1):80–101.
- Wei, F., Dubner, R., Zou, S., Ren, K., Bai, G., Wei, D., et al (2010) Molecular depletion of descending serotonin unmasks its novel facilitatory role in the development of persistent pain. *J. Neurosci.* 30, 8624–8636. doi: 10.1523/jneurosci. 5389-09.2010
- Wen H-B, Zhang Z-X, Wang H, et al (2012) Epidemiology and clinical phenomenology for Parkinson’s disease with pain and fatigue. *Parkinsonism Relat Disord.* 18, 1:S222–5.
- Wiech K, Edwards R, Moseley GL, Berna C, Ploner M, et al (2014) Dissociable Neural Mechanisms Underlying the Modulation of Pain and Anxiety? An fMRI Pilot Study. *PLoS One* 9(12): e110654. doi:10.1371/journal.pone. 0110654
- Wise MG, Taylor SE (1990) Anxiety and mood disorders in medically ill patients. *J Clin Psychiatry* 51(1):27–32.
- Wong, W. S., Lam, H. M. J., Chen, P. P., Chow, Y. F., Wong, S., Lim, H. S., Fielding, R. (2015) The Fear-Avoidance Model of Chronic Pain: Assessing the Role of Neuroticism and Negative Affect in Pain Catastrophizing Using Structural Equation Modeling, *International Journal of Behavioral Medicine*, 22,1,118–131. doi:10.1007/s12529-014-9413-7
- Wurm, M (2018) *Understanding Comorbid Pain and Emotions: A transdiagnostic approach.* PhD Dissertation, Örebro University, Sweden.
- X
- Y
- Z
- Zimmerman, M., Ruggero, C. J., Chelminski, I., & Young, D. (2010) Psychiatric diagnoses in patients previously overdiagnosed with bipolar disorder. *Journal of Clinical Psychiatry*, 71, 26-31.
- Zis, Panagiotis Argyro Daskalaki, Ilia Bountouni, Panagiota Sykioti, Giustino Varrassi Antonella Paladini (2017) Depression and chronic pain in the elderly: links and management challenges, *Clinical Interventions in Aging* 12 709–720 dx.doi.org/10.2147/CIA.S113576
- Zubieta JK, Smith YR, Bueller JA, Xu Y, Kilbourn MR, Jewett DM, et al (2001) Regional mu opioid receptor regulation of sensory and affective dimensions of pain, *Science* 293: 311–5.

A

AAFP, American Academy of Family Physicians: *Definition of PCMH*. Available at: <http://www.aafp.org/online/en/home/membership/initiatives/pcmh/brief.html> (last accessed April 10th, 2009).

Anjum, RL; Copeland, S; Mumford, S & Rocca, E (2015) CauseHealth: integrating philosophical perspectives into person-centered healthcare, *European Journal for Person Centered Healthcare* 3, 4: 427-430.

Arieti, S (ed) (1966) *American Handbook of Psychiatry* 3. Basic Books: NY.

B

Ballerini, A (1997) *La Diagnose in Psiquiatria*, La Nuova Italia Scientifica: Rome.

Barnard, D, Dayringer, R & Cassel, M (1995) Toward a person-centered medicine: religious studies in the medical curriculum, *Academic Medicine* 70 (9), 806–813.

Bartholomew, L. K., Parcel, G. S., Kok, G. & Gottlieb, N. H. (2006) *Planning Health Promotion Programs, An Intervention Mapping Approach*. San Francisco: Wiley.

BDP, British Department of Health (2008) *Code of Practice: Mental Health Act 1983*. London: Department of Health.

Beasley, JW, Hankey, TH, Erickson, R, Stange, KC, Mundt, M, Elliott, M, Wiesen, P & Bobula, J (2004) How many problems do family physicians manage at each encounter? A WReN study, *Annals of Family Medicine* 2 (5): 405–410.

Bechtel, W & Richardson, RC (1993) *Discovering Complexity*, Princeton UP: Princeton.

Benedetti, F (2002) How the doctor's words affect the patient's brain, *Evaluation & The Health Professions* 25: 369–386.

Bensing, J (2000) Bridging the gap. The sepa-

rate worlds of evidence-based medicine and patient-centered medicine, *Patient Education Counseling* 39: 17–25.

Bensing, JM, Tromp, F, van Dulmen, S, van den Brink-Muinen, A, Verheul, W & Scheellevis, FG (2006) Shifts in doctor-patient communication between 1986 and 2002: a study of videotaped General Practice consultations with hypertension patients, *BMC Family Practice* 7, 62.

Bland, M (2009) The tyranny of power: is there a better way to calculate sample size? *British Medical Journal* 339: 1133-1135.

Bertakis, KD & Azari, R (2011) Determinants and outcomes of patient-centered care, *Patient Education and Counseling* 85 (1): 46-52.

Brera, GR (1992) Epistemological aspects of medical science, *Medicine and Mind* 7: 5–12.

Bolt, T & Huisman, F (2015) Towards person-centered healthcare via realistic evidence-based medicine - informing the debate historically, *European Journal for Person Centered Healthcare* 3 (3): 275-278.

Buchanan, A & Brock, D (1990) *Deciding for Others: The Ethics of Surrogate Decision Making*. Cambridge UPL: NY

C

Callieri, B, Castellani, A & de Vincentis, G (1972) *Lineamento de una Psicopatologia Fenomenologica*, Il Pensiero Scientifico: Rome.

Cartwright, ND (1983) *How the Laws of Physics Lie*. Clarendon Press: Oxford

— (1999) *The Dappled World: A Study of the Boundaries of Science*. Cambridge UPL: Cambridge

Cloninger, CR (2004) *Feeling Good: The Science of Well-Being*. Oxford UP: NY.

— (2006) The science of well-being: an integrated approach to mental health and its disorders, *World Psychiatry* 5: 71–76.

Chewning, B, Bylund, CL, Shah, B, Arora, NK, Gueguen, JA & Makoul, G (2012) Patient preferences for shared decisions: A systematic review, *Patient Education & Counseling* 86 (1): 9-18.

Christodoulou, G N (ed.) (1987) *Psychosomatic Medicine*, Plenum: NY.

Cox, J (2010) Medicine of the person and personalised care: a stitch in time saves nine? *Journal of Evaluation in Clinical Practice* 16: 315–317.

## D

Darden, L (2006) *Reasoning in Biological Discoveries*, Cambridge UP: Cambridge.

Datamonitor (July 2007) *Patient Empowerment: empowered patients can change healthcare outcomes and impact the pharmaceutical industry*. Available at: [http://www.researchandmarkets.com/reportinfo.asp?report\\_id=545617](http://www.researchandmarkets.com/reportinfo.asp?report_id=545617) (last accessed February 22nd, 2018).

Deary, V (2005) Explaining the unexplained? Overcoming the distortions of a dualist understanding of medically unexplained illness, *J Ment Health* 14 :213– 221.

Dupré, J (1981) Natural kinds and biological taxa, *Philosophical Review* 90: 66-90.

Dörr-Zegers, O (1995) *Psiquiatría Antropológica*, E de la Universidad de Chile: Santiago de Chile.

## E

Elwyn, G, Stiel, M, Durand, MA & Boivin, J (2011) The design of patient decision support interventions: addressing the theory-practice gap, *Journal of Evaluation in Clinical Practice* 17 (4): 565-574.

Engel, G (1997) From biomedical to biopsychosocial. Being scientific in the human domain, *Psychosomatics* 38 (6): 521–528

—(1988) How much longer must medicine's science be bound by a seventeenth century world view, White, K (ed) *The Task of Medicine: Dialogue at Wickenburg*, 113–116.

Menlo Park: Henry Kaiser Foundation.

Eriksen, TE, Kerry, R, Mumford, S, Lie, SAN & An- jum, RL (2013) At the border of medical reasoning: the aetiological and ontological challenges of medically un- explained symptoms, *Philosophy, Ethics and Humanities in Medicine* 8: 1-11.

## F

Fassaert, T, Jabaaij, L, van Dulmen, S, Timmermans, A, van Essen, T & Schellevis, F (2008) Does familiarity between patient and general practitioner influence the content of the consultation?, *Family Practice* 9: 51.

Fedigan, LM & Fedigan, L (1989) Gender and the Study of Primates, *Critical Reviews of Gender and Anthropology*, 41-64, Am Anthrop As: Washington.

Fehr, C & Plaisance, K (2010) Socially relevant philosophy of science, *Synthese* 177: 301-316.

Fiscella, K, Meldrum, S, Franks, P, Shields, CG, Duberstein, P, McDaniel, SH & Epstein, RM (2004) Patient trust: is it related to patient-centred behavior of primary care physicians?, *Medical Care* 42: 1049-1055.

Fotopoulou, A; Conway, MA; Tyrer, S; Birchall, D; Griffiths, P & Solms, M (2008) Is the content of confabulation positive? An experimental study, *Cortex* 44: 764–772. doi:10.1016/j.cortex.2007.03.001

Flocke, S, Frank, S & Wenger, D (2001) Addressing multiple problems in the family practice office visit, *Journal of Family Practice* 50: 211-216.

Frankel, RM & Stein, T (2001) Getting the most out of the clinical encounter: the four habits model, *Journal of Medical Practice Management* 16: 184–191.

Fuller, S (1988) *Social Epistemology*. Indiana UP: Bloomington.

## G

Galdas, P & Cheater, F (2010) Indian and Pakistani men's accounts of seeking medical

- help for cardiac chest pain in the United Kingdom: constructions of marginalised masculinity or another version of hegemonic masculinity?, *Qualitative Research in Psychology* 7: 122–139.
- Galison, P (2004) Specific theory, *Critical Enquiry* 30, 2: 379–383.
- Galison, P & Stump, DJ (eds.) (1996) *The Disunity of Science: Boundaries, Contexts, and Power*. Stanford UP: Stanford.
- Gask, L, Klinkman, M, Fortes, S & Dowrick, C (2008) Capturing complexity: The case for a new classification system for mental disorders in primary care, *European Psychiatry* 23 (7): 469–476.
- Giere, R (1999) *Science without Laws*, Chicago UP: Chicago.
- (2006a) *Scientific Perspectivism*, Chicago UP: Chicago.
- (2006b) Perspectival pluralism, Kellert, S; Longino, HE & Kenneth Waters, C (eds.) *Minnesota Studies in the Philosophy of Science*, vol XIX, Scientific Pluralism: 26–41, Minnesota UP: London.
- Goffman, E (1968) *Stigma: Notes on the Management of Spoiled Identity*, Pelican: London.
- Goldman, A (1987) Foundations of social epistemics, *Synthese* 73: 109–144.
- (1999) *Knowledge in a Social World*. Oxford UP: Oxford.
- H
- Hacking, I (1986) Making up people, Heller, T (ed.) (1986) *Reconstructing Individualism: Autonomy, Individuality in Self Investigation Thought*, 161–171. Stanford UP: Stanford.
- (1995) The looping effects of human kinds, Sperber, D & Premack, AJ (eds) (1995) *Causal Cognition*, 351–383, Oxford UP: Oxford.
- (1998) *Mad Travellers. Reflections on the Reality of Transient Mental Illnesses*, Virginnia UP: London.
- (2002) *Historical Ontology*, Harper U P: London.
- Haraway, DJ (1976) *Crystals, Frabrics, and Fields: Metaphors that Shape Embryos*, Yale UP: New Haven.
- (1991) *Simians, Cyborgs, and Women*, Routledge: NY.
- Harding, S (1991) *Whose Science? Whose Knowledge?* Cornell UP: NY.
- Hawkins, DM (2004) The problem of overfitting, *Journal of Chemical Information and Computer Science* 44 (1): 1–12.
- Heckman, JJ (1979) Sample selection bias as a specification error, *Econometrica* 47 (1): 153–162.
- Heylighen, F (2000) Evolutionary transitions: how do levels of complexity emerge? *Complexity* 6: 53–57.
- Hickey, DS, Hickey, A & Noriega, LA (2012) The failure of evidence-based medicine?, *European Journal for Person Centered Healthcare* 1, 1: 69–79
- Hickey, S & Roberts, H (2011) *Tarnished Gold: The Sickness of Evidence-based Medicine*, CreateSpace. NP.
- Holmes, D & Hitchcock C (1992) *Gender as a Predictor of Research Topic in Animal Behaviour*, North Carolina UP: Wilmington.
- Hunink, M, Glasziou, P, Siegel, J, Weeks, J, Pliskin, J, Elstein, A & Weinstein, M (2001) *Decision Making in Health and Medicine: Integrating Evidence and Values*. Cambridge UP: Cambridge.
- I
- IHI, Institute for Healthcare Improvement (2009) *Health Partners uses 'BestCare' practices to improve care and outcomes, reduce costs*, Available at: <http://www.ihl.org/NR/rdonlyres/7150DBEF-3853-4390-BBAF-30AC-DCA648F5/0/IHITripleAimHealthPartners-SummaryofSuccessJul09.pdf> (last accessed October 12th, 2017).

Iqbal, SA, Wallach, JD, Khoury, MJ, Schully, SD & Ioannidis, JP (2016) Reproducible research practices and transparency across the biomedical literature, *PLoS Biology* 14: e1002333.

## J

Johnston, BC, Alonso-Coello, P, Friedrich, JO, Mustafa, RA, Tikkinen, KA, Neumann, I, Vandvik, PO, Akl, E.A., da Costa, B.R., Adhikari, N.K., Dalmay, G.M., Kosunen, E., Mustonen, J., Crawford, M.W., Thabane, L. & Guyatt, GH (2016) Do clinicians understand the size of treatment effects? A randomized survey across 8 countries, *Canadian Medical Association Journal* 188: 25-32.

## K

Kappen, T & Van Dulmen, S (2008) General practitioners' responses to the initial presentation of medically unexplained symptoms: a quantitative analysis, *BioPsychoSocial Medicine* 2: 22.

Keller, EF (2003) *Making Sense of Life: Explaining Biological Development with Models, Metaphors, and Machines*, Harvard UP: Cambridge.

— (2005) Ecosystems, organisms, and machines, *Bioscience* 55, 12: 1069-1074.

Kitcher, P (1984) 1953 and all that: a tale of two sciences, *Philosophical Review* 93: 335-373.

— (1992) The naturalists return, *Philosophical Review* 101: 53-114.

— (1993) *The Advancement of Science*, Oxford UP: Oxford.

— (2003) What kind of science should be done?, Lightman, A, Sarewitz, D & Dresser, C (eds.) (2003) *Living with the Genie*, 201-224, Island P: Washington.

— (2004) Evolutionary theory and the social uses of biology, *Biology and Philosophy* 19: 1-15.

Kitcher, P & Salmon, W (eds) (1989) *Scientific Explanation*, Minnesota UP: Minneapolis.

Kitwood, T (1995) *Studies in person-centred*

care: building up the mosaic of good practice, *Journal of Dementia Care* 3 (5): 12-13.

Klinkman, M & van Wheel, C (2011) Prospects for person-centered diagnosis in general medicine, *Journal of Evaluation in Clinical Practice* 17: 365-370.

Krupat, E, Frankel, R, Stein, T & Irish, J (2006) The Four Habits Coding Scheme: validation of an instrument to assess clinicians' communication behaviour, *Patient Education and Counseling* 62: 38-45

## L

Laing, RD (1960) *The Divided Self, a Study of Sanity and Madness*, Tavistock P: London.

— (1961) *Self and Others*, Tavistock P: London.

— (1967) *The Politics of Experience*, Penguin P: Harmondsworth.

Levinson, W., Roter, D. L., Mullooly, J. P., Dull, V. T. & Frankel, R. M. (1997) Physician-patient communication. The relationship with malpractice claims among primary care physicians and surgeons, *JAMA* 277: 553-559.

Lichtenstein, S & Slovic, P (eds) (2006) *The Construction of Preference*, Cambridge UP: NY.

Lilienfeld, SO & Marino, L (1999) Essentialism revisited: Evolutionary theory and the concept of mental disorder, *Journal of Abnormal Psychology* 108: 400-411.

Lindenmayer, A, Hearnshaw, H., Sturt, J., Ormerod, R. & Aitchison, G (2007) Assessment of the benefits of user involvement in health research, *Health Expectations* 10 (3): 268-277.

Longino, HE (1990) *Science as Social Knowledge: Values and Objectivity in Scientific Inquiry*, Princeton UP: Princeton.

— (2000) Reply to P Kitcher, *Philosophy of Science* 69: 573-577.

— (2001) *The Fate of Knowledge*, Princeton UP: Princeton.

## M

Macleod, A & Frank, B (2010) Patient-centredness in a context of increasing diversity: Location, location, location, *Medical Teacher* 32 (10): 799-801.

- MacMahon, JA; Phillips, DL; Robinson, JV & Schimpf, DJ (1978) Levels of biological organization: an organism-centered approach, *Bioscience* 28: 700–704.
- Martin, JC, Avant, RF, Bowman, MR (2004) The future of family medicine, *Annals of Family Medicine* 2 (1): S3–32.
- Matthews, E. (2007) *Body-Subjects and Disordered Minds: Treating the Whole Person in Psychiatry*. Oxford: Oxford University Press.
- May, R & Angel, E & Allenberger, HF (eds) (1958) *Existence. A new Dimension in Psychiatry and Psychology*, Basic Books: NY.
- McCauley, RN & Bechtel, W (2001) Explanatory pluralism and the heuristic identity theory, *Theory Psychol* 11: 736–760.
- McKeown, T & Lowe, R (1967) *Introduction to Social Medicine*, Davis P: Fil
- Mead, N & Bower, P (2000) Patient-centredness: a conceptual framework and review of the empirical literature, *Social Science and Medicine* 51: 1087–1110.
- Melnyk, BM & Feinstein, NF (2009) Reducing hospital expenditures with the COPE (Creating Opportunities for Parent Empowerment) program for parents and premature infants: an analysis of direct health-care neonatal intensive care unit costs and savings, *Nursing Administration Quarterly* 33 (1): 32–37
- Mercer (2008) *Executive summary, 2008 community care of North Carolina evaluation*. (Available at: <http://www.communitycarenc.com/PDFDocs/Mercer%20ABD%20Report%20SFY08.pdf> (last accessed November 2nd, 2018).
- Merton, RK (1973) *Sociology of Science*. Chicago UP: Chicago
- Miles, A, Loughlin, M & Polychronis, A (2008) Evidence-based healthcare, clinical knowledge and the rise of personalised medicine, *Journal of Evaluation in Clinical Practice* 14: 621–649.
- Miller, CG & Miller, DW (2011) The real world failure of evidence-based medicine, *International Journal of Person Centered Medicine* 1 (2): 295–300.
- Mitchell, WJT (2004) Medium Theory, *Critical Inquiry* 30, 2: 324–335.
- Mitchell, S (2002) Integrative Pluralism, *Biology and Philosophy* 17: 55–70.
- Mody, CCM (2005) The sounds of science: Listening to laboratory practice, *Science, Technology, and Human Values* 30, 2: 175–198.
- Mumford, S & Anjum, RL (2011) *Getting Causes from Powers*. Oxford UP: Oxford.
- Musalek, M & Schebenbogen, O (2008) From categorical to dimensional diagnostics: deficiency-oriented versus person-centered diagnostics, *Eur Arch Psychiatry Clin Neurosci* 258:18–21.
- N
- Nejad, AG; Anari, AMZ & Pouya, F (2013) Effect of cultural themes on forming Cotard's syndrome: reporting a case of Cotard's syndrome with depersonalization and out of body experience symptoms, *Iran J Psychiatry Behav Sci* 7, 2: 91–3.
- O
- Olson, V (2010) The ecobiopolitics of space medicine, *Medical Anthropology* 29, 2: 170–193.
- Ong, BN, Yip, MP, Feng, S, Calhoun, R, Meischke, HW & Tu, SP (2012) Barriers and facilitators to using 9-1-1 and Emergency Medical Services in a limited English proficiency Chinese community, *Journal of Immigrant and Minority Health* 14: 307–313.
- P
- PAHO, Pan American Health Organization (2007) *Renewing Primary Health Care in the Americas*, Pan American Health Organization: Washington DC.



PCPC, Patient Centered Primary Care Collaborative (2006) Accessible at: <http://www.pcpc.net> (last accessed January 10th, 2018).

Phillips, RL, Klinkman, MS & Green, L (2007) Harmonizing Primary Care Clinical Classification and Data Standards, *Am Ac Family Physicians*: Washington. NP.

Pongsupap, Y (2007) *Introducing A Human Dimension to Thai Health Care: the Case for Family Practice*. Vrije Universiteit P: Brussels.

## Q

## R

Raman, R (2011) Evidence-based medicine and patient-centered care: cross-disciplinary challenges and healthcare information technology enabled solutions, *International Journal of Person Centered Medicine* 1 (2): 279-294.

Rappaport, J (1987) Terms of empowerment. Exemplars of prevention: towards a theory for community psychology, *American Journal of Community Psychology* 15: 121-144.

Rittenhouse, DR, Shortell, SM & Fisher, ES (2009) Primary care and accountable care: two essential elements of delivery-system reform, *New England Journal of Medicine* 361 (24): 2301-2303.

Rogers, ES, Chamberlin, J, Ellison, ML & Crean, T (1997) A consumer-constructed scale to measure empowerment among users of mental health services, *Psychiatric Services* 48: 1042-1047.

Rosenblatt, A & Attkisson, C (1993) Assessing outcomes for sufferers of severe mental disorder: a conceptual framework and review, *Evaluation and Program Planning* 16: 347-363.

Rossiter, M (1982) *Women Scientists in America*, John Hopkins UP: Baltimore.

## S

Safran, DG, Murray, A., Chang, H., Murphy, J. & Rogers, WH (2000) Linking doctor-patient relationship to quality outcomes, *Journal of General Internal Medicine* 15, S: 116.

Schwenk, TL (1999) The tyranny of names in mental health care, *Journal of the American Board of Family Practice* 12 (1): 99-101.

Shamliyan, T, Kane, R.L. & Jansen, S. (2010) Quality of systematic reviews of observational nontherapeutic studies, *Preventing Chronic Disease* 7 (6): A133.

Smith, MA., Lisabeth, L. D., Bonikowski, F. & Morgenstern, L. B. (2010) The role of ethnicity, sex, and language on delay to hospital arrival for acute ischemic stroke, *Stroke* 41 (5): 905-909.

Solomon, M (2001) *Social Empiricism*, MIT: Cambridge.

Sonnemann, U (1954) *Existence and Therapy: An Introduction to Phenomenological Psychology and Existential Analysis*, Grune & Stratton: NY.

Southwick, C & Smith R (1986) The growth of primate field studies, Mitchell, G & Erwin, J (eds) (1986) *Comparative Primate Biology* 2A, 73-91, ARL: NY.

Stange, KC & Ferrer, RL (2009) The paradox of primary care, *Annals Family Medicine* 7: 293-299.

Stewart, S, Ryan, BL & Bodea, C (2011) Is Patient-Centred Care Associated with Lower Diagnostic Costs?, *Healthcare Policy* 6 (4): 27-31.

Stump, D (1992) Naturalized philosophy of science with a plurality of methods, *Philosophy of Science* 59: 456-60.

Sullivan, HS (1953) *The Interpersonal Theory of Psychiatry*, Norton: NY.

## T

Taleb, NN (2007) *The Black Swan: The Impact of the Highly Improbably*, Random House: NY.

Thagard, P (1999) *How Scientists Explain Disease*. Princeton UP: NJ.

— (2012) Mapping minds across cultures, Sun, R (ed) *Grounding Social Sciences in Cognitive Sciences*: 35–62. MIT: Cambridge.

Thomasma, DC (1983) Beyond medical paternalism and patient autonomy: a model of physician conscience for the physician-patient relationship, *Annals of Internal Medicine* 98 (2): 243-248.

## U

## V

van Dulmen, S (2011) The value of tailored communication for person-centred outcomes, *Journal of Evaluation in Clinical Practice* 17 (2): 381-383.

van Fraassen, BC (1976) To save the phenomena, Boyd, P; Gasper, P & Trout, JD (eds) (1992) *The Philosophy of Science*, 187-194, MIT: Cambridge.

— (1980) *The Scientific Image*. Oxford UP: Oxford.

van Staden, CW (2006) Mind, brain and person: reviewing psychiatry's constituency, *South African Psychiatry Review* 9: 93–96.

## W

Walsh, B & Gillett, G (2011) A post-structuralist view of evidence-based medicine (EBM): what EBM contributes to philosophy, *International Journal of Person Centered Medicine* 1 (2) 223-231.

Weed, E & Rooney, E (2010) What's the difference? The question of theory, *Differences* 21, 1: SI.

WHO, Health Education Network (2006) *What is the evidence on effectiveness of empowerment to improve health?*, Official Report.

WHO, Sixty-Second World Health Assembly (2009) *Primary Health Care, Including Health System Strengthening*. WHO. WHA62.12: Geneva.

Woodbridge, K & Fulford, KWM(2004) *Whose Values? A Workbook for Values-Based Practice in Mental Health Care*, The Sainsbury Centre for Mental Health: London.

WPA, World Psychiatric Association (2003) Essentials of the World Psychiatric Association's International Guidelines for Diagnostic Assessment (IGDA), *British Journal of Psychiatry* 182, 45: 37–s66.

## Y

Young, HN, Bell, RA, Epstein, RM, Feldman, MD & Kravitz, RL (2008) Physicians' shared decisionmaking behaviors in depression care, *Archives of Internal Medicine* 168 (13): 1404-1408.

## Z

Zangrilli, A, Ducci, G, Bandinelli, PL, Dooley, J, Mc-Cabe & Priebe, S (2014) How do psychiatrists address delusions in first meetings in acute care? A qualitative study, *BMC Psychiatry* 14: 178. doi:10.1186/1471-244X-14-178.

A

- Aisyaturridha A, Naing L, Nizar AJ. (2006) Validation of the Malay Brief Pain Inventory Questionnaire to measure cancer pain. *J Pain Symptom Manage* 31:13e21.
- Anderson KO, Dowds BN, Pelletz RE, et al (1995) Development and initial validation of a scale to measure self-efficacy beliefs in patients with chronic pain, *Pain* 63:77–83.
- Anderson KO, Syrjala KL, Cleeland CS: How to assess cancer pain, Turk DC, Melzack R, (eds.): *Handbook of pain assessment*, 579–600. Guilford Press: NY.
- Arnstein P (2000) The mediation of disability by self efficacy in different samples of chronic pain patients, *Disabil Rehabil* 22:794–801.
- Asghari A, Nicholas MK. An investigation of pain self-efficacy beliefs in Iranian chronic pain patients: a preliminary validation of a translated English-language scale. *Pain Med*. 2009;10:619–632.
- Asmundson, G. J., & Katz, J. (2009) Understanding the co-occurrence of anxiety disorders and chronic pain: state-of-the-art. *Depression and anxiety* 26(10), 888-901. doi:10.1002/da.20600
- Atkinson, T.M., Rosenfeld, B.D., Sit, L., Mendoza, T.R., Fruscione, M., Lavene, D., Shaw, M., Li, Y., Hay, J., Cleeland, C.S., Scher, H.I., Breitbart, W.S., Basch, E (2011) Using confirmatory factor analysis to evaluate construct validity of the Brief Pain Inventory, *Journal of Pain and Symptom Management* 41,3:558-565

B

- Bandura A (1977) Self-efficacy — toward a unifying theory of behavioral change, *Psychol Rev* 84:191–215
- Bandura A (1989) Human agency in social cognitive theory. *Am Psychol* 44:1175–1184.
- Bech P, Rasmussen N-A, Olsen LR, Noerholm V, Abildgaard W (2001) The sensitivity and specificity of the Major Depression Inventory, using the Present State Examination as

the index of diagnostic validity. *J Affect Disord* 66: 159-164.

- Beck, A.T., Epstein, N., Brown, G., & Steer, R.A. (1988) An inventory for measuring clinical anxiety: Psychometric properties. *Journal of Consulting and Clinical Psychology* 56, 893-897.
- Beck AT, Steer RA, Brown GK (1996) *Manual for the Beck Depression Inventory-II*, San Antonio, TX, Psychological Corporation.
- Beck, A. T., Ward, C. H., Mendelson, M. M., Mock, J., & Erbaugh, J (1961) An inventory for measuring depression. *Archives of General Psychiatry* 4, 561-571.
- Benyon K, Hill S, Zadurian N, et al (2010) Coping strategies and self-efficacy as predictors of outcome in osteoarthritis: a systematic review, *Musculoskeletal Care* 8:224–236.
- Bowling A (2005) Mode of questionnaire administration can have serious effects on data quality, *Journal of public health* 27 (3): 281–91.
- Brazier, J., Deverill, M., Green, C., Harper, R. and Booth, A (1999) A review of the use of health status measures in economic evaluation. NHS R&D HTA programme, *Health Technology Assessment* 3(9). NP.
- Broderick JE, Junghaenel DU, Turk DC (2004) Stability of patient adaptation classifications on the multidimensional pain inventory, *Pain* 109(1-2):94-102.
- Brown GK, Nicassio PM (1987) Development of a questionnaire for the assessment of active and passive coping strategies in chronic pain patients, *Pain* 31:53–64.
- Bunketorp L, Carlsson J, Kowalski J, Steiner-Victorin E (2005) Evaluating the reliability of multi-item scales: a non-parametric approach to the ordered categorical structure of data collected with the Swedish version of the Tampa Scale for Kinesiophobia and the Self-Efficacy Scale. *J Rehabil Med*. 37(5):330-4.
- Burn, D (2002) Beyond the iron mask: Towards better recognition and treatment of depression associated with Parkinson's disease, *NJJM* 17, Issue3 445-454
- Busch V, Haas J, Cronlein T, Pieh C, Geisler P, Hajak G, Eichhammer P (2012) Sleep deprivation in chronic somatoform pain-effects on mood and pain regulation. *Psychiatry Res* 195:134–43.

Buysse, Daniel J.; Reynolds, Charles F.; Monk, Timothy H.; Berman, Susan R.; Kupfer, David J. (1989) The Pittsburgh sleep quality index: A new instrument for psychiatric practice and research, *Psychiatry Research* 28 (2): 193–213. doi:10.1016/0165-1781(89)90047-4.

## C

Cartwright, ND (1999) *The Dappled World: A Study of the Boundaries of Science*. Cambridge UP: Cambridge.

Chibnall JT Tait RC (1994) The Pain Disability Index: Factor Structure and Normative Data. *Arch Phys Med Rehabil* 75: 1082-1086.

Chou R, Shekelle P (2010) Will this patient develop persistent disabling low back pain? *JAMA*: 303:1295–1302.

Cleeland CS, Ryan KM (1994) Pain assessment: global use of the Brief Pain Inventory, *Annals of the Academy of Medicine*, Singapore 23:129–138.

Cohen TR, Wolf ST, Panter AT, Insko CA (2011) Introducing the GASP Scale: A New Measure of Guilt and Shame Proneness. *J Pers Soc Psychol* 100(5):947–66. doi: 10.1037/a0022641 PMID: 21517196

Cole, J.C.; Motivala, S.J.; Buysse, D.J.; Oxman, M.N.; Levin, M.J.; Irwin, M.R. (2006) Validation of a 3-factor scoring model for the Pittsburgh Sleep Quality Index in older adults, *SNYTW* 29(1): 112–116. doi:10.1093/sleep/29.1.112.

## D

Daut RL, Cleeland GS, Flanery RC (1983) Development of the Wisconsin Brief Pain Questionnaire to assess pain in cancer and other diseases. *Pain* 17:197e210.

de Gagné TA, Mikail SF, D'Eon JL (1995) Confirmatory factor analysis of a 4-factor model of chronic pain evaluation. *Pain* 60:195–202.

deGood DE, & Cook AJ (2011) Psychosocial assessment: comprehensive measures and measures specific to pain beliefs and coping, Turk DC, Melzack R (eds.) *Handbook of pain assessment*, 67–97. Guilford: NY.

Dworkin RH, Turk DC, Farrar JT, Haythornthwaite JA, Jensen MP, Katz NP, Kerns RD,

Stucki G, Allen RR, Bellamy N, Carr DB, Chandler J, Cowan P, Dionne R, Galer BS, Hertz S, Jadad AR, Kramer LD, Manning DC, Martin S, McCormick CG, McDermott MP, McGrath P, Quessy S, Rappaport BA, Robbins W, Robinson JP, Rothman M, Royal MA, Simon L, Stauffer JW, Stein W, Tollett J, Wernicke J, Witter J (2005) Core outcome measures for chronic pain clinical trials: IMMPACT recommendations. *Pain* 113(1-2):9-19.

## E

Edwards AL (1957) *Techniques of attitude scale construction*. New York: Appleton.

Elliott, T, Shewchuk, R, & Richards, J.S. (2001) Family caregiver problem solving abilities and adjustment during the initial year of the caregiving role. *Journal of Counseling Psychology* 48, 223-232.

Erdman RAM, Passchier J, Kooijman M, et al (1993) The Dutch version of the Nottingham Health Profile: Investigations of psychometric aspects. *Psych Reports*; 72: 1027-1035.

Essink-Bot M, Krabbe PFM, Bonsel GJ, et al. (1997) An empirical comparison of four generic health status measures: The Nottingham Health Profile, the Medical Outcomes Study 36-item Short-Form Health Survey, the COOP/WONCA Charts, and the Euro-Qol Instrument. *Med Care* 35: 522-537.

## F

Fairbank JC, Couper J, Davies JB, O'Brien JP (1980) The Oswestry Low Back Disability Questionnaire. *Physiotherapy* 66:271-3.

Fava GA (1983) Assessing depressive symptoms across cultures: Italian validation of the CES-D self-rating scale. *J Clin Psychol* 39(2):249-51.

Finan PH, Goodin BR, Smith MT (2013) The association of sleep and pain: an update and a path forward. *J Pain* 14:1539–52.

## G

- Giere, RN (2006a) *Scientific Perspectivism*. Chicago: University of Chicago Press.
- (2006b) Perspectival pluralism, Kellert, S; Longino, HE & Kenneth Waters, C (eds.) *Minnesota Studies in the Philosophy of Science*, vol XIX, Scientific Pluralism: 26-41, Minnesota UP: London.
- Gilbert, P., & Procter, S. (2006) Compassionate mind training for people with high shame and self-criticism: overview and pilot study of a group therapy approach. *Clinical psychology and Psychotherapy* 13, 353–379.
- Gilbert, P. (2009) *The Compassionate Mind*. London: Copyright.
- Goldberg DP, Rickels K, Downing R, et al (1976) A comparison of two psychiatric screening tests, *British Journal of Psychiatry* 129:61–67.
- Goldie, PL (2000) *The Emotions*, Oxford UP: Oxford.
- (2002a) Emotions, Feelings and Intentionality, *Phenomenology and the Cognitive Sciences* 1: 235-254
- (2002b) Emotion, personality and simulation», Goldie, PL (ed.) (2002) *Understanding Emotions: Mind and Morals*, 97-109. Ashgate P: Aldershot.
- (2003) Narrative and perspective; values and appropriate emotions, Hatzimoyssis, A (ed.) (2003) *Philosophy and the Emotions*, 201-220. Cambridge UP: Cambridge.
- Grenon P, Smith B, Goldberg L (2004) Biodynamic ontology: applying BFO in the biomedical domain. *Stud Health Technol Inform*, 102:20–38.
- Grove, J.R., & Prapavessis, H. (1992) Preliminary evidence for the reliability and validity of an abbreviated Profile of Mood States. *International Journal of Sport Psychology*, 23, 93-109.

## H

- Hamilton, M (1980) Rating depressive patients. *Journal of Clinical Psychiatry* 41: 21-24.

- Harding, S (1991) *Whose Science? Whose Knowledge?* Cornell UP: NY.
- (1993) Rethinking standpoint epistemology: what is strong objectivity?, Alcoff, L & Potter, E (eds.) (1993) *Feminist Epistemologies*, Routledge: London.
- Harland, N & Georgieff, K (2003) Development of the Coping Strategies Questionnaire 24, a Clinically Utilitarian Version of the Coping Strategies Questionnaire. *Rehabilitation Psychology* 48,4, 296–300.
- Harmon-Jones E, Harmon-Jones C (2010) On the relationship of trait PANAS positive activation and trait anger: Evidence of a suppressor relationship. *J Res Pers* 44(1):120–3.
- Harmon-Jones C, Bastian B, Harmon-Jones E (2016) The Discrete Emotions Questionnaire: A New Tool for Measuring State Self-Reported Emotions. *PLoS One* 11(8):e0159915. doi:10.1371/journal.pone.0159915
- Haythornthwaite JA, Hegel MT, Kerns RD (1991) Development of a sleep diary for chronic pain patients, *Journal of Pain and Symptom Management* 6:65–72.
- Helsel, W. J., & Matson, J. L (1984) The assessment of depression in children: The internal structure of the Child Depression Inventory (CDI). *Behavior Research and Therapy*, 22(3), 289–298.
- Hishinuma, E.S., Miyamoto, R.H., Nishimura, S.T., y Nahulu, L.B. (2000) Differences in State-Trait Anxiety Inventory Scores for ethnically diverse adolescents in Hawaii. *Cultural Diversity and Ethnic Minority*, 6, 73-83.
- Hockenberry MJ, Wilson D (2009) *Wong's Essentials of Pediatric Nursing, 8th Edition*. St. Louis: Mosby.
- Hodges, K. & Craighead, W. E. (1990) Relationship of Children's Depression Inventory factors to diagnosed depression. *Psychological Assessment* 2(4), 489–492.
- Hunt SM, McKenna SP, McEwen J, et al (1980) A quantitative approach to perceived health status: a validation study, *Journal of Epidemiology and Community Health* 34:281–286.
- Hunt SM, McEwen J, McKenna SP. (1985) Measuring health status: A new tool for clinical

- cians and epidemiologists. *J R Coll Gen Pract* 35: 185-188
- Huskinson, E.C., Visual analogue scales. In: R. Melrack (ed.) (1983) *Pain Measurement and Assessment*, 33-37. Raven Press, NY.
- I
- J
- Jans, M.P., Schellevis, F.G., Eijk, J.T.M (1999) The Nottingham Health Profile: score distribution, internal consistency and validity in asthma and COPD patients. *Quality of Life Research*: 8(6), 501-507 .
- Jensen MP, Turner JA, Romano JM, Lawler BK. (1994) Relationship of pain-specific beliefs to chronic pain adjustment. *Pain* 57(3):301-9.
- Jensen MP, Turner JA, Romano JM, Strom SE. (1995) The Chronic Pain Coping Inventory: development and preliminary validation. *Pain* 60(2):203-16.
- Jensen MP, Turner JA, Romano JM (2001) Changes in beliefs, catastrophizing, and coping are associated with improvement in multidisciplinary pain treatment. *J Consult Clin Psychol.* 69(4):655-62.
- Jensen MP, Ehde DM, Hoffman AJ, et al (2002) Cognitions, coping and social environment predict adjustment to phantom limb pain, *Pain* 95:133–142.
- Jensen MP (2003) The validity and reliability of pain measures in adults with cancer, *Journal of Pain* 4:2–21.
- Johannesson, M, Jonsson, B and Karlsson, G. (1996) Outcome measurement in economic evaluation. *Health Economics* 5: 279-96.
- Johns MW (1991) A new method for measuring daytime sleepiness: the Epworth sleepiness scale , *Sleep.* 14 (6): 540–5.
- K
- Kerns, RD & Turk, DC (1983) Conceptual issues in the assessment of clinical pain. International, *Journal of Psychiatry Medical* 13, 15-26.
- Kerns, RD & Turk, DC, & Rudy, TE (1985) The West Haven-Yale Multidimensional Pain Inventory (WHYMPI) *Pain*, 23, 345-356.
- Kitcher, P (1993) *The Advancement of Science*, Oxford U P: Oxford.
- Klepstad P, Håvard L, Borchgrevink PC, et al (2002) The Norwegian Brief Pain Inventory Questionnaire: translation and validation in cancer pain patients. *J Pain Symptom Manage* 24:517e525
- Klevsgård R, Froberg BL, Risberg B, et al (2002) Nottingham Health Profile and Short-Form 36 Health Survey questionnaires in patients with chronic lower limb ischemia: before and after revascularization, *Journal of Vascular Surgery* 36:310–317.
- Kozaki, K; Kou, H; Yamagata, Y; Imai, T; Ohe; K & Mizoguchi R (2012) *Browsing causal chains in a disease ontology*, Poster & Demo Notes of 11th International Semantic Web Conference. The Semantic Web Science Association (SWSA): Boston.
- L
- Lallukka T, Overland S, Haaramo P, Saastamoinen P, Bjorvatn B, Sivertsen B (2014) The joint contribution of pain and insomnia to sickness absence and disability retirement: a register-linkage study among Norwegian and Finnish employees. *Eur J Pain* 18:883–92.
- Lefebvre JC, Keefe FJ (2002) Memory for pain: the relationship of pain catastrophizing to the recall of daily rheumatoid arthritis pain, *Clinical Journal of Pain* 18:56–63.
- Li D, Puntillo K, Miaskowski C (2008) A review of objective pain measures for use with critical care adult patients unable to self-report. *J Pain* 9:2–10.
- Longino, H (1990) *Science as Social Knowledge*, Princeton UP: Princeton.
- (2001) *The Fate of Knowledge*, Princeton UP: Princeton.
- Loomes, G., Jones-Lee, M.W. and Robinson, A. (1994) *What do visual analogue scales really measure?* HESG: Newcastle.
- Lundberg MKE, Styf J, Carlsson SG (2004) A psychometric evaluation of the Tampa Scale for Kinesiophobia – from a physiotherapeu-

tic perspective. *Physiotherapy Theory and Practice* 20(2):121-133.

## M

McCracken, L (1998) Learning to live with pain: acceptance of pain predicts adjustment in persons with chronic pain. *Pain* 74, 21-27.

—(2005) Social context and acceptance of chronic pain: the role of solicitous and punishing responses. *Pain* 113, 155-159.

McCracken LM, Dhingra L (2002) A short version of the Pain Anxiety Symptoms Scale (PASS-20): preliminary development and validity. *Pain Res Manag* 7(1):45-50.

McCracken, L., & Eccleston, C. (2003) Coping or acceptance: What to do about chronic pain? *Pain* 105, 197-204.

McCracken LM, Samuel VM (2007) The role of avoidance, pacing, and other activity patterns in chronic pain, *Pain* 130:119-125.

McCracken, L., Vowles, K. & Eccleston, C. (2004). Acceptance of chronic pain: Component analysis and a revised assessment method. *Pain*, 107, 159-166. —Also in *Research and Therapy*, 43, 1335-1346.

McCracken, L., & Vowles, K. (2008) A prospective analysis of acceptance of pain and values-based action in patients with chronic pain. *Health Psychology* 27, 215-220.

McCracken, L., & Yang, S. (2006) The roles of values in a contextual cognitive-behavioral approach to chronic pain. *Pain* 123, 137-145.

McCracken LM, Zayfert C, Gross RT (1992) The Pain Anxiety Symptoms Scale: development and validation of a scale to measure fear of pain, *Pain* 50:67- 73.

McCullough ME, Emmons RA, Tsang JA (2002) The grateful disposition: a conceptual and empirical topography. *J Pers Soc Psychol.* 82(1):112.

McGrath PA, Seifert CE, Speechley KN, et al (1996) A new analogue scale for assessing children's pain: an initial validation. *Pain* 64: 435-43.

McGrath PA, Gillespie J (2001) Pain assessment in children and adolescents, Turk DC,

Melzack R, (eds.) *Handbook of Pain Assessment*, 97-118.

McNair et al. (NP) (1971) *Manual for the Profile of Mood States*. Educational and Industrial Testing Service: San Diego, CA.

McWilliams LA, Goodwin RD, Cox BJ (2004) Depression and anxiety associated with three pain conditions: results from a nationally representative sample, *Pain* 111:77-83.

Melzack, R (1961) The perception of pain, *Sci Am* 204: 197-210.

Melzack R & Wall P.D. (1962) On the nature of cutaneous sensory mechanisms. *Brain*, 85: 331-356.

Melzack R. & Wall P.D. Pain mechanisms: a new theory. *Science*, 150: 971-979, 1965.

Melzack R. & Casey K.L. (1968) Sensory, motivational and central control determinants of pain, Kenshalo D.R (ed.) *The Skin Senses*, 423-439. Charles C. Thomas Publisher: Springfield, Illinois.

Melzack R & Torgerson WS (1971) On the language of pain. *Anesthesiology* 34:50-9.

Melzack R. (1975) The McGill Pain Questionnaire: Major properties and scoring methods. *Pain* 1: 277-299.

—(1987) The short-form McGill Pain Questionnaire. *Pain* 30:191-7.

Meyer-Rosberg K, Burckhardt CS, Huizar K, et al (2001) A comparison of the SF-36 and Nottingham Health Profile in patients with chronic neuropathic pain, *European Journal of Pain* 5:391-403.

Miles, CL, Tamar Pincus, MSc, MPhil, Dawn Carnes, BSc, Stephanie J.C. Taylor, & Martin Underwood (2011) Measuring Pain Self-efficacy, *The Clinical journal of pain* 2011, NP: DOI: 10.1097/AJP.0b013e318208c8a2

Miller RP, Kori SH, Todd DD (1991, original v.) *The Tampa Scale*, Tampa, FL, 1991, NP.

Miró J, Huguet A, Nieto R, Paredes S, Baos J. (2005) Assessment of the faces pain scale-revised for measuring pain severity in children. *Rev Soc Esp Dolor* 12: 407-416.

Montgomery SA, Åsberg M (1979) A new depression scale designed to be sensitive to change, *British Journal of Psychiatry* 134 (4): 382-9.

- Monti JM, Monti D (2007) The involvement of dopamine in the modulation of sleep and waking. *Sleep Med Rev* 11:113–33.
- Monticone, M., Ferrante, S., Giorgi, I., Galandra, C., Rocca, B., & Foti, C. (2014) The 27-item coping strategies questionnaire-revised: confirmatory factor analysis, reliability and validity in Italian-speaking subjects with chronic pain. *Pain research & management* 19(3), 153-8.
- Mphahlele, Noko, Duncan Mitchell, Peter Karmnerman (2008) Validation of the Wisconsin Brief Pain Questionnaire in a Multilingual South African Population of 2008, *Journal of Pain and Symptom Management* 36, 4, 396-412.
- Mystakidou K, Mendoza T, Tsilika E, et al (2001) Greek Brief Pain Inventory: validation and utility in cancer pain. *Oncology* 60:35e42.

## N

- Neff, K. (2003a) The development and validation of a scale to measure. Self Compassion Scale. *Self and Identity* 2, 223– 250.
- (2003b) Self-compassion: An alternative conceptualization of a healthy attitude toward oneself. *Self and Identity* 2, 85–101.
- Nicholas MK (2007) The pain self-efficacy questionnaire: taking pain into account. *Eur J Pain*. 11:153–163.

## O

- O'Brien EM, Waxenberg LB, Atchison JW, Gremlion HA, Staud RM, McCrae CS, Robinson ME (2010) Negative mood mediates the effect of poor sleep on pain among chronic pain patients. *Clin J pain* 26:310–19.
- Olsen LR, Jensen DV, Noerholm V, Martiny K, Bech P (2003) The internal and external validity of the Major Depression Inventory in measuring severity of depressive states. *Psychol Med* 33, 351-356.

## P

- Pan South African Language Board (2000) *Language use and language interaction in South Africa: A national sociolinguistic survey*. Pan South African Language Board: Pretoria
- Pollard CA (1984) Preliminary validity study of the pain disability index. *Perceptual and Motor Skills* 59: 974.
- Price DD, McGrath PA, Rafii A, Buckingham B. (1983) The validation of visual analogue scales as ratio scale measures for chronic and experimental pain. *Pain* 17:45–56.
- Prieto L, Alonso J, Ferrer M, et al (1997) Are results of the SF-36 Health Survey and the Nottingham Health Profile similar?: A comparison in COPD patients. *J Clin Epidemiol* 50: 463-473.

## Q

## R

- Radloff LS (1977) The CES-D scale: a self report depression scale for research in the general population, *Applied Psychological Measures* 1:385–401.
- Radloff LS, Locke BZ (1977) The Community Mental Health Assessment Survey and the CES-D scale, Weissman M, Myers J, Ross C, (eds.) *Community Surveys*. Piscataway: 177–189. Rutgers UP: NY.
- Robinson, A., Loomes, G. & Jones-Lee, M. (2001) Visual Analogue Scales, Standard Gamble and Relative risk aversion. *Medical Decision Making* 21(1):17-27.
- Robinson ME, Riley JL 3rd, Myers CD, Sadler IJ, Kvaal SA, Geisser ME, Keefe FJ (1997) The Coping Strategies Questionnaire: a large sample, item level factor analysis, *Clin J Pain* 13(1):43-9.
- Roehrs T, Hyde M, Blaisdell B, Greenwald M, Roth T (2006) Sleep loss and REM sleep loss are hyperalgesic. *Sleep* 29:145–51.
- Roelofs J, van Breukelen G, Sluiter J, et al (2011) Norming of the Tampa Scale for kinesiophobia across pain diagnoses and various countries, *Pain* 152:1090–1095.



- Rosenstiel AK, Keefe FJ (1983) The use of coping strategies in chronic low back pain patients: relationship to patient characteristics and current adjustment, *Pain* 17:33–44.
- Rudy TE (1989) *Multiaxial assessment of pain. Multidimensional pain inventory*. U Pittsburgh, School of Medicine: Pittsburgh.
- S
- Schuh-Hofer S, Wodarski R, Pfau DB, Caspani O, Magerl W, Kennedy JD, Treede RD (2013) One night of total sleep deprivation promotes a state of generalized hyperalgesia: a surrogate pain model to study the relationship of insomnia and pain. *Pain* 154:1613–21.
- Shiota MN, Keltner D, John OP (2006) Positive emotion dispositions differentially associated with Big Five personality and attachment style. *J Posit Psychol* 1; 1(2):61–71.
- Smith MT, Perlis ML, Smith MS, et al (2000) Sleep quality and presleep arousal in chronic pain, *Journal of Behavioral Medicine* 23:1–13.
- Spielberger, C.D. (1989) *State-Trait Anxiety Inventory: A comprehensive bibliography* (2a ed.) Consulting Psychologists Press: PA.
- Spielberger, C.D., y Díaz-Guerrero, R. (eds.) (1976) *Cross-cultural anxiety*. Hemisphere/Wiley: Washington DC.
- (1983) *Cross-cultural anxiety II*. Hemisphere/Wiley: Washington DC.
- (1986) *Cross-cultural anxiety III* Hemisphere/Wiley: Washington DC.
- (eds.) (1990) *Cross-cultural anxiety IV*. Hemisphere/Wiley: Washington DC.
- Spielberger, C.D., Gorsuch, R., y Lushene, R. (1970) *Manual for the State-Trait Anxiety Inventory*, Consulting Psychologist Press: PA.
- Spielberger, C.D., Gorsuch, R.L., y Lushene, R. (1982) *Manual del Cuestionario de Ansiedad Estado/Rasgo (STAI)*, TEA: Madrid.
- Spielberger, C. D., Gorsuch, R. L., Lushene, R., Vagg, P. R., & Jacobs, G. A. (1983) *Manual for the State-Trait Anxiety Inventory*. Consulting Psychologists Press: PA
- Stacey BR, Swift JN (2006) Pregabalin for neuropathic pain based on recent clinical trials, *Current Pain and Headache Reports* 10:179–184, 2006.
- Strong J, Ashton R, Chant D (1992) The measurement of attitudes towards and belief about pain. *Pain* 38(2):227–36.
- Svanborg, P; Åsberg, M (2001) A comparison between the Beck Depression Inventory (BDI) and the self-rating version of the Montgomery Åsberg Depression Rating Scale (MADRS), *J. Affective Disorders*. 64 (2-3): 203–216.
- Suzuki, T., Tsukamoto, K., y Abe, K. (2000) Characteristic factor structures of the Japanese version of the State-Trait Anxiety Inventory: Coexistence of positive-negative and State-Trait Factor Structures. *Journal of Personality Assessment*, 74, 447–458.
- T
- Tait RC Chibnall JT Krause S (1990) The pain disability index: psychometric properties. *Pain* 40: 171–182.
- Tait RC, Chibnall JT (1997) Development of a brief version of the Survey of Pain Attitudes. *Pain* 70(2/3):229–35.
- Tait RC, Pollard CA, Margolis RB, et al (1987) The Pain Disability Index: psychometric and validity data, *Archives of Physical Medicine and Rehabilitation* 68:438–441.
- Thompson M, McCracken LM (2011) Acceptance and related processes in adjustment to chronic pain, *Current Pain and Headache Reports* 15:144–151.
- Tompkins M, Plante M, Monchik K, et al (2011) The use of a non-benzodiazepine hypnotic sleep-aid (zolpidem) in patients undergoing ACL reconstruction: a randomized controlled clinical trial. *Knee Surgery, Sports Traumatology, Arthroscopy* 19:787–791.
- Turk DC, Okifuji A, Sinclair JD, et al (1998) Interdisciplinary treatment for fibromyalgia syndrome: clinical and statistical significance, *Arthritis Care Research* 11:186–195.
- Turk, D. C., & Monarch, ES (2002) Biopsychosocial perspective on chronic pain, D. C. Turk & R. J. Gatchel (eds.), *Psychological approaches to pain management: A practitioner's handbook* (2nd ed.) Guilford: NY.

- Turk, DC & Rudy, TE (1986) Assessment of cognitive factors in chronic pain: a worthwhile enterprise?, *Journal of Consulting and Clinical Psychology*, 54(6), 760-768.
- U
- V
- Veehof MM, Oskam MJ, Schreurs KM, et al (2011) Acceptance-based interventions for the treatment of chronic pain: a systematic review and meta-analysis, *Pain* 152:533–542.
- Viane, I., Crombez, G., Eccleston, C., Poppe, C., Devulder, J., Van Houdenhove, B., & De Corte, W. (2003) Acceptance of pain is an independent predictor of mental well-being in patients with chronic pain: empirical evidence and reappraisal, *Pain* 106, 65–72.
- Vowles KE, McCracken LM, McLeod C, et al (2008) The Chronic Pain Acceptance Questionnaire: confirmatory factor analysis and identification of patient subgroups, *Pain* 140:284–291.
- Vowles KE, Wetherell JL, Sorrell JT (2009) Targeting acceptance, mindfulness, and values-based action in chronic pain: findings of two preliminary trials of an outpatient group-based intervention, *Cognitive Behavioural Practice* 16:49–58.
- W
- Waddell G, Main CJ (1984) Assessment of severity in low back disorders. *Spine* 9:204-8.
- Waddell G, Newton M, Henderson I, et al (1993) A Fear-Avoidance Beliefs Questionnaire (FABQ) and the role of fear-avoidance beliefs in chronic low back pain and disability, *Pain* 52:157–168.
- Waldman, D (2009) Ch. §222 - Pain Assessment Tools for Adults, *Pain Review* 2009, 375-380.
- Wall, PD (1960) Cord cells responding to touch, damage and temperature skin, *J Neurophysiol* 23: 197-210.
- Ward SE, Goldberg N, Miller-McCauley V, et al (1993) Patient-related barriers to management of cancer pain, *Pain* 52:319–324.
- Wilson, K. G., Mikail, S. F., D'Eon, J. L., & Mins, J. E. (2001) Alternative criteria for major depressive disorder in patients with chronic pain. *Pain*, 91, 227-234
- Wu, J.S.Y., Beaton, D., Smith, P.M., Hagen, N.A (2010) Patterns of Pain and Interference in Patients with Painful Bone Metastases: A Brief Pain Inventory Validation Study, *J Pain Symptom Manage* 39: 230-240
- X
- Y
- Yamagata, Y; Kou, H; Kozaki, K; Imai, T; Ohe, K & Mizoguchi, R (2013) Ontological model of abnormal states and its application in the medical domain, *4th International Conference on Biomedical Ontology: 28–33*. ICBO2013: Montreal.
- Z
- Zuckerman M, Lubin B, Robins S (1965) Validation of the multiple affect adjective check list in clinical situations. *J Consult Psychol* 31; 29(6):594.
- Zung WW (1965) A self-rating depression scale. *Archives of General Psychiatry* 12: 63-70

A

Arias, M (2011) Neurología de la risa y del humor: risa y llanto patológicos, *Rev Neurol* 53: 415-21.

B

BonJour, L. (2010) *Recent work on the internalism-externalism controversy. A Companion to epistemology*. Blackwell: Oxford.

Bourke, J (2003) Fear and anxiety: Writing about emotion in modern history, *History Workshop Journal* NP: 111-133.

—(2014) *The story of pain, from prayer to painkillers*, Oxford UP: NY.

C

Castañeda, HN (1968) On the logic of attributions of self-knowledge to others, *The Journal of Philosophy* 65:439-456.

D

E

Eichenbaum, H (2008) *Learning and Memory*, Norton: NY.

F

G

Gammerl, B (2012) Emotional styles: Concepts and challenges, *Rethinking history: The journal of theory and practice* 16: 161-175.

Goldie, PL (2000) *The Emotions*, Oxford UP: Oxford.

—(2002a) Emotions, Feelings and Intentionality, *Phenomenology and the Cognitive Sciences* 1, 235-254.

—(2002b) Emotion, personality and simulation, Goldie, PL (ed.) (2002) *Understanding Emotions: Mind and Morals*, 97-109. Ashgate P: Aldershot.

—(2003) Narrative and perspective; values and

appropriate emotions, Hatzimoysis, A (ed.) (2003) *Philosophy and the Emotions*, 201-220, Cambridge UP: Cambridge.

—(2004) What people will do: personality and prediction, *Richmond Journal of Philosophy* 7 (Summer): 1-9.

Goldman, A (1979) What Is Justified Belief?, G. Pappas (ed), *Justification and Knowledge*, 1-23. Dordrecht: Reidel.

Green, M (2017) Illocution and Empathy, *Philosophia* 45:881-893 doi 10.1007/s11406-017-9872-6

Griffiths, PE & Scarantino, A (2009) Emotions in the wild: The situated perspective on emotion, Robbins, P & Aydede, M (ed.) *The Cambridge handbook of situated cognition*, Cambridge UP: Cambridge.

H

Hatfield, E., Cacioppo, J. T., & Rapson, R. L. (1992) Primitive emotional contagion, M. S. Clark (ed.) *Emotion and Social Behavior: Review of Personality and Social Psychology*: 151-177. NP.

Hatfield, E., Rapson, R. L., & Le, Y.-C. L. (2009) Emotional contagion and empathy, J. Decety & W. Ickes (eds.), *The social neuroscience of empathy*, 19-31. MIT Press. Cambridge.

Haugh, M (2013) Speaker meaning and accountability in interaction, *Journal of pragmatics* 48: 41-56.

Hebb, DO (1949) *Organization of Behavior: a Neuropsychological Theory*, Wiley: NY.

I

J

K

Kaplan, D (1977) Demonstratives, J. Almog, J. Perry & H. Wettstein (eds.) *Themes from Kaplan*, 481-563. OUP: Oxford.

Kim, JJ & Baxter, MG (2001) Multiple brain-memory systems: the whole does not equal the sum of its parts, *Trends Neurosci* 24: 1030-1038.

- Kölbel, M (2002) *Truth Without Objectivity*. London: Routledge.
- Kölbel, M (2008) “True” as ambiguous, *Philosophy and Phenomenological Research* 77: 359–384.
- Kripke, S (1979) A puzzle about belief, A. Margalit (ed.) *Meaning and Use*, 239–83. Dordrecht: Reidel.
- Kurth, F, Zilles, K, Fox, PT, Laird, AR & Eickhoff, SB (2010) A link between the systems: functional differentiation and integration within the human insula revealed by meta-analysis, *Brain Struct Funct* 214 (5–6): 519–534.
- L
- Le Géner, A (ed.) (2002) *Olfaction and cognition: a philosophical and psychological view, Olfaction, Taste and Cognition*, Cambridge UP: NY.
- Leys, R (2011) The turn to affect: a critique, *Critical Inquiry* 37: 434–472.
- M
- MacFarlane, John (2005). Making sense of relative truth, *Proceedings of the Aristotelian Society*, 105: 321–339.
- (2007) Relativism and disagreement, *Philosophical Studies* 132: 17–31.
- (2014) *Assessment sensitivity: Relative Truth and its Applications*. Oxford UP: Oxford.
- McDowell, JH (1998) *Meaning, Knowledge and Reality*, Harvard UP: Cambridge.
- McGurk, H & McDonald, J (1976) Hearing lips, seeing voices, *Nature* 264: 746–8.
- Melero, H, Peña-Melián, A, Ríos-Lago, M, Pajares, G, Hernández-Tamames, JA & Álvarez-Linera, J (2013) Grapheme-color synesthetes show peculiarities in their emotional brain: cortical and subcortical evidence for VBM analysis of 3D-T1 and DTI data, *Exp Brain Res* 227: 343–353.
- Mobbs, D, Hagan, CC, Azim, E, Menon, V & Reiss, AL (2005) Personality predicts activity in reward and emotional regions associated with humor, *Proc Natl Acad Sci USA* 102, 16502–6.
- Morrot, G, Brochet, F & Dubourdieu, D (2001) The color of odors, *Brain Lang* 79: 309–320.
- N
- Nagel, J. (2014) *Knowledge*. Oxford UP: NY.
- O
- Overgaard, S (2007) *Wittgenstein and other minds*, Routledge: SP.
- P
- Parvizi, J, Coburn, KL, Shillcutt, SD, Coffey, CE, Lauterbach, EC & Méndez, MF (2009) Neuroanatomy of pathological laughing and crying: a report of the American Neuropsychiatric Association Committee on Research, *J Neuropsychiatry Clin Neurosci* 21: 75–87.
- Patel, R, Lloyd, Th, Jackson, R, Ball, M, Shetty, H, Broadbent, M, Geddes, JR, Stewart, R, McGuire, P & Taylor, M (2015) Mood instability is a common feature of mental health disorders and is associated with poor clinical outcomes, *BMJ Open*, e007504. doi:10.1136/bmjopen-2014-007504.
- Perry, J (1979) The problem of the essential indexical, *Noûs* 13: 3–21.
- Predelli, S (2002) Intentions, indexicals, and communication, *Analysis* 62, 310–16 .
- Q
- R
- Read, S (1994/2002) Formal and material consequence, *JPL* 23: 247–65.
- Reddy, WM (2001) *The navigation of feeling: A framework for the history of emotions*, Cambridge UP: Cambridge.
- Reger, J (ed) (2005) *Different Wavelengths:*

- Studies of the Contemporary Women's Movements*, Routledge: NY.
- Reich, W (2010) *Análisis del Carácter*, Paidós Surcos 5a: Madrid.
- Rosenwein, B (2006) *Emotional communities in the early middle ages*, Cornell University: Ithaca-New York.
- Rugema, L, Mogren, I, Ntaganira, J & Krantz, G (2015) Traumatic episodes and mental health effects in young men and women in Rwanda, 17 years after the genocide, *BMJ Open*, e006778. doi:10.1136/bmjopen2014-006778.
- S
- Salmon, N (1986) *Frege's Puzzle*. MIT Press: cambridge.
- Scheer, M (2012) Are emotions a kind of practice (and is that what makes them have history)? A Bourdieuan approach to understanding emotion, *History and theory* 51: 193-220.
- Schiffer, S (1987) The "Fido"-Fido theory of belief, Tomberlin, J (ed.) (1987) *Philosophical Perspectives*, 455-480. Ridgeview: Atascadero.
- Shepherd, G (2012) *Neurogastronomy. How the Brain Creates Flavor and Why It Matters* Columbia UP: NY.
- Shoemaker, S (1968) Self reference and self-awareness. *The Journal of Philosophy*, 65, 555-567 .
- Skorupski (2007) Internal reasons and the scope of blame, Alan Thomas (ed.) *Bernard Williams*, 74. Cambridge UP: Cambridge
- T
- Tanaka, M & Sumitsuji, N (1991) Electromyographic study of facial expressions during pathological laughing and crying, *Electromyo Clin Neurophysiol* 31:399-406.
- U
- V
- W
- Wikan, U (1990) *Managing Turbulent Hearts*, Chicago UP: Chicago.
- (1992) Beyond the words: the power of resonance, *American Ethnologist* 19: 460-482.
- Williams, B (1981) *Internal and External Reasons* (Moral Luck) Cambridge: Cambridge University Press.
- (1995) Internal Reasons and the Obscurity of Blame, 1989, reprinted — *Making Sense of Humanity, and Other Philosophical Papers 1982–1993*, Cambridge UP: Cambridge.
- (2001) Postscript: Some Further Notes on Internal and External Reasons, Elijah Millgram (ed.) *Varieties of Practical Reasoning*, Cambridge: MIT Press,.
- Witek, M (2014) An interactional account of illocutionary practice, *Language Sciences* 47 (2015) 43–55 <http://dx.doi.org/10.1016/j.langsci.2014.08.003>
- X
- Y
- Yu, Y, Lui, Zi-wei, Hu, Mi, Liu, Xi-guang, Liu, Hui-ming, Yang, JP, Zhou, L & Xiao, SY (2015) Assessment of mental health literacy using a multifaceted measure among a Chinese rural population, *BMJ Open*, e009054. doi:10.1136/bmjopen-2015-009054.
- Z
- Zald, DH & Pardo, JV (1997) Emotion, olfaction, and the human amygdala: amygdala activation during aversive olfactory stimulation, *Proc Nat Acad Sci USA* 94, 4119-4124.

A

Abbott, A (2002) Brain implants show promise against obsessive disorder, *Nature* 419 (octubre), 658.

Agmon-Snir, H & Segev, I (1996) The concept of decision points as a tool in analyzing dendritic computation, Bower, JM (ed.) *Computational Neuroscience*, 41-46, Academy P: NY.

Aucher, G. (2003) *A Combination System for Update Logic and Belief Revision*, Master's thesis, ILLC, University of Amsterdam.

Austin, JL (1975) *How to do things with words*. Oxford: Clarendon Press [Orig. 1962]

B

Baltag, A, & Smets, S (2006) Dynamic Belief Revision over Multi-Agent Plausibility Models, *Proceedings of the 7th Conference on Logic and the Foundations of Game and Decision Theory* (LOFT 06), Liverpool.

Bakhtin, MM (1981) *The dialogic imagination, four essays by MM Bakhtin*, Michael Holquist (comp.), University of Texas: Austin.

—(1986) *Speech genres and other late essays*, Caryl Emerson & Michael Holquist (comps.), University of Texas: Austin.

Barker, SJ (2003) *Renewing meaning: a speech-act theoretic account*. Oxford: Clarendon Press

Bishop, J (1989) *Natural agency: an essay on the causal theory of action*. Cambridge UP: Cambridge

Björdal, F (1996) On Beliefs», *Nordic Journal of Philosophical Logic* 1:79-94.

BonJour, L (2010) *Recent work on the internalism-externalism controversy. A Companion to epistemology*. Blackwell: Oxford.

Bourke, J (2003) Fear and anxiety: Writing about emotion in modern history, *History Workshop Journal* 111-133.

—(2014) *The story of pain, from prayer to painkillers*, Oxford UP: NY.

Boutilier, C (1996) Iterated Revision and minimal change of conditional beliefs, *Journal of Philosophical Logic* 25:262-305.

Brenner, JE (2009) *Logic in Reality*. Springer: Berlin.

Brenner, A (2015) Mereological nihilism and the special arrangement question, *Synthese* 192, 5: 1295-1314.

Brinegar, MG & Salvi, L & Stiles, W & Greenberg, L (2006) Building a meaning bridge: therapeutic progress from problem formulation to understanding, *Journal of Counseling Psychology* 53, 2:165-180.

C

Cameron, RP (2007) The contingency of compositio, *Philosophical Studies* 136: 99–121.

—(2010) How to have a radically minimal ontology, *Philosophical Studies*, 151: 249–64.

—(2012) Why Lewis's analysis of modality succeeds in its reductive ambitions, *Philosophers' Imprint* 12:1–21.

Carassa, A & Colombetti, M (2009) Joint meaning, *Journal of pragmatics* 41: NP.

Cartwright, N (1999) *The Dappled World*, Cambridge UP: Cambridge.

Chang, H (2012) *Is Water H2O? Evidence, Realism and Pluralism*, Springer: Dordrecht.

Craig, A D (2008) Interoception of Emotion: a Neuroanatomical Perspective, Lewis, M et al. (ed.) *Handbook of Emotions*, 272-289. The Guilford Press: NY.

D

Davidson, D. (1963/1980) *Actions, reasons, and causes*. Clarendon Press: Oxford.

—(1980) *Essays on actions and events*. Oxford: Clarendon.

—(1991a) Epistemology externalized, *Dialectica* 45:191-202.

—(1991b) Three varieties of knowledge, Davidson, D (2001) *Subjective, Intersubjective, Objective*, 205-220. Oxford UP: NY.

- (1997) Indeterminism and antirealism, Kulp, CB (ed.) (1997) *Realism/Antirealism and Epistemology*, Rowman & Littlefield: Lanham, Davidson, D (2001) *Subjective, Intersubjective Objective*, NSP, Oxford UP: NY.
- (2001) *Subjective, Intersubjective, Objective*, Oxford UP: NY.
- Dayan, P & Abbott, L (2001) *Theoretical neuroscience: Computational and mathematical modeling of neural systems*, MIT Press: Cambridge.
- E
- Eeckman, F (ed.) (1993) *Computation and the Neural Systems*, Kluwer: Norwell.
- F
- Fehr, C & Plaisance, K (2010) Socially relevant philosophy of science: An introduction, *Synthese* 177: 301-316.
- Ford, MK, C. Glymour and P. J. Hayes (eds.) (1995) *Android Epistemology*. The MIT Press: Cambridge.
- Fiedler, K & Bless, H (2000) The Formation of Beliefs at the Interface of Affective and Cognitive Processes, Frijda, N H & Manstead, A S R & Bem, S (2000), *Emotions and Beliefs: How Feelings Influence Thoughts*, 144-170. Cambridge UP: Paris.
- Fischer, D (1987) Knowledge acquisition via incremental conceptual clustering, *Machine Learning* 2: 139-172.
- Fischer, A H & Manstead, A S R (2008) Social Functions of Emotion, Lewis, M et al. (ed.) *Handbook of Emotions*, 456-470. The Guilford Press: Nueva York.
- Frankfurt, HG (1978) The problem of action. *American Philosophical Quarterly*, 15, 157-162.
- Friederici, AD et al (2006) The brain differentiates human and non-human grammars: Functional localization and structural connectivity, *Proc Natl Acad Sci USA* 103: 2548-63.
- Friederici, AD (2011) The brain basis of language processing: From structure to function, *Physiological Review* 91: 1357-92.
- Frijda, N H & Mesquita, B (2000) Beliefs through Emotions, Frijda, N H & Manstead, A S R & Bem, S (2000) *Emotions and Beliefs: How Feelings Influence Thoughts*, 45-77. Cambridge UP: Paris.
- Fuller, S (1988) *Social Epistemology*. Indiana UP: Bloomington.
- G
- Galison, P & Stump, DJ (eds.) (1996) *The Disunity of Science: Boundaries, Contexts, and Power*. Stanford UP: Stanford.
- Gallister, C.R. (1980) *The organization of action: a new synthesis*. Hillsdale, NJ: Erlbaum.
- Gammerl, B (2012) Emotional styles: Concepts and challenges, *Rethinking history: The journal of theory and practice* 16:161-175.
- Gärdenfors, P (1988) *Knowledge in flux: modeling the dynamics of epistemic states*, MIT Press, Cambridge.
- Gärdenfors, P, Rott, H (1995) Belief Revision, at *Handbook of Logic in Artificial Intelligence and Logic Programming*, 4, OUP.
- Geller, P & Stockett (eds) (2006) *Feminist Anthropology: Past, Present and Future*, Pennsylvania UP: Philadelphia.
- Gell-Mann, M (1995) *Complexity*. Wiley: NY.
- Giere, RN (1985) Philosophy of Science Naturalized, *Philosophy of Science*. 52, 331-356.
- (2006a) *Scientific Perspectivism*. Chicago UP: Chicago.
- (2006b) Perspectival pluralism, Kellert, S; Longino, HE & Kenneth Waters, C (eds.) *Minnesota Studies in the Philosophy of Science*, vol XIX, Scientific Pluralism: 26-41, Minnesota UP: London.
- Gliozzi, V (2002) *Conditional Logic and Belief Revision*, PhD thesis in Computer Science, University of Turin, Italy.
- Goldie, PL (2000) *The Emotions*, Oxford UP: Oxford.
- (2002a) Emotions, Feelings and Intentionality, *Phenomenology and the Cognitive Sciences* 1: 235-254.

- (2002b) «Emotion, personality and simulation» in Goldie, PL (ed.) (2002) *Understanding Emotions: Mind and Morals*, 97-109. Ashgate P: Aldershot.
- (2003) Narrative and perspective; values and appropriate emotions, Hatzimoysis, A (ed.) (2003) *Philosophy and the Emotions*, 201-220, Cambridge UP: Cambridge.
- (2004) What people will do: personality and prediction, *Richmond Journal of Philosophy* 7 (Summer): 1-9.
- Goldman, A (1979) What Is Justified Belief?, G. Pappas (ed), *Justification and Knowledge*. 1-23. Dordrecht: Reidel.
- (1987) Foundations of social epistemics, *Synthese* 73: 109-144.
- (1989) Epistemic Folkways and Justification and Scientific Epistemology, A. Goldman (ed) (1992), *Liaisons*, 155-175. Cambridge, MA: MIT Press.
- (1999) *Knowledge in a social world*. Oxford UP: Oxford.
- Gombert, JE (rev. 2015; orig.1993) Metacognition, metalanguage and metapragmatics, *International Journal of Psychology* (1993): 572-580.
- Green, M (2008) Empathy, expression, and what artworks have to teach, G. Hagberg (Ed.), *Art and Ethical Criticism*, 95-122. Blackwell: NP.
- (2010) How and what can we learn from literature?, G. Hagberg and W. Jost (Eds.), *The Blackwell Companion to the Philosophy of Literature*, 350-66. Wiley-Blackwell: NP.
- (2016) Learning to be good (or bad) in (or through) literature, G. Hagberg (Ed.), *Fictional Characters, Real Problems: The Search for Ethical Content in Literature* 282-304. Oxford UP: Oxford.
- (2017) Illocution and Empathy, *Philosophia* 45:881-893 DOI 10.1007/s11406-017-9872-6
- Grenon P, Smith B, Goldberg L (2004) Biodynamic ontology: applying BFO in the biomedical domain. *Stud Health Technol Inform* 102:20-38.
- Grice, PH (1975) Logic and conversation, Cole, P., Morgan, J.L. (Eds.), *Syntax and Semantics, Speech Acts*, 3: 41-58. Academic Press, NY.
- Griffiths, PE (1997) *What Emotions Really Are: The Problem of Psychological Categories*. Chicago UP: Chicago.
- (2004) Is Emotion a Natural Kind?, RC Solomon (ed.), *Thinking about Feeling*: NP Oxford University Press: Oxford.
- Griffiths, PE & Scarantino, A (2009) Emotions in the wild: The situated perspective on emotion, Robbins, P & Aydede, M (ed.) *The Cambridge handbook of situated cognition*, Cambridge UP: Cambridge.
- Gustafsson, M & Balkenius, C (2004) Using semantic web techniques for validation of cognitive models against neuroscientific data, *Swedish Artificial Intelligence Society-Swedish Society for Learning Systems Workshop* (On Line) -www.lucls.lu.se/People/Christian.Balkenius/PDF/Gustafsson.Balkenius.2004.pdf.- consultado en 8.1.2005.
- H
- Harding, S (1991) *Whose Science? Whose Knowledge?* Cornell UP: NY.
- (1993) Rethinking standpoint epistemology: what is strong objectivity?, Alcof, L & Potter, E (eds.) *Feminist Epistemologies*, Routledge: London.
- Haugh, M (2013) Speaker meaning and accountability in interaction, *Journal of pragmatics* 48: 41-56.
- Hebb, DO (1964) *Organization of Behaviour*, Wiley: NY.
- Heylighen, F (2000) Evolutionary transitions: how do levels of complexity emerge?, *Complexity* 6: 53-57.
- Holland, J (1996) *How Adaptation Builds Complexity*. Wesley: Reading.
- (1998) *Emergence: From Chaos to Order*. Wesley: Reading.
- I
- J



## K

- Kaplan, D (1977) Demonstratives, J. Almog, J. Perry and H. Wettstein (Eds.) *Themes from Kaplan*, 481–563. Oxford: OUP.
- Keller, EF (1995) *Refiguring Life: Metaphors of Twentieth-Century Biology*, Columbia UP: NY.
- (2003a) *Making Sense of Life: Explaining Biological Development with Models, Metaphors, and Machines*, Harvard: Cambridge.
- (2003b) Models, simulation, and “computer experiments”, Radder, H (ed.) *The Philosophy of Scientific Experimentation*, 198-215, Pittsburg UP: Pittsburg.
- (2005) Ecosystems, organisms, and machines, *Bioscience* 55, 12: 1069-1074.
- Kitcher, P (1984) 1953 and All That: A Tale of Two Sciences, *Philosophical Review*, 93, 335-373.
- (1992) The Naturalists Return, *Philosophical Review*, 101, 53-114.
- (1993) *The Advancement of Science*, Oxford UP: Oxford.
- (2003) What kind of science should be done?, Lightman, A; Sarewitz, D & Dresser, C (eds.) (2003) *Living with the Genie*, 201-224, Island P: Washington.
- (2004) Evolutionary theory and the social uses of biology, *Biology and Philosophy* 19, pg. 1-15.
- Kitcher, P & Salmon, W (eds) (1989) *Scientific Explanation*: Minnesota UP: Minneapolis.
- Korn, R. W. (2005) The emergence principle in biological hierarchies, *Biol. Philos.* 20: 137–151.
- Kripke, S (1979) A puzzle about belief, A. Margalit (ed.), *Meaning and Use*, 239–83. Dordrecht Reidel.

## L

- Longino, HE (1990) *Science as social knowledge: Values and objectivity in scientific inquiry*. Princeton UP: Princeton.
- (1996) Cognitive and Non-Cognitive Values

in Science, (ed.) L. H. Nelson and J. Nelson, *Feminism, Science, and the Philosophy of Science*, 39–58. Dordrecht: Kluwer.

- (2000) Reply to P Kitcher, *Philosophy of Science* 69, 573-577.
- (2001) *The Fate of Knowledge*, Princeton UP: Princeton.
- (2006) Theoretical pluralism and the scientific study of behavior, Kellert, S; Longino, HE & Kenneth Waters, C (eds.) *Minnesota Studies in the Philosophy of Science*, vol XIX, Scientific Pluralism: 102-131, Minnesota UP: London.

## M

- McDowell, JH (1998) *Meaning, Knowledge and Reality*, Harvard UP: Cambridge.
- MacMahon, JA; Phillips, DL; Robinson, JV & Schimpf, DJ (1978) Levels of biological organization: an organism-centered approach, *Bioscience* 28: 700–704.
- McCauley, RN (2009) Time is of the essence: explanatory pluralism and accommodating theories about long-term processes, *Philos. Psychol.* 22: 611–635.
- McCauley, RN & Bechtel, W (2001) Explanatory pluralism and the heuristic identity theory, *Theory Psychol.* 11: 736–760.
- Merton, RK (1973) *Sociology of science*. ChicagoUP: Chicago.
- Michalski, RS (1980) Knowledge acquisition through conceptual clustering: A theoretical framework and algorithm for partitioning data into conjunctive concepts, *International Journal of Policy Analysis and Information Systems*, 4, 219-243.
- Mitchell, S (2002) Integrative Pluralism, *Biology and Philosophy* 17: 55–70.
- (2003) *Biological Complexity and Integrative Pluralism*. Cambridge UP: Cambridge.
- Moser, U (1970) Computer simulation of a model of neurotic defence process, *International Journal of Psychoanalysis* 50; 53-64.

## N

- Nagel, J. (2014) *Knowledge*. Oxford UP: NY.

## O

- Ogden, J (2003) Some problems with social cognition models: A pragmatic and conceptual analysis, *Health Psychology* 22, 424–428.
- Öhman, A (1979) The orienting response, attention, and learning: An information processing perspective, Kimmel, HD & van Olst, HE & Orlebeke, JF (eds.) *The orienting reflex in humans*, 443–472. Hillsdale, NJ: Erlbaum.

## P

- Perry, J (1979) The problem of the essential indexical, *Noûs* 13: 3–21.
- (2000) Myself and I, J. Perry, *The problem of the essential indexical and other essays*, 325–339). CSLI: California.
- Predelli, S (2002) Intentions, indexicals, and communication. *Analysis*, 62, 310–16

## Q

## R

- Rall, W (1964) Theoretical significance of dendritic trees for neuronal input-output relations, *Neural Theory and Modeling*: 73–97.
- (1970) Cable properties of dendrites and effect on synaptic location, Andersen, P & Jansen, JKS (eds.) *Excitatory Synaptic Mechanisms*, 175–187, Universitetsforlaget: Oslo.
- Reddy, WM (2001) *The navigation of feeling: A framework for the history of emotions*, Cambridge UP: Cambridge.
- Reger, J (ed) (2005) *Different Wavelengths: Studies of the Contemporary Women's Movements*, Routledge: NY.
- Rieger, CJ (1975) Conceptual memory and inferences, Schank, RC (ed.) *Conceptual information processing*, 157–288, Elsevier: NY.
- Rosenblatt, F (1962) *Principles of Neurodynamics*, Spartan: NY.
- Rosenwein, B (2006) *Emotional communities in the early middle ages*, Cornell University: Ithaca-New York.

## S

- Salmon, N (1986) *Frege's Puzzle*. MIT Press: Cambridge.
- Sbisà, M (2014) The Austinian conception of illocution and its implications for value judgments and social ontology. *Etica & Politica / Ethics & Politics* 16/2: 619–631.
- Scheer, M (2012) Are emotions a kind of practice (and is that what makes them have history)? A Bourdieuan approach to understanding emotion, *History and theory* 51: pg. 193–220.
- Schwarz, N (2000) Emotion, cognition, and decision making. *Cognition and Emotion*, 14, 433–440.
- Searle, JR (1969) *Speech Acts: an Essay in the Philosophy of Language*. Cambridge UP, Cambridge.
- Searle, JR & Vanderveken, D (1985) *Foundations of illocutionary logic*. Cambridge UP: Cambridge.
- Shoemaker, S (1968) Self reference and self-awareness. *The Journal of Philosophy*, 65, 555–567
- Skarda, CA & Freeman, WJ (1990) Chaos and the new science of the brain, *Concepts in Neuroscience* 1, 2:275–85.
- Solomon, M (2001) *Social Empiricism*. MIT Press: Cambridge.
- Solomon, M & Richardson, A (2005) A critical context for Longino's critical contextual empiricism, *Studies in History and Philosophy of Science* 36: 211–222.
- Solomon, R C (2008) The Philosophy of Emotions, Lewis, M et al. (ed.), *Handbook of Emotions*, 3–16, The Guilford Press: NY.
- Sperber, D, Wilson, D (2002) Pragmatics, modularity and mind-reading. *Mind Lang.* 17, 3–23.
- Stalnaker, R (1968) A Theory of Conditional, N. Rescher (ed.) *Studies in Logical Theory, American Philosophical Quarterly, Monograph Series no.2*, 98–112. Blackwell, Oxford.
- Stepp, R (1984) *Conjunctive conceptual clustering: A methodology and experimentation*

- (*Technical Report UIUCDCS-R-84-1189*).  
 Doctoral dissertation, Department of Computer Science, University of Illinois, Urbana.
- Stapp, RE & Michalski, RS (1986) Conceptual clustering: Inventing goal-directed classifications of structured objects, R. S. Michalski, J. G. Carbonell, & T. M. Mitchell (eds.), *Machine learning: An artificial intelligence approach 2*; NP. Morgan Kaufmann: Los Altos.
- Strawson, PF (1964) Intention and convention in speech acts. *Philos. Rev.* 73, 439–460.
- T
- Tesdale, J (1999) Metacognition, Mindfulness and the Modification of Mood Disorders, *Clinical Psychology and Psychotherapy* 6, 146-155.
- Tomkins, SS & Messick, S (eds.) (1963) *Computer simulation of personality: Frontiers to psychological research*, Wiley: NY.
- Toulmin, S (2003) *The uses of argument*. Cambridge UP: Cambridge [Orig. 1958]
- U
- V
- Voloshinov, NV (1973) *Marxism and the philosophy of language*, Seminar Press: NY
- (1988) *Freudianism, a critical sketch*, Indiana University Press: Bloomington.
- Vygotsky, LS (1986) *Thought and language*, The MIT Press: Cambridge.
- W
- Walton, Douglas and Erik C. W. Krabbe (1995) *Commitment in dialogue: Basic concepts of interpersonal reasoning*. SUNY Press: NY.
- Wertsch, JV (1993) *Voces de la mente: un estudio sociocultural para el estudio de la Acción Mediada*, Visor: Madrid.
- White, M & Epston, D (1990), *Narrative Means to Therapeutic Ends*. Norton, NY.
- Wimsatt, WC (2007) *Re-Engineering Philosophy for Limited Beings*. Harvard UP: Cambridge.
- Witek, M (2014) An interactional account of illocutionary practice, *Language Sciences* 47 (2015) 43–55 <http://dx.doi.org/10.1016/j.langsci.2014.08.003>
- Wittgenstein, L (1986) *Philosophical Investigations*, Basil Blackwell: Oxford.
- (2015) *Investigaciones Filosóficas, Wittgenstein*, v. II, Gredos: BCN.
- X
- Y
- Yablo, S (2003) Abstract objects: A case study, Sosa, E & Villanueva, E (ed.) *Philosophical issues on realism and relativism*, Blackwell: Oxford.
- Yamagata, Y; Kou, H; Kozaki, K; Imai, T; Ohe, K & Mizoguchi, R (2013) Ontological model of abnormal states and its application in the medical domain, *4th International Conference on Biomedical Ontology*: 28–33. ICBO2013: Montreal.
- Z
- Zhu, J, Thagard, P (2002) Emotion and action *Phil Psych*, 15, 1: 19-36.
- Zipser, D (1992) Identification models of the nervous system, *Neurosc* 47: 853-862.
- Zlateva, P (ed.) (1993) *Translation as social action*, Rourledge: Cornwall.



Alejandro Cardeña Martínez

2019