EFECTIVIDAD DEL PROGRAMA DE REHABILITACIÓN NEUROPSICOLOGICA GRADIOR EN PERSONAS CON DETERIORO COGNITIVO LEVE (DCL) Y DEMENCIA LEVE. ENSAYO CLÍNICO ALEATORIZADO

TESIS DOCTORAL

Presentada por:
Angie Alejandra Diaz Baquero

Directores:
Dr. Manuel Ángel Franco Martín
Dra. María Victoria Perea Bartolomé
Dra. Henriëtte van der Roest

VNiVERSiDAD D SALAMANCA
CAMPUS DE EXCELENCIA INTERNACIONAL

TESIS DOCTORAL

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TESIS POR COMPENDIO DE PUBLICACIONES
PRESENTADA POR: ANGIE ALEJANDRA DIAZ BAQUERO

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SALAMANCA
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CERTIFICAN:

Que Dña. Angie Alejandra Diaz Baquero, ha realizado bajo su dirección la Tesis Doctoral: "**Efectividad del programa de rehabilitación neuropsicológica GRADIOR en personas con deterioro cognitivo leve (DCL) y demencia leve. Ensayo Clínico Aleatorizado**" para optar al grado de ***Doctor con mención internacional*** por la Universidad de Salamanca. La presente Tesis Doctoral se presenta en la modalidad de Tesis por Compendio de artículos.

Salamanca, a 8 de Octubre de 2022.

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Fdo. Henriëtte van der Roest

Sin continuo crecimiento y perseverancia, palabras como mejora, logro y éxito no tienen significado (Benjamin Franklin)

Para mí no existió y nunca existirá la palabra imposible, todo será posible. Disfrutar del camino, aprender de cada cosa que percibe mis sentidos, levantarse y tener esperanza, observar oportunidades son parte de este logro.

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A mis padres, por motivarme a elegir este camino como parte de mi proyecto de vida, por su tiempo y apoyo emocional durante este trayecto, sobre todo cuando el

camino se tornaba con más obstáculos y se percibía más estrecho. Aunque con la distancia a cuestas, siempre tuve su apoyo incondicional. Este trabajo fue posible por ustedes.

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A todos. Gracias por ese cariño.

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INDUCT: Interdisciplinary Network for Dementia Using Current Technology.

H2020 Marie Skłodowska Curie Actions – Innovative Training Networks, 2015.

Departamento de Investigación y Desarrollo, Fundación INTRAS, Zamora, España.

Resumen

El deterioro cognitivo leve (DCL) ha sido definido de muchas maneras, entre ellas como un estado pre a la demencia o un estado entre el envejecimiento normal y la demencia. Sin embargo, no siempre estas personas avanzan hacia una demencia, esto dependerá de diferentes factores. La demencia es una enfermedad neurodegenerativa que progresa a lo largo de diversas fases y se caracteriza por déficits a nivel físico, cognitivo, emocional, social, entre otros. Actualmente, existe una gran incidencia de personas con demencia a nivel mundial (50 millones), cifra que se prevé incrementará en los siguientes años. Esto constituye un problema de salud pública y, por tanto, el diagnóstico y el tratamiento precoz será de importancia, para que estas personas no avancen hacia su completo deterioro de una forma rápida. Para esto, desde un enfoque médico y psicosocial se han propuesto múltiples terapias. En los últimos años, han venido desarrollando programas de entrenamiento cognitivo por ordenador. Estos programas incluyen una serie de ejercicios cognitivos con el fin de mantener y/o mejorar el funcionamiento cognitivo de personas con DCL y demencia leve. En este orden de ideas, esta investigación tuvo el objetivo de evaluar la efectividad de un programa de rehabilitación cognitivo (GRADIOR) en personas con DCL y demencia leve. Para lograr responder a este objetivo, se incluyeron una serie de estudios.

Método: este trabajo incluyó la caracterización de GRADIOR con respecto a sus interfaces y requerimientos, así mismo también se referenciaron estudios previos sobre GRADIOR y cómo estos aportaron al desarrollo de la última versión de GRADIOR. Evaluar e identificar el diseño metodológico aplicado en el desarrollo de programas de entrenamiento cognitivo computarizado (ECC) para personas con DCL y demencia leve fue una revisión sistemática que encontró 13 estudios que describieron una metodología centrada en el usuario para el desarrollo de 11 programas de ECC para personas con DCL y demencia leve. Posteriormente, se propuso un Ensayo Clínico Aleatorizado (ECA) multicéntrico simple ciego para evaluar la efectividad de GRADIOR en esta población. Para esto, se reclutó un total de 140 personas entre 60-90 años y se aleatorizo 89 personas, estos fueron diagnosticadas con DCL y demencia leve y, asignados a uno de los dos grupos (experimental y control), todos fueron evaluados con escalas cognitivas y emocionales. Las personas que siguieron la intervención con GRADIOR asistieron dos o tres veces por semana durante 12 meses. Así mismo, también se evaluó los determinantes de la

adherencia o no a este programa, para esto se propusieron variables sociodemográficas, físicas, cognitivas, psicológicas y tecnológicas como posibles predictores de adherencia. Para lo anterior, sólo se incluyó el grupo experimental, el cual se dividido en personas adherentes y no adherentes.

Resultados y Discusión: Esta investigación describió el desarrollo de la última versión de GRADIOR con respecto a su usabilidad y experiencia de usuario tomando como referencia puntos de mejora de estudios previos con este software. También de identificó y describió el diseño metodológico centrado en el usuario referenciado por estudios sobre programas de ECC, y, por tanto, se tomó en cuenta los criterios de: entendimiento del contexto, requerimientos de usuario, desarrollo del programa y evaluación del mismo. Sin embargo, no todos los estudios incluidos en esta revisión sistemática los señalaron. Un total de 45.5% de los estudios no definieron los requerimientos de usuario, aspecto que resulta importante cuando se trata del desarrollo de estos programas y su dirección sobre personas con DCL y demencia leve. Así mismo, GRADIOR fue considerado como un programa efectivo que ayudó en el mantenimiento y mejora leve de funciones cognitivas y del estado afectivo-emocional en personas con DCL y demencia leve, estos cambios fueron más notorios hacia los 12 meses, por el contrario, el grupo control disminuyó su rendimiento. Por lo cual se plantea el efecto que tiene el incluir un ECC extenso o prolongado en el tiempo con el fin de afianzar estos cambios. Esta investigación también reveló una tasa del 83.3% de adherencia y variables como la atención, memoria de trabajo (MT), razonamiento numérico, fluidez verbal fonológica y flexibilidad cognitiva como predictores de la adherencia a GRADIOR, así mismo, las personas adherentes presentaron un mejor rendimiento en estos dominios en comparación con personas no-adherentes. Por último, se escribió un capítulo sobre GRADIOR.

Palabras claves: demencia; deterioro cognitivo leve (DCL); diseño de desarrollo, ensayo clínico aleatorizado, entrenamiento cognitivo, programa basado en ordenador, rehabilitación;

Abstract

Mild cognitive impairment (MCI) has been defined in many ways, including as a pre-dementia state or a state between normal aging and dementia. However, these people do not always progress towards dementia, this will depend on different factors. Dementia is a neurodegenerative disease that progresses through various phases and is characterized by deficits at the physical, cognitive, emotional, and social levels, among others. Currently, there is a high incidence of people with dementia worldwide (50 million), a figure that is expected to increase in the coming years. This constitutes a public health problem and, therefore, early diagnosis and treatment will be important so that these people do not rapidly progress towards complete deterioration. For this, multiple therapies have been proposed from a medical and psychosocial approach. In recent years, computer-based cognitive training programs have been developed. These programs include a series of cognitive exercises in order to maintain and/or improve the cognitive functioning of people with MCI and mild dementia. In this order of ideas, this research had the objective of evaluating the effectiveness of a cognitive rehabilitation program (GRADIOR) in people with MCI and mild dementia. To achieve this objective, a series of studies were included.

Method: This work included the characterization of GRADIOR with respect to its interfaces and requirements, as well as previous studies on GRADIOR and how these contributed to the development of the latest version of GRADIOR. Evaluate and identify the methodological design applied in the development of computerized cognitive training (CCT) programs for people with MCI and mild dementia was a systematic review that found 13 studies that described a user-centered methodology for the development of 11 CCT programs for people with MCI and mild dementia. Subsequently, a single-blind multicenter Randomized Clinical Trial (RCT) was proposed to assess the effectiveness of GRADIOR in this population. A total of 140 people between 60-90 years old were recruited and 89 people were randomized, they were diagnosed with MCI and mild dementia and assigned to one of the two groups (experimental and control), all were evaluated with cognitive and emotional scales. And people who followed the intervention with GRADIOR attended two or three times a week for 12 months. Likewise, the determinants of adherence or not to this program were also evaluated, for this sociodemographic,

physical, cognitive, psychological, and technological variable were proposed as possible predictors of adherence. For the above, only the experimental group (EG) was included, which was divided into adherent and non-adherent people.

Results and Discussion: The research described the development of the latest version of GRADIOR with respect to its usability and user experience, taking as reference improvement points from previous studies with this software. The user-centered methodological design was also identified and described, taking as reference the criteria of understanding the context, user requirements, program development and its evaluation. Not all the studies included in this systematic review indicated all the criteria. A total of 45.5% of the studies did not define the user requirements, aspect that was important when it comes to the development of these programs and their direction on people with MCI and mild dementia. Likewise, GRADIOR was considered an effective program that helped in the maintenance and slight improvement of cognitive functions and of the affective-emotional state in people with MCI and mild dementia, these changes were more noticeable towards 12 months, on the contrary the control group decreased their performance. Therefore, the effect of including an extensive or prolonged CCT in time in order to further strengthen these changes is raised. This research also revealed an 83.3% adherence rate and variables such as attention, working memory (WM), numerical reasoning, phonological verbal fluency, and cognitive flexibility as predictors of adherence to GRADIOR. Likewise, adherent people presented a better performance in these domains compared to non-adherent people. Finally, a chapter on GRADIOR was written.

Key Words: cognitive training, computer-based program, dementia; development design, mild cognitive impairment (MCI); randomized clinical trial, rehabilitation.

Organización de la tesis

El RD 99/2011, del 28 de enero regula las enseñanzas oficiales de Doctorado. Así mismo, la Comisión de Doctorado y Postgrado por medio del artículo 17 del Reglamento de Doctorado de la Universidad de Salamanca establece y acepta como posible formato de tesis doctoral, la modalidad de tesis por compendio de artículos y/o publicaciones en revistas especializadas. Por lo anterior, esta Tesis Doctoral se presenta bajo esta modalidad. Las publicaciones científicas incluidas y objeto de defensa serán:

1. Franco-Martín, M.A., **Diaz-Baquero, A.A.,** Bueno-Aguado, Y., Cid-Bartolomé, M. T., Parra Vidales, E., Perea Bartolomé, M. V., de la Torre Diez, I., van der Roest, H. (2020). Computer-based cognitive rehabilitation program GRADIOR for mild dementia and mild cognitive impairment: new features. *BMC Med Inform Decis Mak, 20, 274.* https://doi.org/10.1186/s12911-020-01293-w

BMC Medical Informatics and Decision Making – Journal Citation Reports (2020)
Factor de impacto: 2.796
Nombre de la categoría: Medical Informatics
Ranking de la categoría: 18/30
Cuartil de la categoría: Q3

2. **Diaz-Baquero, A. A.,** Dröes, R.-M., Perea Bartolomé, M. V., Irazoki, E., Toribio-Guzmán, J. M., Franco-Martín, M. A., van der Roest, H (2021). Methodological Designs Applied in the Development of Computer-Based Training Programs for the Cognitive Rehabilitation in People with Mild Cognitive Impairment (MCI) and Mild Dementia. Systematic Review. *J. Clin. Med, 10(6):1222.* https://doi.org/10.3390/jcm10061222

Journal of Clinical Medicine – Journal Citation Reports (2020)
Factor de impacto: 4.242
Nombre de la categoría: Medicine, General & Internal
Ranking de la categoría: 39/167
Cuartil de la categoría: Q1

3. **Diaz-Baquero, A. A.,** Franco-Martin, M.A., Parra Vidales, E, Toribio-Guzmán, J. M, Bueno-Aguado, Y, Martínez Abad, F, Perea Bartolomé, M. V, Asl, A. M & van der Roest, H. G (2022). The Effectiveness of GRADIOR: A Neuropsychological Rehabilitation Program for People with Mild Cognitive Impairment and Mild Dementia. Results of a Randomized Controlled Trial After 4 and 12 Months of Treatment. *J Alzheimers Dis, 86*(2). Doi: 10.3233/JAD-215350. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9028667/

Journal of Alzheimer's Disease – Journal Citation Reports (2021)
Factor de impacto: 4.160
Nombre de la categoría: Neurosciences
Ranking de la categoría: 121/274
Cuartil de la categoría: Q2

4. **Diaz-Baquero, A. A.**, Perea Bartolomé, M. V., Toribio-Guzmán, J. M., Martínez Abad, F., Parra Vidales, E., Bueno Aguado, Y., van der Roest, H., & Franco-Martín, M. A. (2022). Determinants of Adherence to a "GRADIOR" Computer-Based Cognitive Training Program in People with Mild Cognitive Impairment (MCI) and Mild Dementia. *Journal of Clinical Medicine, 11*(6):1714. https://doi.org/10.3390/jcm11061714

Journal of Clinical Medicine – Journal Citation Reports (2021)
Factor de impacto: 4.964
Nombre de la categoría: Medicine, General & Internal
Ranking de la categoría: 54/172
Cuartil de la categoría: Q2

Publicaciones aceptadas y en proceso de publicación.

5. **Diaz-Baquero A. A**., Irazoki, E., Conteras Somoza, l. M., Toribio-Guzmán, J. M., Parra, E., Perea Bartolomé, M. V., . . . van der Roest, H. G. (in press). Chapter 13: Implementation and Usefulness of Cognitive Stimulation Computer Based – GRADIOR Software. In M. Orrell, D. Oliveira, O. McDermott, F. R. J. Verhey, F. C. M. Dassen, & R.-M. Dröes (Eds.), *Improving the Lives of People with Dementia Through Technology. Interdisciplinary Network for Dementia Utilising Current Technology* (Routledge Taylor & Francis Group ed., pp. 173-183). https://doi.org/10.4324/9781003289005-17.

   https://www.routledge.com/Improving-the-Lives-of-People-with-Dementia-through-Technology-Interdisciplinary/Orrell-Oliveira-McDermott-Verhey-Dassen-Droes/p/book/9781032226675

Routledge Taylor & Francis Group – Journal Citation Reports (2019)
Factor de impacto 3.514
Nombre de la categoría Aging & Mental Health Research
Ranking de la categoría 28/67
Cuartil de la categoría Q2

Colaboraciones

La Doctoranda ha contribuido con diferentes trabajos de investigación durante su doctorado. Sin embargo, estas colaboraciones no será objeto de defensa.

- Shiells, K., **Diaz Baquero, A.A.,** et al. Staff perspectives on the usability of electronic patient records for planning and delivering dementia care in nursing homes: a multiple case study. *BMC Med Inform Decis Mak* 20, 159 (2020). https://doi.org/10.1186/s12911-020-01160-8

- Shiells, K., Sêtêpánková, O., **Diaz-Baquero A. A,** Dostálová, V., & Holmerová, I. (2023). Chapter 14: The role of Electronic Patient Records (EPR) for planning and delivery dementia care in nursing homes. In M. Orrell, D. Oliveira, O. McDermott, F. R. J. Verhey, F. C. M. Dassen, & R.-M. Dröes (Eds.), *Improving the Lives of People with Dementia Through Technology. Interdisciplinary Network for Dementia Utilising Current Technology* (Routledge Taylor & Francis Group ed., pp. 184-197). https://doi.org/10.4324/9781003289005-17

Nota: Estas publicaciones están incluidas en el ANEXO 1

La siguiente publicación hace parte de la ***Guía de Mejores Prácticas: Interacción humana con la tecnología en la demencia***. Esta guía fue construida con el aporte de todos los Investigadores en etapa primaria asociados al proyecto INDUCT. La Doctoranda fue colaboradora en la realización de esta guía. Y será incluida dentro de la tesis (Anexo 2).

- **Diaz Baquero, A. A. (**2019). Technology design focused on the characteristics of the population provides usability [3.1.3.6].

Consider user-centered design in the development of computer-based cognitive rehabilitation programs for people with dementia [3.1.3.7]

Ecological validity contributes to the effectiveness of a technology [3.2.1.1]

Consider the factors that potentially determine adherence to a computer-based cognitive rehabilitation program to generate corresponding adaptations [3.2.3.5]

Accessibility to technology should be ensured for all people with dementia [3.3.3.6]

Take into account the level of cognitive impairment when implementing technologies [3.3.3.7]. In R. M. Dröes, et al. Best Practice Guidance: Human Interaction with Technology in Dementia. Recommendations based on the research conducted in the Marie Sklodowska Curie International Training Network INDUCT. Retrieved from https://www.dementiainduct.eu/guidance/

Otras Publicaciones: NEWSLETTERS

Estas son publicaciones cortas que la doctoranda realizó durante su trabajo en INDUCT con el objetivo de difundir su proyecto. Debido a su naturaleza, estas no serán objeto de defensa.

- 31 August: Introducing the newest addition to the INDUCT project. Alzheimer Europe Newsletter. September 2018.
- Our Induct Experiences. Interdisciplinary Network for Dementia Using Current Technology. Spring 2019 https://www.dementiainduct.eu/wp-content/uploads/2019/06/INDUCT-newsletter-Spring-2019.pdf
- INDUCT consortium members greatly contributed to the 29th Alzheimer Europe conference in The Hague. Induct Web. October 2019. https://www.dementiainduct.eu/news/induct-consortium-members-greatly-contributed-to-the-29th-alzheimer-europe-conference-in-the-hague/
- Meeting Centers in the Netherlands and Spain. MeetingDem Newsletter. December 2019 https://www.meetingdem.eu/wp-content/uploads/2019/12/MeetingDem-Newsletter-December- 2019_v1.0DEF.pdf

Nota: Estos newsletters están incluidos en el ANEXO 3

Tabla de contenido

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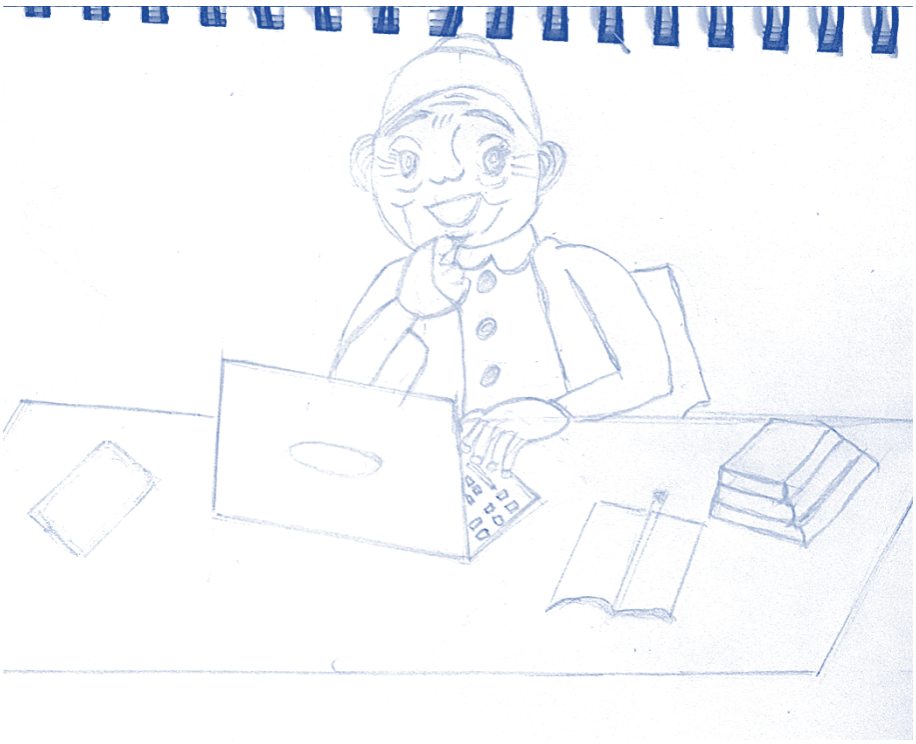

Capítulo I

Introducción y Justificación

Deterioro Cognitivo Leve y Demencia

La demencia como una enfermedad neurodegenerativa, constituye un problema de salud pública en la actualidad. The World Alzheimer Report 2019 estimó que hay más de 50 millones de personas con esta enfermedad a nivel mundial y para el 2050, este número incrementará a 152 millones (Alzheimer's Disease International, 2019). En este orden de ideas, este tema merece ser estudiado para desarrollar programas de prevención e intervención con el objetivo de mantener el estado funcional y, disminuir la incidencia de personas con esta patología.

Es importante distinguir entre deterioro cognitivo leve (DCL) y demencia leve. Aunque en ambos se notifique un deterioro y exista una línea muy fina entre estos, cada uno cuenta con unas características específicas, tomando en consideración los criterios de Petersen (2011) para el diagnóstico de DCL y del Manual Diagnóstico y Estadístico de los Trastornos Mentales (DSM-V) (American Psychiatric Association, 2013) para demencia leve.

Estudios como el de Leung et al. (2013) señaló la presencia de pequeñas tasas de aceleración con respecto a la atrofia del hipocampo en personas con DCL y, por tanto, su progreso a demencia leve. No obstante, no siempre personas con DCL evolucionan a una demencia leve, esto dependerá de diferentes factores de riesgo, por ejemplo: factores genéticos, psicológicos, ambientales, etc. Al respecto, Rivas-Fernández et al. (2022) sugirieron la resonancia magnética estructural como un instrumento, que permite diferenciar entre personas con DCL con y sin biomarcadores para desarrollar demencia de Alzheimer

Así mismo, se ha encontrado una disminución del hipocampo y la región mesial hipocampal bilateral en personas con Alzheimer, pero esta disminución no mostró diferencias significativas tras un año en comparación con personas con demencia frontotemporal, en cuya patología se vio una atrofia frontotemporal bilateral que progresó tras un año (Marino et al., 2019). Es decir que, el progreso dependerá del tipo de demencia y la atrofia cortical.

La demencia como un cuadro clínico neurodegenerativo va creando una atrofia a nivel cerebral y, como consecuencia se va evidenciando un múltideterioro debido a que afecta diversas

áreas: física (Wang et al., 2006), cognitiva (Weintraub et al., 2012), emocional (Kitching, 2015), social (Hackett et al., 2019), etc. No obstante, estas áreas se deterioran en función de las distintas etapas que se van produciendo a medida que avanza la enfermedad y también dependiendo del tipo de demencia. A nivel físico, la persona podrá presentar problemas para coordinar y movilizarse. A nivel cognitivo, alteraciones de las funciones y procesos cognitivos, tales como orientación, memoria, atención, lenguaje, razonamiento, etc. Con respecto a la parte emocional, algunos trastornos como ansiedad, depresión y apatía. Por último, la perdida de redes sociales y la vida en soledad hace parte de las alteraciones a nivel social (Diaz Baquero et al., 2021).

La elevada incidencia, los cambios a nivel cerebral y su impacto a nivel de las diferentes áreas, hace necesario un diagnóstico temprano y con ello un tratamiento eficaz para paliar los síntomas. Una de las primeras perspectivas en aportar una solución ha sido la farmacología desde el campo de la medicina, cuyo objetivo ha de ser el de disminuir los síntomas de la enfermedad. Algunos de los fármacos como los inhibidores de la acetilcolinesterasa (ej. donepezilo, rivastigmina y galantamina) y los antagonistas de N-metil-D-aspartato (NMDA) (ej. memantina) (Arnedo Montoro et al., 2012). Actualmente se evidencia diversos ECAs, cuyo objetivo es el de probar su eficacia (Birks, 2006; McShane et al., 2019; Russ & Morling, 2012)

Sin embargo, el tratamiento para personas con demencia deberá centrarse en una intervención multidisciplinar que combine el uso de fármacos con otras terapias. Las terapias psicosociales aportaran un bienestar cognitivo, psicológico y social a personas con demencia. Entre estas se distinguen la terapia de orientación a la realidad (Rands, 1998), la estimulación cognitiva de lápiz y papel (Kang et al., 2019), musicoterapia (Moreno-Morales et al., 2020), terapia de reminiscencia (Woods et al., 2018), terapia cognitivo-conductual (Kraus et al., 2008), terapia con perros (Lai et al., 2019), entre otras.

A lo anterior, se añade el uso de ordenadores para realizar entrenamiento físico y cognitivo e incluso para provocar un apoyo emocional. Un enfoque que cada vez más toma fuerza debido a los múltiples estudios asociados a su desarrollo y eficacia para personas con DCL y demencia leve. Sin embargo, este enfoque plantea un reto para las personas mayores, quienes, y en su gran mayoría nunca han utilizado un ordenador, smartphone o tablet.

Programas de entrenamiento cognitivo computarizado (ECC)

GRADIOR

En 1997, se inició la aplicación de GRADIOR en el campo clínico. Desde entonces, GRADIOR fue planteado como un programa de entrenamiento cognitivo para personas con diferentes síndromes neurológicos y psiquiátricos. Sin embargo, ha sido mayormente usado en personas con DCL y demencia. GRADIOR no sólo permite el entrenamiento, sino que también permite obtener una evaluación neuropsicológica sobre el perfil y nivel cognitivo del paciente (Diaz-Baquero et al., in press). El diseño de GRADIOR cuenta con unos requisitos (funcionales, no funcionales, técnicos y de implementación) y su arquitectura es de "cliente/servidor" admitiendo tres opciones de instalación (Franco-Martin et al., 2020)

GRADIOR incluye ejercicios cognitivos alrededor de 8 funciones cognitivas: orientación, memoria, atención, cálculo, función ejecutiva, percepción, lenguaje y razonamiento. Cada función está constituida por procesos cognitivos. Por ejemplo, se incluye el proceso "memoria verbal inmediata" para la función "memoria". A su vez, cada ejercicio incluye una serie de niveles de dificultad. Tanto los procesos cognitivos y los niveles de dificultad permiten personalizar el plan de entrenamiento cognitivo al tipo y nivel cognitivo del paciente con el fin de que este no resulte fácil, produciendo aburrimiento, pero tampoco difícil, lo que daría lugar a frustración.

Diseño metodológico asociado al desarrollo

El desarrollo y diseño de los programas de entrenamiento cognitivo es un tema que merece ser estudiado. En la actualidad hablamos de los programas de entrenamiento cognitivo y visualizamos un gran número de ellos que se ofertan a partir de la web o incluso, en eventos públicos. Pero cuántos de estos programas han sido inspirados y desarrollados para personas con

demencia, o cuántos de estos programas incluyen estudios rigurosos sobre su desarrollo y la accesibilidad a los mismos desde la literatura científica, donde se especifique sus fases tanto de diseño, evaluación, rediseño, construcción y/o cuáles han sido las técnicas usadas en cada una de estas fases, qué población fue usada por primera vez y cuáles son sus estándares de usabilidad, experiencia de usuario, validez y efectividad. Este es el tipo de cuestionamientos que investigadores y profesionales clínicos deberían tratar de contestar cuando intentan diseñar una intervención para personas con DCL o demencia basada en estos programas ECC.

Programas como CogMed (Klingberg, 2010), CogniPlus (Yang et al., 2019) y CogniFit (Shatil et al., 2010) son programas que no reportan gran detalle de su desarrollo en personas con demencia por medio de estudios publicados o en sus propias páginas de comercialización. Esto no quiere decir que estos programas carezcan de estudios previos sobre su desarrollo, pero lo que si quiere decir es que esta información no está disponible para su revisión, haciendo más visibles los anteriores interrogantes.

Los interrogantes anteriormente presentados sugieren el uso de un diseño centrado en el usuario (DCU). Un diseño que focalice su atención y se centre en las particularidades, características y necesidades de una población específica, para el caso, personas con DCL y demencia leve. La ISO9241-210 (2019) plantea y define una serie de estándares que caracterizan el desarrollo de programas bajo un DCU:

- Entender y especificar el contexto de uso.
- Especificar los requerimientos de usuario.
- Diseño del programa.
- Evaluación del programa (Usabilidad y experiencia de usuario).

Entender y especificar el contexto de uso hace referencia al conocimiento que se tiene y al nuevo que se pueda añadir sobre la población en particular. Se trata de especificar y delimitar el tipo de población para la cual se dirige el programa (ej. tipo de diagnóstico, edad, sexo y demás datos sociodemográficos) y el contexto en el cual se usará el mismo (ej. centro de memoria, clínica, hospital o casa).

Especificar los *requerimientos de usuario* implica reclutar, incluir e implicar al grupo de personas o usuarios finales, es decir la población a la cual se dirige el programa a desarrollar. Tras esto, evaluar y definir los requerimientos de usuario implica atender a las necesidades y características propias de la población con el objetivo de adaptar el programa a este usuario final y que no ocurra lo contrario, es decir que la persona trate de adaptarse a la tecnología.

Se hace referencia a "necesidad" al definir a las personas con DCL y demencia con una serie de características particulares a nivel físico, cognitivo, emocional y social. Y, por tanto, algunas tecnologías deberán adaptarse a estas características y/o necesidades. También tomar en consideración el nivel de motivación de las personas con demencia para usar estas tecnologías o lo qué estas podrían aportan a sus necesidades es importante para lograr su uso. Finalmente, establecer requisitos de usuario podría estar asociado a implementar programas en línea con el fin de que no implique un desplazamiento de personas mayores a un centro debido a sus problemas de movilidad y, el uso de colores, texto, sonidos apropiados podrían contrarrestar las alteraciones visuales y auditivas de estas personas (Diaz Baquero, 2019b).

Cada persona con DCL y demencia presenta un nivel y tipo de deterioro diferente, por tanto, diseñar y seleccionar ejercicios y actividades acorde al nivel y perfil cognitivo del paciente es algo fundamental. El componente emocional también está muy asociado con el nivel de motivación, en algunos tipos de demencia como la demencia frontotemporal, la apatía es algo característico (Bozeat et al., 2000) y, por tanto, estas personas podrían presentar problemas al momento de quererse involucrar (motivación) en programas de ECC y sobre todo cuanto estos son extensos.

Para llevar a cabo esta fase, el uso de herramientas cualitativas es de bastante importancia, las entrevistas, cuestionarios, observación a nivel individual y grupal son técnicas que aportan información muy detallada (ISO9241-210, 2019).

Especificar los requisitos de usuario resulta funcional para el *desarrollo y diseño del programa de entrenamiento cognitivo*. Tras esto, la *evaluación del programa* ayudará a

determinar la experiencia y la adaptación que presenta los usuarios al programa con el fin de proponer mejoras inmediatas y futuras.

Aunque estos estándares están propuestos, creemos que son pocos los estudios que diseñan y desarrollan programa de ECC con base en estos y aún más, son pocos los estudios que involucran al usuario final (por ejemplo, personas con DCL y demencia leve) desde las fases iniciales de desarrollo (Contreras-Somoza et al., 2021). Por tanto, surgió el interés de estudiar e investigar sobre el diseño metodológico usado en el desarrollo de programas de entrenamiento cognitivo en personas DCL y demencia leve (Artículo 2) (Diaz Baquero et al., 2021).

Efectividad

Los estudios de efectividad de programas de ECC son muy comunes. Cavallo and Angilletta (2019) indicaron una mejora cognitiva en pacientes con Alzheimer tras el uso de un programa de ECC estructurado durante 12 semanas, efecto que se mantuvo incluso 6 meses después. Estos autores subrayaron la ventaja que existe en desarrollar estudios longitudinales con fases de seguimiento e incluir programas de entrenamiento cognitivo estructurado y adaptado a las necesidades de las personas con demencia. En esta misma línea, Flak et al. (2019) destacaron la mejora en la memoria de trabajo (MT) tras un programa de entrenamiento personalizado frente a uno no personalizado en personas con DCL.

Otros estudios han indicado la mejora en la MT después de 5 semanas y su consiguiente mantenimiento hacia los 3 meses siguientes en pacientes con DCL (Vermeij et al., 2016). Así mismo, Yang et al. (2019) mencionó tras su ECA de 3 meses de seguimiento, el mantenimiento de la MT en personas con DCL y resaltó la importancia que tiene el entrenamiento cognitivo para retrasar el deterioro cognitivo.

Sin embargo, se encuentran estudios que no incluyen un periodo de seguimiento para monitorear el mantenimiento de los cambios a largo plazo, tal es el caso del estudio de Hyer et al. (2016), en el que se indicó una mejora de la memoria de trabajo tras 7 semanas de

intervención en adultos con DCL. También han estudiado otros tipos de memoria diferentes a la MT. Hwang et al. (2015) mencionaron la mejora en la memoria tardía, reciente y el reconocimiento visual en pacientes con Alzheimer tras 5 sesiones semanales durante 4 semanas de entrenamiento cognitivo.

Al igual que el estudio Flak et al. (2019), en el ECA realizado por Peretz et al. (2011) se incluyó la comparación entre un programa de entrenamiento computarizado personalizado y juegos computarizados y, por tanto, destacaron la mejora en la MT visoespacial, el aprendizaje y la atención. Otros estudios también encontraron mejoras en esta última función (González-Palau et al., 2014; Hagovská et al., 2017)

Mejoras en el funcionamiento ejecutivo en adultos mayores también fueron reportadas por Barban et al. (2016), Djabelkhir et al. (2017) y Shatil et al. (2014). Así mismo, en la velocidad de procesamiento, coordinación mano-ojo, denominación y procesamiento visuoespacial en un programa de entrenamiento combinado (cognitivo y físico) durante 4 meses (Shatil, 2013). Estudios como el anterior, muestran un enfoque más amplio y atractivo debido a que incluye dos intervenciones y las ventajas sobre el rendimiento cognitivo cuando ambas son combinadas.

Otros estudios han intentado observar y comparar cómo se producen estas mejoras en relación con la edad, encontrando que los adultos más jóvenes tienen una mayor probabilidad de mejora significativa en comparación con las personas mayores (Mendoza Laiz et al., 2018). En cuanto a los factores psicológicos, algunos estudios han indicado mejoras en la ansiedad (Gaitán et al., 2013) y depresión (García-Casal et al., 2017) en personas con DCL y demencia leve.

Para ampliar el espectro frente a la variedad de programas de ECC, la revisión sistemática realizada por Irazoki et al. (2020), ofrece detalles sobre algunos de estos programas de entrenamiento cognitivo. También, es de apreciar el esfuerzo de desarrollar diversas investigaciones con el fin de probar la efectividad del ECC en personas con DCL y demencia. Sin embargo, los hallazgos de algunos de estos estudios merecen ser tomados con cautela debido a las dos limitaciones más importantes y casi siempre señaladas por todos ellos, el tamaño de la

muestra (Klimova & Maresova, 2017) y los cortos periodos de intervención (Lee et al., 2018). Esto sugiere una problemática y un punto a mejorar por parte de futuros estudios. Por tanto, se hace necesario incluir muestras más grandes y representativas y, periodos de entrenamiento más amplios (Yang et al., 2019)

La revisión sistemática realizada por Bahar-Fuchs et al. (2013) hace mención a la baja y moderada calidad de dichos estudios y concluye con la necesidad de realizar estudios que describan de forma detallada sus intervenciones. Así mismo, la revisión sistemática de García-Casal et al. (2017) indicó una aceptable calidad metodológica de aquellos estudios cuyo objetivo fue evaluar la efectividad de estos programas. Esta revisión planteó la existencia de grandes problemas en la validez externa, es decir, en determinar si los participantes representan a la población, y finalmente, enfatizó en la dificultad de comparar los resultados de estos estudios debido al uso variado de diseños e intervenciones. Por lo tanto, los esfuerzos científicos deben enfocarse en desarrollar investigaciones que suplan estas principales críticas, brindando un mejor valor a cada una de las investigaciones.

La efectividad de GRADIOR ha sido poco estudiada. Sin embargo, GRADIOR ha sido eficaz para tratar síntomas conductuales (Franco Martín & Bueno Aguado, 2002), cognitivos, mejorar la calidad de vida e independencia (Fumero Vargas et al., 2015). No obstante, la mayoría de los estudios al respecto se han centrado en la usabilidad y experiencia de usuario (Góngora Alonso et al., 2020; Irazoki et al., 2021; Toribio Guzmán, 2016). Por lo tanto, resulta interesante desarrollar un estudio a partir del cual se pueda evaluar la efectividad de GRADIOR sobre la cognición y emoción en personas con DCL y demencia leve tras un periodo extenso de entrenamiento (12 meses) (Artículo 3) (Diaz Baquero, Franco Martín, et al., 2022).

Adherencia

La adherencia ha sido un tema comúnmente estudiado y relacionado con el uso de medicamentos (Organization, 2003). Sin embargo, la adherencia no podría quedar restringida a un solo contexto. De este modo, podríamos referirnos a la adherencia vista desde la aplicación de los programas de ECC a persona con DCL y demencia leve. Son pocos los estudios desde esta

perspectiva. No obstante, algunos estudios también han tratado de señalar pequeños matices con respecto al tema.

La OMS define la adherencia como el grado en que el comportamiento de una persona corresponde con las indicaciones y/o recomendaciones proporcionadas por un profesional de la salud (Sabaté, 2003). De esta manera, el cumplimiento (Cramer et al., 2008) y más recientemente, la persistencia (Dilla et al., 2009) han sido dos términos utilizados para operacionalizar el concepto de adherencia desde la Sociedad Española de Farmacia, Clínica, Familia y Comunidad (SEFAC) (SEFAC, 2010). Aunque, no siempre una persona es cumplidora y a su vez, persistente (Alfian et al., 2019).

Factores a nivel socioeconómico, personal, terapéutico, ambiental, del sistema de salud y el equipo médico de atención han sido referenciados como posibles determinantes de la adherencia (SEFAC, 2010). El estudio de Scase et al. (2017) mencionó de una forma puntual, pero no amplia algunas variables como el nivel leve de deterioro, la interacción social y la disponibilidad de soporte tecnológico, que podrían estar asociadas a la adherencia a un entorno gamificado basado en computadora en personas con DCL.

El bajo rendimiento inicial en las pruebas de memoria, atención y fluidez verbal semántica (FVS), predijo una mayor adherencia en personas mayores (Evers et al., 2011). En esta misma línea, el buen rendimiento de memoria ha sido señalado como predictor de adherencia, en personas mayores con riesgo de demencia tras un programa de entrenamiento cognitivo (Turunen et al., 2019) y en personas con DCL que participaron en un programa de entrenamiento de rehabilitación y avance de la memoria basado en la recuperación espaciada ubicua (USMART) (Han et al., 2014). Así mismo, las estrategias compensatorias de memoria podrían influir en la adherencia de personas con DCL (de Wit et al., 2019). Por consiguiente, la mejora en el funcionamiento cognitivo ha sido asociada con la adherencia a programas de entrenamiento de Realidad Virtual (RV) (Park et al., 2020). Por último, variables de tipo psicológicas como las expectativas positivas al inicio de un programa de ECC podrían ayudar a predecir la adherencia (Turunen et al., 2019).

Los anteriores estudios, han señalado variables asociadas a la adherencia. Sin embrago, la mayoría de estos estudios no pretendían indagar sobre los determinantes de la adherencia a programas de ECC porque son estudios cuyo objetivo inicial y/o primordial ha sido el de evaluar la efectividad o desarrollar un programa de ECC. Por lo cual, el concepto de adherencia ha sido tratado de forma muy superficial y no ha sido estudiado en su amplio espectro. De esta forma, el artículo 4 tuvo el objetivo de identificar determinantes sociodemográficos, cognitivos, psicológicos y físicos que ayudaran a predecir la adherencia o no a un programa de ECC GRADIOR en personas con DCL y demencia leve (Diaz Baquero, Perea Bartolomé, et al., 2022).

Capítulo II

Objetivos e hipótesis

Objetivo general

Evaluar la efectividad del programa de rehabilitación neuropsicológica GRADIOR en personas con DCL y demencia leve a partir de la consecución de un ensayo clínico aleatorizado (ECA) multicéntrico.

Objetivos específicos

1. Describir el desarrollo de la última versión del programa de rehabilitación cognitiva basado en computadora GRADIOR en personas con DCL y demencia leve.

    1.1. Detallar los requerimientos no-funcionales, funcionales, tecnológicos, de implementación, y arquitectura de la última versión de GRADIOR.

    1.2. Caracterizar las diferentes interfaces de GRADIOR (gestión clínica, gestión de historia clínica, gestión del tratamiento, gestión de reportes).

    1.3. Exponer los aspectos de usabilidad y experiencia de usuario de la última versión de GRADIOR tomando como referencia aspectos claves reseñados por estudios previos.

2. Identificar el diseño metodológico aplicado en el desarrollo de programas de ECC para la rehabilitación del funcionamiento cognitivo en personas con DCL y demencia leve.

    2.1. Identificar y caracterizar el tipo de participantes (diagnóstico), el número de grupos usados, el tamaño de la muestra y la edad de la población empleada durante el desarrollo de programas de ECC para la rehabilitación del funcionamiento cognitivo en personas con DCL y demencia leve.

    2.2. Caracterizar y describir el diseño metodológico empleado para el desarrollo de programas de ECC para la rehabilitación del funcionamiento cognitivo en personas con DCL y demencia leve.

3. Evaluar la efectividad del programa de ECC GRADIOR sobre la cognición y la situación afectivo-emocional en personas con DCL y demencia leve a los 4 y 12 meses de tratamiento.

    3.1. Comparar a nivel intergrupal el rendimiento cognitivo y la situación afectivo-emocional entre el grupo experimental (GE) y control para cada una de las condiciones (T_o: línea base, T_1: a los 4 meses y T_2: a los 12 meses).

    3.2. Comparar a nivel intra-grupo el rendimiento cognitivo y la situación afectivo-emocional para ambos grupos (experimental y control), es decir, evaluar los cambios entre cada una de las condiciones (T_o- T_1) y (T_1-T_2) respecto a cada grupo de manera independiente.

    3.3. Evaluar y comparar los cambios en el rendimiento cognitivo y la situación afectivo-emocional a lo largo del tiempo (T_o-T_1-T_2) y su interacción con los grupos de estudio (experimental y control).

    3.4. Evaluar y comparar los cambios en el rendimiento cognitivo y la situación afectivo-emocional tomando en consideración la interacción entre tiempo (T_o- T_1-T_2), grupo clínico (DCL y demencia leve) y grupo de estudio (experimental y control).

4. Platear un modelo de adherencia que señale los determinantes a nivel sociodemográfico, físico, cognitivo y psicológico y que, ayude a predecir o no la adherencia a un programa de ECC GRADIOR en personas con DCL y demencia leve.

    4.1. Determinar el grupo de adherentes o no y, por tanto, la tasa de adherencia, tomando en consideración el nivel de cumplimiento y la persistencia al programa de ECC GRADIOR en personas con DCL y demencia leve.

    4.2. Comparar el rendimiento de las personas adherentes con respecto a las personas no-

adherentes, con base en las variables que conformen el modelo de adherencia al programa de ECC GRADIOR.

4.3. Asociar el rendimiento de personas con DCL y demencia leve de cada grupo (adherente y no adherente), con base en las variables que conformen el modelo de adherencia al programa de ECC GRADIOR.

4.4. Evaluar diferencias en el rendimiento de personas adherentes y no-adherentes por cada uno de los grupos clínicos (DCL y demencia leve) con base en las variables que conformen el modelo de adherencia al programa de ECC GRADIOR.

5. Recopilar estudios previos y actuales sobre la implementación del programa de ECC GRADIOR en personas con DCL y demencia leve.

Hipótesis

A continuación, se presentará la formulación de hipótesis (nula y alterna) en el caso de los estudios experimentales asociados al objetivo 3 y 4 (citados anteriormente). Cada una de las hipótesis corresponde con cada uno de los objetivos específicos incluidos para el objetivo 3 y 4.

Objetivos Específicos del artículo 3.

3.1.

3.1.1. (H_0) El rendimiento en los dominios cognitivos y/o de afecto-emoción no presentará diferencia entre el GE y el grupo control (GC) para cada una de las condiciones (T_O-T_1 Y T_2).

3.1.2. (H_1) El rendimiento en los dominios cognitivos y/o de afecto-emoción asociado al GE será diferente al del GC para cada una de las condiciones (T_O-T_1 Y T_2).

3.2.

3.2.1. (H_0) El rendimiento (cognitivo y/o afectivo-emocional) no mostrará diferencias entre línea

base-4 meses y/o 4 meses-12 meses a nivel intra-grupo (GE y GC).

3.2.2. (H_1) Presencia de cambios por mantenimiento y/o mejora del rendimiento (cognición y afecto-emoción) entre línea base-4 meses y/o 4 meses-12 meses en el GE.

3.2.3. (H_1) Presencia de cambios por empeoramiento en el rendimiento (cognición y/o afecto-emoción) entre línea base-4 meses y/o 4 meses-12 meses en el GC.

3.3.

3.3.1. (H_0) El GE no presentará diferencias en su rendimiento (cognición y afecto-emoción) a lo largo de la intervención en comparación con el GC.

3.3.2. (H_1) El GE presentará cambios por mantenimiento y/o mejora de su rendimiento (cognición y afecto-emoción) a lo largo de la intervención en comparación con el GC.

3.4.

3.4.1. (H_0) El grupo con DCL-GE y/o demencia leve-GE no presentará diferencias en su rendimiento (cognición y afecto-emoción) a lo largo de la intervención en comparación con el grupo con DCL-GC y/o demencia leve-GC.

3.4.2. (H_1) El grupo con DCL-GE y/o demencia leve-GE presentará cambios por mejora y/o mantenimiento de su rendimiento (cognición y afecto-emoción) a lo largo de la intervención en comparación con el grupo de DCL-GC y/o demencia leve-GC.

Objetivos Específicos del artículo 4.

4.1.

4.1.1. (H_0) El grupo adherente no tendrá diferencia con respecto al grupo no-adherente en la tasa de adherencia para el programa de entrenamiento cognitivo GRADIOR.

4.1.2. (H_1) El grupo adherente tendrá una tasa de adherencia representativa para el programa de entrenamiento cognitivo GRADIOR en comparación con el grupo no-adherente.

4.2.

4.2.1. (H_0) El rendimiento del grupo adherente y no adherente será similar en las variables que conformen el modelo de adherencia.

4.2.2. (H_1) El grupo adherente tendrá un mejor rendimiento con base en las variables que conformen el modelo de adherencia en comparación con el grupo no-adherente.

4.3.

4.3.1. (H_0) El rendimiento entre las personas con DCL-adherentes y demencia leve-adherentes no se diferenciará con base en las variables que conformen el modelo de adherencia.

4.3.2. (H_1) El rendimiento de las personas con DCL-adherentes con base en las variables que conformen el modelo de adherencia, será mejor con respecto a las personas con demencia leve adherentes.

4.4.

4.4.1. (H_0) El rendimiento entre las personas con DCL-adherentes y DCL - no adherentes no se diferenciará con base en las variables que conformen el modelo de adherencia.

4.4.2. (H_1) El rendimiento de las personas con DCL-adherentes con base en las variables que conformen el modelo de adherencia, será mejor con respecto a las personas con DCL-no adherentes.

4.4.3. (H_0) El rendimiento entre las personas con demencia leve-adherentes y demencia leve-no adherentes no se diferenciará con base en las variables que conformen el modelo de adherencia.

4.4.4. (H_1) El rendimiento de las personas con demencia leve-adherentes con base en las variables que conformen el modelo de adherencia, será mejor con respecto a las personas con demencia leve-no adherentes.

Capítulo III

Metodología

Cada publicación incluida en esta tesis por compendio incluyó una metodología especifica (ver cada una de las publicaciones en el capítulo IV). A continuación, se especifica brevemente cada una de estas metodologías.

Artículo 1.

Computer-based cognitive rehabilitation program GRADIOR for mild dementia and mild cognitive impairment: new features.

Programa de rehabilitación cognitiva basado en ordenador GRADIOR para demencia leve y deterioro cognitivo leve: Nuevas características.

Este artículo es de carácter descriptivo sobre el desarrollo del programa de entrenamiento cognitivo GRADIOR. Inicia mostrando una perspectiva de la demencia a nivel de España y el mundo y, describiendo las particularidades y beneficios de los programas de intervención psicosocial por medio del uso de dispositivos tecnológicos en personas con DCL y demencia leve. Posteriormente, señala los requisitos funcionales, no funcionales, técnicos y de implementación y, la arquitectura de GRADIOR. En la sección de resultados, se describe el programa de forma extensa y se incluye los estudios previos sobre usabilidad y experiencia de usuario de GRADIOR, lo cual, plantea una base para hablar sobre el desarrollo de la última versión de GRADIOR y cómo esta versión satisface mejoras respecto a las versiones anteriores y las necesidades actuales de los pacientes. Finalmente, la discusión se enfoca en las ventajas, pero también señala limitaciones sobre GRADIOR con respecto a su usabilidad y experiencia de usuario.

Artículo 2.

Methodological Designs Applied in the Development of Computer-Based Training Programs for the Cognitive Rehabilitation in People with Mild Cognitive Impairment (MCI) and Mild Dementia. Systematic Review.

Diseños Metodológicos Aplicados en el Desarrollo de Programas de Entrenamiento por Ordenador para la Rehabilitación Cognitiva en Personas con DCL y Demencia Leve. Revisión sistemática.

Revisión sistemática de la literatura

Para esta revisión sistemática, se empleó las bases de datos PubMed y PsycINFO. El protocolo fue registrado en el Registro Prospectivo Internacional para Revisiones Sistemáticas (PROSPERO) bajo el número de registro CRD42020159027 or EC626091945 en abril de 2020 y actualizado en Octubre de 2020 (Diaz Baquero et al., 2020). El protocolo fue diseñado de acuerdo con Preferred Reporting Items for Systematic Review and Meta-Analysis-PRISMA statements (Moher et al., 2009).

Estrategias de búsqueda

El autor principal realizó la búsqueda inicial el 5 de noviembre de 2019. Las palabras claves alrededor de las cuales giro la búsqueda fueron: dementia-MCI AND computer-based program AND development or design AND cognitive. Elaborándose una estrategia de búsqueda para cada una de las bases de datos (Anexo 4).

Criterios de elegibilidad

Se seleccionaron artículos publicados entre enero del 2000 y octubre de 2019, escritos en inglés y español. También, aquellos estudios que incluyeran a personas con DCL o demencia leve. Se excluyeron los estudios que no describieron el desarrollo de programas de ECC y cuyo tema principal y único fue la efectividad o usabilidad. También, se tuvieron en cuenta revisiones sistemáticas y metaanálisis con el fin de rastrear estudios que no fueron identificados por la estrategia de búsqueda inicial.

Síntesis de datos

Inicialmente, se llevó a cabo la caracterización de la muestra (tamaño de muestra, distribución por sexo, grupo de estudio, diagnostico), país o centro dónde se llevó a cabo la recolección de la muestra y abandonos (cantidad de sujetos que abandonaron el estudio y principales motivos).

Posteriormente, se empleó un análisis crítico con el objetivo de identificar, describir y caracterizar el diseño metodológico aplicado en el desarrollo de programas de ECC para la rehabilitación de la función cognitiva en personas con DCL y demencia leve y, se obtuvo la siguiente información: 1) Diseño metodológico y 2) Acorde con los estándares de la ISO9241-210 (2019): a) contexto de uso, b) requisitos de usuario, c) producción de soluciones de diseño y d) evaluación del diseño.

Selección de estudios

El proceso de selección y exclusión de estudios para la revisión sistemática se muestran en el diagrama de flujo PRISMA (Figura 1). Un total de 13 estudios cumplieron con los criterios de inclusión.

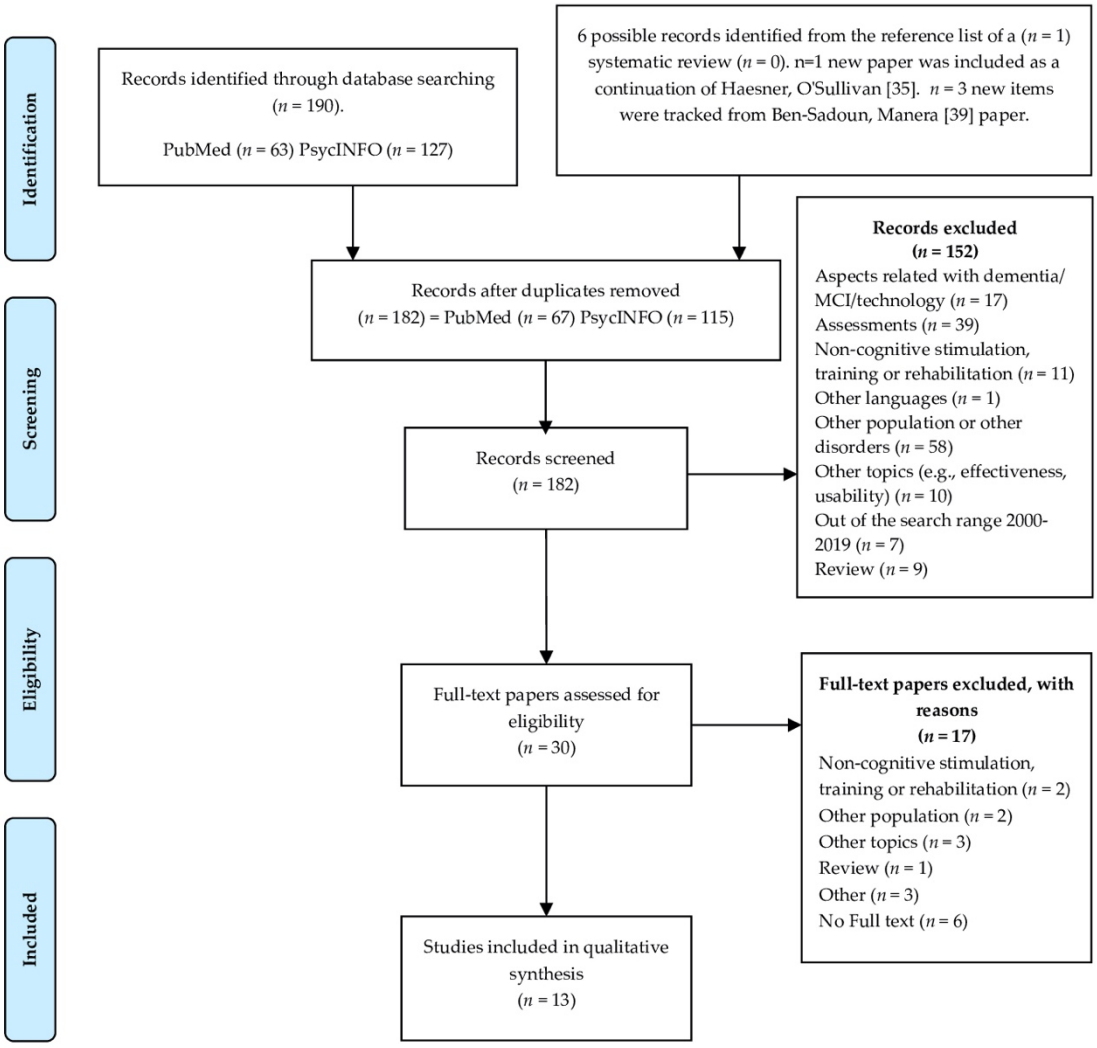

Figura 1. Diagrama de Flujo PRISMA. Proceso de selección de la revisión sistemática (From: (Moher et al., 2009). [1] (Haesner et al., 2014). [2] (Ben-Sadoun et al., 2018).

Tomado de "Methodological Designs Applied in the Development of Computer-Based Training Programs for the Cognitive Rehabilitation in People with Mild Cognitive Impairment (MCI) and Mild Dementia. Systematic Revie"w (p.5), por A. A. Diaz Baquero., et al, 2021, J. Clin. Med, 10(6).

Artículo 3.

The Effectiveness of GRADIOR: A Neuropsychological Rehabilitation Program for People with Mild Cognitive Impairment and Mild Dementia. Results of a Randomized Controlled Trial After 4 and 12 Months of Treatment.

La efectividad de GRADIOR: un programa de rehabilitación neuropsicológica para personas con deterioro cognitivo leve y demencia leve. Resultados de un ensayo controlado aleatorio después de 4 y 12 meses de tratamiento.

Diseño

El diseño utilizado fue un ECA multicéntrico, simple ciego (ISRCTN: 15742788) (Franco-Martín, 2017). Los participantes fueron aleatorizados (1:2) a uno de los dos grupos (experimental y control) (Figure 2). Así mismo, cada uno de los investigadores, que llevaron a cabo la evaluación, fueron ciegos para el tratamiento seguido por cada participante. Los participantes del GE asistieron a 2 o 3 sesiones semanales (dependiendo de la disponibilidad del centro), cada una de 30 minutos durante 12 meses y los participantes del GC continuaron con su tratamiento usual. Este estudio fue aprobado el 17 de mayo del 2017 por el comité ético de Investigación de Medicamentos del Área de Salud de Zamora (Número: 387-EC). Y fue empleado un consentimiento informado para el participante y los cuidadores.

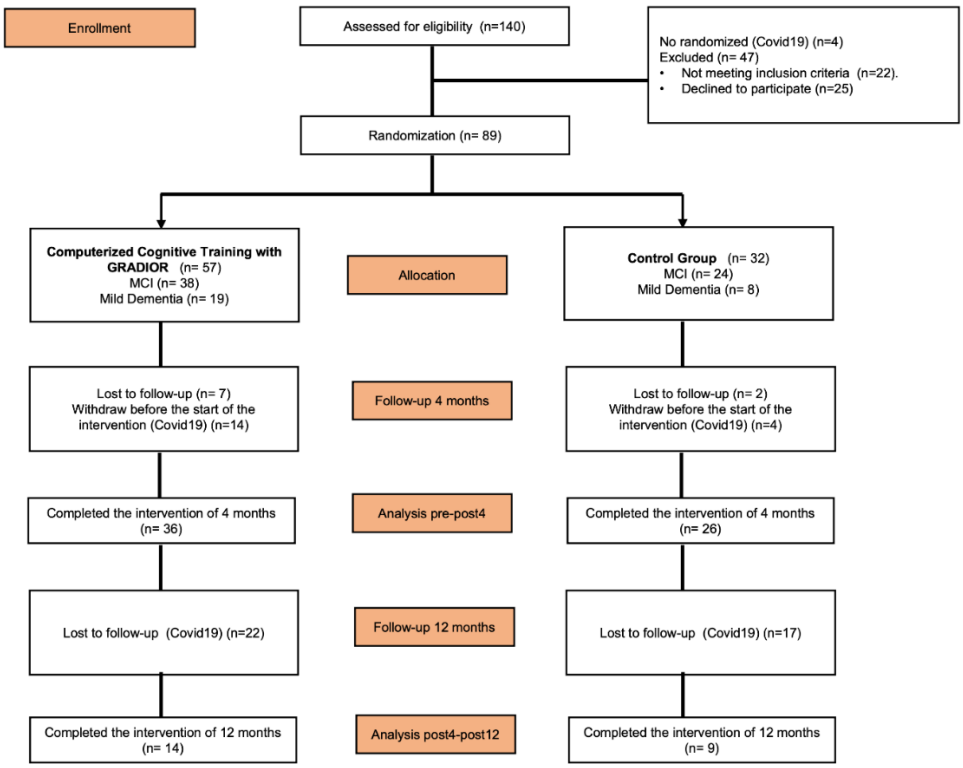

Figura 2. Proceso de reclutamiento y Randomización.

Tomado de "The Effectiveness of GRADIOR: A Neuropsychological Rehabilitation Program for People with Mild Cognitive Impairment and Mild Dementia. Results of a Randomized Controlled Trial After 4 and 12 Months of Treatment"(p.713), por A.A. Diaz Baquero, M.A. Franco Martín, 2022, J Alzheimers Dis, 86(2).

Participantes

Un total de 89 personas fueron aleatorizadas a los grupos. Sin embrago, sólo 62 participantes completaron los 4 meses del ECA y 23 personas llegaron a los 12 meses antes del inicio de la pandemia por COVID-19, situación que comprometió la continuación del ECA.

Los participantes tenían entre 60-90 años y fueron diagnosticados con DCL por los criterios Clínicos de Petersen (2011) y con demencia leve por el Manual Diagnóstico y Estadístico de los Trastornos Mentales (American Psychiatric Association, 2013). Cada diagnóstico fue confirmado por un psiquiatra y neurólogo contemplando la historia clínica individual de cada paciente. El tipo de DCL fue amnésico, y los tipos de demencia incluidos fueron los siguientes: enfermedad de Alzheimer, demencia vascular, demencia mixta y frontotemporal.

Puntajes obtenidos en el Mini-Examen del Estado Mental (MMSE) fueron adicionales, ≤ 27 para DCL y un MMSE= $20 \geq X \leq 25$ para demencia leve. También, fue necesario una puntuación en la Escala Geriátrica de Yesavage (GDS) de ≤ 5. Así mismo, cada participante debía asistir voluntariamente, tener un cuidador de referencia, hablar y comprender el español.

Los criterios de exclusión fueron: pacientes con comorbilidad física severa, alteración sensorial significativa (oído-visual), trastornos neurológicos (enfermedad de Huntington, lesión cerebral, enfermedad de Parkinson), trastornos psicopatológicos clínicamente significativos (depresión, ansiedad, trastorno bipolar, psicosis) y/o antecedentes de consumo de sustancias psicoactivas (alcohol o tabaco).

Evaluación Neuropsicológica

Los participantes asociados a ambos grupos fueron evaluados en tres momentos diferentes a lo largo de la intervención (T_o: línea base, T_1: a los 4 meses, T_2: a los 12 meses). Las principales escalas cognitivas empleadas fueron: MMSE (Folstein et al., 1975), la sub-escala cognitiva de Alzheimer's Disease Assessment Scale (ADASCog) (Rosen et al., 1984), the Trail Making Test (TMT) A-B (Tombaugh, 2004), el test del Dibujo del Reloj (Kokmen et al., 1991), Dígitos-símbolos, Aritmética y Dígitos del Wechsler Adult Intelligence Scale (WAIS-III) (Wechsler, 1997), Memoria visual del Rivermead Behavioural Memory Test (RBMT) (Wilson et al., 1989), Razonamiento visual del Cambridge Cognitive Examination (CAMCOG) (Roth et al., 1986), y el test de Fluidez Verbal (Benton, 1968; Peña-Casanova et al., 2009). La medida de resultado secundaria fue el GDS (Yesavage & Sheikh, 2018). Estos y otros instrumentos no incluidos para esta tesis (principalmente escalas físicas y sociales) fueron descritos a gran detalle en el protocolo publicado para este ECA (Vanova et al., 2018). La razón por la que no se incluyó estas medidas de resultado, fue porque actualmente se encuentran bajo análisis y serán objeto de futuras publicaciones.

Entrenamiento cognitivo basado en computadora con GRADIOR

GRADIOR fue el programa de entrenamiento cognitivo basado en computadora empleado para este ECA (Diaz-Baquero et al., in press). El plan de intervención cognitiva de este ECA se diseñó según el perfil cognitivo (Figura 3) y, el nivel de dificultad de cada ejercicio se ajustó al nivel cognitivo de cada persona a lo largo del periodo de tratamiento. Los participantes asistieron a dos o tres sesiones semanales de 30 minutos durante un período de 12 meses. Las sesiones se llevaron a cabo en salas especializadas con ordenadores en residencias, clínicas de memoria y hospitales.

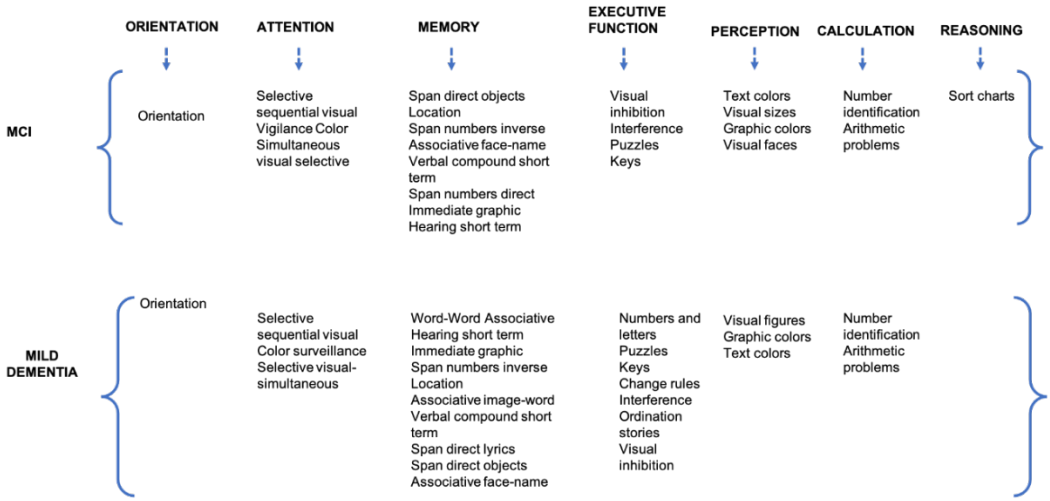

Figura 3. Plan de estimulación cognitiva GRADIOR en personas con Deterioro Cognitivo Leve (DCL) y demencia leve

Análisis estadístico

El análisis estadístico se realizó utilizando el Paquete Estadístico software de Ciencias Sociales (SPSS) (IBM-Corp, 2017). Se utilizó la prueba de normalidad de Shapiro-Wilk. La comparación entre el GE - GC se realizó mediante el Test U de Mann-Whitney respecto a cada uno de los tiempos T_o-T_1-T_2 (Inter grupo). Se utilizó el Test de Rangos con Signo de Wilcoxon para comparar el rendimiento cognitivo entre los tiempos T_o-T_1 y T_1-T_2 para cada uno de los grupos (intragrupo). El umbral de significación establecido para cada uno de los análisis fue $\leq .05$.

El análisis con ANOVA de medidas repetidas nos permitió ver: 1) el factor tiempo (cambios en el tiempo en la muestra en general), 2) la interacción entre los factores “tiempo vs grupos de estudio” y 3) la interacción entre factores “tiempo, grupos clínicos y grupos de estudio”.

Artículo 4.

Determinants of Adherence to a "GRADIOR" Computer-Based Cognitive Training Program in People with Mild Cognitive Impairment (MCI) and Mild Dementia.

Determinantes de la Adherencia a un Programa de Entrenamiento Cognitivo Basado en Computador "GRADIOR" en DCL y Demencia Leve.

Diseño

El diseño de este artículo partió del diseño de ECA descrito en el artículo 3 (Diaz Baquero, Franco Martín, et al., 2022). Sin embargo, este estudio sólo se centró en el GE. A partir del cual, se formaron dos grupos: adherentes (cumplimiento y persistencia) y no adherentes (aquellos que no cumplieron con alguna o ninguna de las condiciones) (Figure 4).

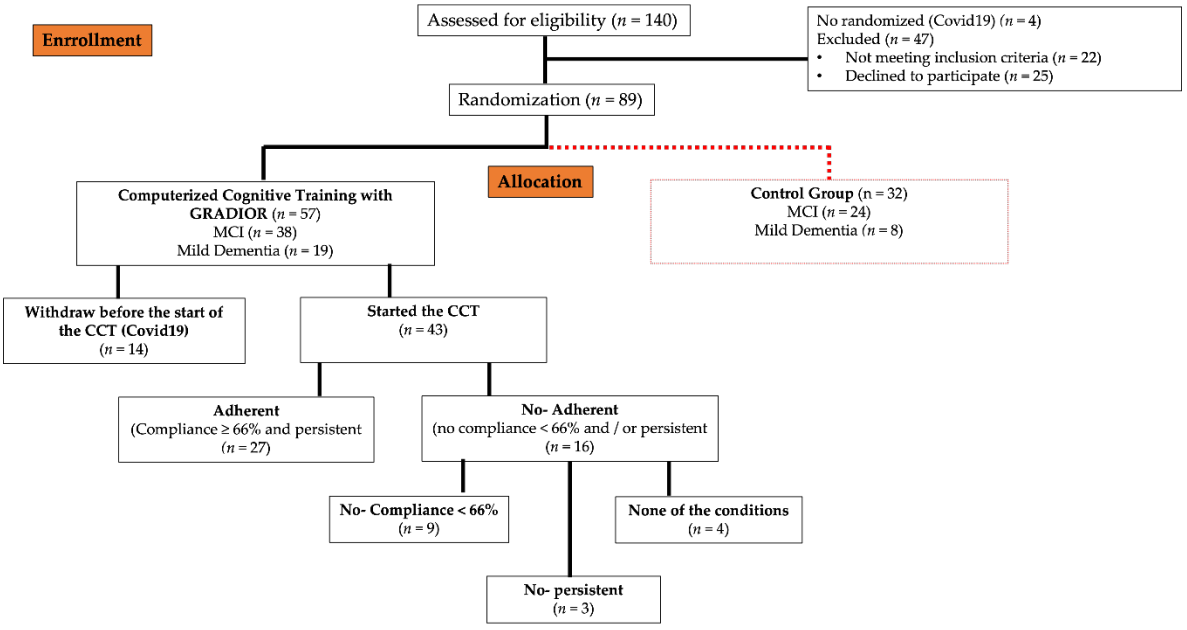

Figura 4. Proceso de aleatorización de muestra del Ensayo Clínico Aleatorizado (ECA). Y conformación del grupo adherente y no adherente asociado al grupo experimental (GE).

Tomado de "Determinants of Adherence to a "GRADIOR" Computer-Based Cognitive Training Program in People with Mild Cognitive Impairment (MCI) and Mild Dementia", (p. 6), por A.A. Diaz Baquero, M. V. Perea Bartolomé, 2022, Journal of Clinical Medicine, 11(6).

Participantes

La muestra de este estudio incluyó a 43 participantes de entre 60 a 86 años, y el 72,1% presentaron un nivel educativo básico primario. Los participantes fueron seleccionados de centros de día, clínicas de memoria y hospitales de Castilla y León y Galicia, España. Los criterios de inclusión y exclusión de personas con DCL y demencia leve fueron los mismos que los incluidos en el artículo 3.

Para conformar el grupo de adherentes se consideraron las condiciones de cumplimiento y persistencia. Respecto al cumplimiento terapéutico, las personas debían asistir al menos al 66% de las sesiones del máximo número de sesiones, cada sesión con una duración de 30-40 minutos. Así mismo, una persona fue considerada persistente si asistía semanalmente durante 16 semanas (4 meses) de intervención y, por lo tanto, no excedía el único "período de gracia" o intervalo permitido de ausencia del ECC de dos semanas continuas. Si la persona no cumplía con alguna o ninguna de las dos condiciones (cumplimiento y persistencia) se consideró no adherente.

Evaluación neuropsicológica

Las posibles variables predictores de la adherencia se asociaron con los procesos evaluados durante la línea de base del ECA. El protocolo de evaluación para el ECA incluía varias escalas que evaluaban diferentes aspectos (Vanova et al., 2018). Sin embargo, seleccionamos las variables de nuestro interés para nuestro estudio, considerando la literatura y nuestros objetivos. Se evaluaron aspectos sociodemográficos como edad, sexo, nivel educativo y años de educación. Las escalas cognitivas fueron las mismas que las usadas para el artículo 3 (Tabla 1).

Tabla 1. Descripción de los instrumentos

Determinantes	Test	Sub-escala	Evalúa	Escala de medida
Cognición	MMSE		Estado cognitivo general	Puntaje: 0-30
	ADAS-Cog		Estado cognitivo general	Puntaje: 0-70. 70 = Peor o menor rendimiento cognitivo
		Memoria de palabras	Memoria: Recuerdo libre verbal	10= número máximo de palabras no recordadas
		Reconocimiento de palabras	Memoria: reconocimiento verbal	12= número máximo de palabras no recordadas

Determinantes	Test	Sub-escala	Evalúa	Escala de medida
Psicológico	TMT-A	Tiempo	Velocidad de procesamiento	Tiempo (Percentil): 5-95
		Errores	FE: Atención selectiva-sostenida. Flexibilidad cognitiva.	Errores = 0-4. 4 = Número máximo de errores
	WAIS-III	Total Dígitos	FE: MT. Atención y memoria inmediata auditiva.	Puntuación escalar: 1-19
		Dígitos y Símbolo	FE: MT y atención	
		Aritmética	FE: atención. WM. Razonamiento numérico	
	CAMCOG	Razonamiento visual	FE: Razonamiento abstracto visual	Puntuación: 0-6. 6 = Número máximo de aciertos
	RBMT	Reconocimiento de dibujos	Memoria: reconocimiento visual	Puntuación: 0-10. 10 = Número máximo de aciertos
	FVS		EF: fluidez, flexibilidad cognitiva, categorización y monitorización del rendimiento	Puntuación escalar: 2-18
	FVL-P			
	FVL -M			
	FVL -R			
	GDS		Nivel de Depresión	Puntuación: 0-15. 15 = síntomas máximos de depresión
	Motivación	Atención	¿Necesitas que alguien te anime a asistir a GRADIOR?	Puntuación: 1-5. 1 = Nada. 2 = Algo. 3 = No estoy seguro. 4 = Bastante. 5 = mucho
	Expectativas	Memoria	¿Creo que GRADIOR ayudará a mi memoria?	
		Calidad de vida	¿Creo que mi calidad de vida mejorará después de GRADIOR?	
		Tiempo libre	¿Creo que el taller con GRADIOR ocupará mi tiempo de forma agradable?	
		Relacionarse	¿Me gustaría conocer gente nueva en el taller con GRADIOR?	
Salud física	EQ-5D-5L	Movilidad	Percepción subjetiva de los problemas de movilidad	Puntaje: 1-5. 1 = No tengo problemas. 2 = problemas menores. 3 = problemas moderados. 4 = problemas graves. 5 = no puedo
		Autocuidado	Percepción subjetiva de problemas para bañarse y vestirse	
		Actividades de la vida diaria	Percepción subjetiva de problemas para realizar AVD	
		Dolor y Malestar	Percepción subjetiva del dolor o malestar.	
		Ansiedad y depresión	Percepción subjetiva de depresión o ansiedad.	
	Estado de salud		Percepción subjetiva del estado general de salud	Puntuación: 0-100. 100 = Salud excelente
Tecnología	Uso previo de tecnología			1 = Si. 2 = No

Note: CAMCOG, Cambridge Cognition Examination; EQ-5D-5L, EuroQol; FE, Función ejecutiva; FVS; Fluidez Verbal Semántica; FVL, Fluidez Verbal Lexical; GDS, Geriatric Depression Scale; MMSE, Mini Mental State Examination; MT, Memoria de trabajo; RBMT, The Rivermead Behavioural Memory Test; TMT, Trail Making Test; WAIS-III, Wechsler Adult Intelligence Scale

No obstante, también se evaluó el estado afectivo, la motivación y las expectativas como parte de la dimensión psicológica. El componente afectivo se evaluó mediante el GDS (Yesavage & Sheikh, 2018). La motivación y las expectativas se evaluaron mediante una serie de preguntas. Y, se utilizó el test EuroQol (EQ-5D-5L) (Herdman et al., 2011) para evaluar la percepción de los pacientes sobre la dimensión físico-salud y la percepción de los participantes con respecto a su estado de salud actual (Tabla 1).

Entrenamiento cognitivo basado en computadora (ECC) y adherencia

Para el ECC se usó el programa GRADIOR (Diaz-Baquero et al., in press). La intervención y/o entrenamiento cognitivo con GRADIOR para el GE se realizó de la misma manera que la especificada en el artículo 3.

Para calcular la tasa de adherencia, esta se obtuvo dividiendo el número de sesiones a las que asistió cada persona al ECC durante los 4 meses por el número máximo de sesiones a las que debía asistir, el resultado se multiplicó por cien, excepto para los participantes que fallecieron o abandonaron por razones médica, para los cuales se calculó la tasa de adherencia sólo hasta el momento de la deserción. Consideramos el punto de corte del 66% para la tasa de adherencia o cumplimiento terapéutico según la literatura (Coley et al., 2019; Heesch et al., 2003; Sjösten et al., 2007). La persistencia o no se consideró como una variable dicotómica (Leslie et al., 2008) y se midió teniendo en cuenta si la persona completó o no los 4 meses de intervención, considerando el período de gracia.

Análisis estadístico

El análisis estadístico se realizó con el Paquete Estadístico de Software para Ciencias Sociales (SPSS) (IBM-Corp, 2017). Se utilizó la correlación biserial puntual para encontrar el grado de asociación entre la variable dicotómica-dependiente (adherente y no adherente) y las variables cuantitativas e independientes (sociodemográficas, cognitivas, psicológicas y físico-salud). Y la correlación Phi para encontrar la asociación entre variables dicotómicas.

Las variables independientes que se correlacionaron significativamente con la variable dependiente fueron posibles variables predictoras de la adherencia y, por tanto, se introdujeron en el análisis con Regresión Logística Múltiple con el objetivo de hallar el modelo de adherencia.

Utilizamos un análisis no paramétrico para dos muestras independientes (Mann Whitney) debido al tamaño de la muestra y a la distribución no-normal (Shapiro-Wilk). Este análisis nos

permitió 1) comparar el desempeño entre el grupo adherente y no-adherente, 2) investigar si había diferencias significativas entre las personas con DCL y demencia leve en relación con cada grupo (adherente y no-adherente) y, 3) evaluar si existían diferencias significativas entre adherente con DCL vs no-adherente con DCL y adherentes con demencia leve vs no-adherentes con demencia leve con respecto a las variables que conformaron el modelo de adherencia.

Capítulo IV

Compendio de Publicaciones

En este capítulo, se incluye una copia de cada una de las publicaciones originales que constituyen esta Tesis Doctoral. Se presenta también, el resumen en castellano de cada publicación científica. Cada artículo y capítulo se presenta conforme las normas de la revista científica en la que fueron publicados.

Artículo 1

Programa de rehabilitación cognitiva basado en ordenador GRADIOR para demencia leve y deterioro cognitivo leve: Nuevas características.

Manuel A. Franco-Martín[1,2,3,4], **Angie A. Diaz-Baquero[3,4*]** , Yolanda Bueno-Aguado[5] , María T. Cid-Bartolomé[6] , Esther Parra Vidales[7] , María V. Perea Bartolomé[8] , Isabel de la Torre Díez[9] and Henriëtte G. van der Roest[10]

Resumen

Introducción: El creciente número de personas mayores y, con ello, el aumento de alteraciones neurológicas como la demencia ha llevado a implementar el uso de programas informáticos para la rehabilitación cognitiva en personas con demencia. Desde hace 20 años, se ha venido desarrollando el programa de rehabilitación cognitiva GRADIOR y se ha realizado varios estudios asociados a su usabilidad y efectividad. Este artículo describe el desarrollo de la última versión del programa de rehabilitación cognitiva computarizado GRADIOR para personas con diferentes etiologías neurológicas, especialmente deterioro cognitivo leve y demencia leve.

Resultados: GRADIOR es un programa que permite la evaluación y rehabilitación cognitiva de personas afectadas por deterioro cognitivo. La nueva versión de GRADIOR se caracteriza por una estructura dinámica y flexible tanto para el usuario como para el terapeuta, compuesto por un: Gestor Clínico, Gestor de Historia Clínica, Gestor de Tratamiento y Gestor de Informes. Por una estructura basada en requerimientos específicos, GRADIOR incluye una serie de modalidades y sub-modalidades, cada modalidad está constituida por una serie de ejercicios con diferentes niveles de dificultad.

Discusión: Estudios previos asociados con versiones anteriores de GRADIOR han permitido el desarrollo de una nueva versión de GRADIOR. Teniendo en cuenta aspectos asociados a la experiencia de usuario, usabilidad y efectividad. Aspectos que han permitido obtener un programa que pueda cubrir las necesidades de las personas mayores con demencia.

Palabras clave: Demencia, Software, Rehabilitación neurológica, Cognición, Servicios comunitarios de salud mental.

BMC Medical Informatics and Decision Making

SOFTWARE

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Computer-based cognitive rehabilitation program GRADIOR for mild dementia and mild cognitive impairment: new features

Manuel A. Franco-Martín[1,2,3,4], Angie A. Diaz-Baquero[3,4*], Yolanda Bueno-Aguado[5], María T. Cid-Bartolomé[6], Esther Parra Vidales[7], María V. Perea Bartolomé[8], Isabel de la Torre Díez[9] and Henriëtte G. van der Roest[10]

Abstract

Background: The growing number of older people and, with it, the increase of neurological impairments such as dementia has led to the implementation of the use of computer programs for cognitive rehabilitation in people with dementia. For 20 years, we have been developing the GRADIOR cognitive rehabilitation program and conducted several studies associated with its usability and effectiveness. This paper describes the development of the latest version of the GRADIOR computer-based cognitive rehabilitation program for people with different neurological etiologies, especially mild cognitive impairment and mild dementia.

Results: GRADIOR is a program that allows cognitive evaluation and rehabilitation of people affected by cognitive impairment. The new version of GRADIOR is characterized by a structure that is dynamic and flexible for both user and therapist, consisting of: Clinical Manager, Clinical History Manager, Treatment Manager and Report Manager. As a structure based on specific requirements, GRADIOR includes a series of modalities and sub-modalities, each modality comprising a series of exercises with different difficulty levels.

Discussion: Previous studies associated with earlier versions of GRADIOR have allowed the development of a new version of GRADIOR. Taking into account aspects associated with user experience, usability and effectiveness. Aspects that have made it possible to achieve a program that can meet the needs of older people with dementia.

Keywords: Dementia, Software, Neurological rehabilitation, Cognition, Community mental health services

Background

Europe is an ageing society. Eurostat's population projections anticipate that in the coming decades the number of people aged over 60 will increase by approximately two million people per year, accounting for around 30% of the total population by 2060 [1]. Dementia and cognitive impairment are age-related conditions that involve very high healthcare demands. The overall crude prevalence rate for mild cognitive impairment (MCI) in the over-60 population is between 6 and 42% [2], and with 20–40% of such cases progressing into dementia [3]. Approximately 5–7% of the world population has developed some form of dementia [4]. In Spain alone, over 800,000 people are affected by dementia [5].

Due to its high prevalence and consequences in the older population, dementia has become a major public health challenge [6] and a healthcare priority in many countries [4]. Projections based on current healthcare policies predict an increase in age-related public expenditure from 4.1% to around 29% of Gross Domestic Product by 2060 [7]. Such rising costs will put a strain on the sustainability of existing healthcare systems [8]. To counteract the rising health care expenditures, European

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policies are increasingly focussing on independent living for older adults, since community care is cheaper than care in a facility.

In recent decades, many different psychosocial approaches aimed at improving and maintaining cognitive ability have been developed to slow down the progression of dementia as much as possible and to enable people affected by it to age healthily [9, 10]. Various studies have proven the positive effects of cognitive rehabilitation as an individualised cognitive intervention explicitly focused on a person's objectives and needs (cognitive profile) [11]. Huckans, Hutson [12] reported improvements in performance in people with MCI in at least one cognitive domain, which shows that adults with MCI are still able to learn. Another study found that cognitive rehabilitation had a long-lasting effect on the overall cognition of older adults experiencing age-related cognitive decline [13]. Recent studies suggest that slowing the progression of dementia by one year would lead to a better quality of life for its sufferers [14, 15] and to a significant cut in the related socioeconomic costs [16–18].

The most common implementation of cognitive rehabilitation is based on pen and paper exercises and training that is conducted by a neuropsychologist. This makes the treatment very costly, which added to the fact that it is not easy to have a neuropsychologist available in every treatment location (e.g. community or primary care center), means that accessibility to this approach can be poor. It is well known that people with dementia in Europe have trouble in getting access to adequate treatment, especially to psychosocial therapies [19]. Particularly in rural and semirural regions of the vast majority of European Union countries, where the percentage of people over 65 years of age is above national averages and resources for services or treatment are scarce [20, 21].

Since timely treatment is crucial to achieve better results and fewer complications, it is important to improve accessibility to services and treatments [21]. A good opportunity to increase accessibility to treatments could lie in Information and Communications Technology (ICT) solutions for health and wellness coaching. There are already studies that have shown that computer-based cognitive interventions are effective in improving cognition, anxiety and mood in people with dementia, and can lead to better results than non-computer-based interventions [22, 23]. Nevertheless, despite technological progress, the improved user-friendliness of ICT devices and the spread of smart phones, tablets and other wearables, the use of new ICT solutions for people with dementia is still very low.

Cognitive computer-based training programs still face the challenge of being accepted by elderly people who are not very familiar with technology [24]. In addition, these solutions must be embedded into the strategies and goals of the end-user organisations, service providers and business partners, which requires these tools to be user-friendly and useful for therapists, and well-accepted by carers and patients. From the INTRAS foundation, we have tried to improve care for people with cognitive impairment by developing a new computer-based tool for cognitive rehabilitation called GRADIOR (Fig. 1). In constant development for the last 20 years, the earliest version of GRADIOR has been used in clinical practice since 1997, adding improvements ever since. This paper describes the development of the latest version of the GRADIOR computer-based cognitive rehabilitation program for people with different neurological etiologies, especially mild cognitive impairment and mild dementia.

Fig. 1 Person with dementia performing cognitive stimulation with software GRADIOR

GRADIOR is a computer-based program used for neuropsychological rehabilitation in people suffering from one or more cognitive disorders of different etiology, as well as for cognitive stimulation in healthy people [25]. GRADIOR was designed to stimulate the full range of cognitive skills and also includes tools for neuropsychological assessment. The program uses a touch screen in order to make its use easier for people lacking computer literacy. The development of GRADIOR started 20 years ago, ever since combining knowledge on neuropsychological advances in the field of clinical expertise with the experiences of end-users and stakeholders in its development process.

The first GRADIOR version was funded and validated by the Social Affairs Minister [26]. The third GRADIOR version was acknowledged by the 2007–2010 Alzheimer Plan of Andalucía (Spanish region) as recommended software for cognitive stimulation. Currently, there are more than 500 clinical and social settings in Spanish cities that use and support different GRADIOR versions

as a good rehabilitation and stimulation cognitive tool. GRADIOR is used by more than 11,000 people.

Requirements

Non-functional

In this regard, the new GRADIOR version was designed pursuing the following objectives: (a) a familiar looking interface, (b) to facilitate the role of professionals through the creation of new exercises, making it possible to obtain user-performance reports and digitized evaluations, (c) an easy-to-use program based on a tactile interface, (d) a program with exercises that allow the improvement or maintenance of cognitive functions, (e) as well as, a program to promote the socialization of older adults with other people who have the same needs and/or problems.

GRADIOR is based on a series of essential features that make it an easy access program that offers adequate user experience. Thus, it is (a) flexible: it has been developed for a broad variety of disorders such as: neurodegenerative diseases, brain damage, stroke, mental retardation, mental illnesses, and epilepsy. Therapists can tailor the rehabilitation approach to the patient's cognitive profile, personal preferences, and needs; (b) dynamical: it allows the addition of new tools; (c) user-friendly: it can be used by users who lack computer-literacy; (d) economical: it is easily accessible and accommodates the economic needs of its target population; (e) highly accessible: it can be easily implemented in any setting, including rural areas; (f) useful: studies on earlier versions reveal positive results for this program [26].

Functional

Likewise, certain functional requirements were established for the program, which should enable therapists to: (a) obtain a neuropsychological profile of each user based on the neuropsychological evaluation of each of the cognitive processes included: orientation, attention, memory, language, reasoning, calculus, executive function; (b) design and implement an individualized cognitive training plan according to the cognitive processes affected and the level of deterioration in each of them; (c) periodically adjust the treatment plan to the patient's performance and continuous improvement; (d) draw up user performance reports based on the exercises, sessions, modalities and sub-modalities, thus facilitating work on adjusting the plan and producing progress reports.

Technical

GRADIOR software is compatible with a Windows operating system (the current version of GRADIOR requires Windows 7 SP1 or later) and is specifically designed for touchscreen computers, although it can be also used with the mouse or keypad. To run smoothly, the system requirements are: RAM (2 GB/4 GB recommended), graphics card (RAM) (256 MB minimum/1 GB recommended for optimal graphical performance) and Microsoft Office 2003 or later versions. We are currently working on a tablet version.

Minimum requirements for the PC where the server is to be installed:

- Windows server 2008, 2 GB RAM + 3.2 GHz + .NET Framework 3.5 SP1.
- Configuration of antivirus exclusions to allow remote access.
- Wired internet connection.
- IP publishes FIXED and configuration of the necessary ports to access the SQLSERVER from an external client (if the server is not in the same NETWORK).
- Local administrator permissions.

Minimum customer equipment requirements:

- Operating System: Windows 7 ServiPack1 + .NET Framework 3.5 SP1.
- RAM: 2 GB minimum—4 GB recommended.
- Graphical performance: 3.0 MHz minimum—4.5 MHz recommended.
- RAM graphics card: 256 MB minimum—1 GB recommended.
- Tools installed: Microsoft Office 2003 or higher.
- Configuration of antivirus exclusions to allow the running of the GRADIOR program.
- Wired internet connection.
- Local administrator permissions.

Implementation

Microsoft Visual Studio is used as an integrated development framework for GRADIOR. The object-oriented programming language that brings together all the necessary components for developing applications is Visual Basic.NET. SQL Server acts as the database management system.

Easy development methodology: Scrum is an agile, incremental and iterative development framework. It allows the planning and managing of the development, focusing on achieving high productivity and quality levels while mitigating the risks of software development thanks to a regular review and adjustment of the process and product.

Some of the benefits for which Scrum has been selected are:

- Project status and progress visibility.

- Systematic mitigation of risks by means of intensive phases. The complexity of the development is reduced (requirements, technology) to what fits in one sprint.
- Enhancement of product internal quality to be built incrementally and at a constant pace.

Architecture and deployment

GRADIOR 4 has been developed according to a "client/server" architecture that allows users to execute the "client" on their own device, which connects to a server that stores the data shared by all the "clients". This architecture is supported by the Microsoft Framework.NET platform. In this way, GRADIOR can be easily implemented in home care.

In short, GRADIOR 4 supports three installation options:

- Basic installation (single-user system): For local use, both "server" and the "client" are installed on the same device (internet connection not required).
- Installation in local area network (intranet): GRADIOR is installed according to a standard "client/server" architecture. Data are stored on a local server (internet connection not required).
- Remote mode installation: GRADIOR is installed according to a multi-site architecture. The "server" (database management system) is installed on the main premises while "clients" can be deployed in far-away facilities (internet connection required) or in main facilities (intranet access or internet access).

Through the server, the therapist has access to the data of every treatment session, while also acting as an administrator who can modify and personalize treatments for every user from the server computer. Likewise, the "server" computer allows the therapist to video contact the client. GRADIOR is available in Spanish and English, but its contents can be easily changed and culturally adapted to any language or environment.

Results

This section describe different structural and functional aspects of the GRADIOR rehabilitation program: the modules that comprise it, the different steps to plan an intervention plan and preliminary data on usability from previous versions of GRADIOR. Finally, this section places special emphasis on aspects of usability and user experience of the new GRADIOR 4 version, citing studies that support it.

Description of the program

GRADIOR has been developed to design and manage personalized cognitive rehabilitation treatments, save patient clinical features, overview results and adapt exercise difficulty to the patient's cognitive level. The current version includes eight different moduli (orientation, memory, attention, calculus, executive function, perception, language and reasoning) for clients to follow.

Therapists have the following five GRADIOR functionalities at their disposal:

Clinical management

The Clinical Management provides an overview of the user accounts of all the patients under treatment by a specific therapist, also allowing the addition of new users to GRADIOR (a picture and password are required for every patient), the modification of information and the deletion of user accounts. The therapist can see the centre, appointed therapists and condition of every patient (Figs. 2, 3).

Clinical history manager

The Clinical History Manager stores the (socio) demographic and clinical data of every GRADIOR user. Client files such as personal data, clinical observation, medication and results of clinical assessments are stored in a session that can be resumed. The therapist is the only person authorized to access this session through two-step authentication. In a clinical observation session, the therapist can record the diagnosis from the International Classification of Diseases 10 (ICD-10), record the patient's illnesses and family background. In the medication session, the therapist can register information about medication, e.g. dose, duration, start date and end date.

In results of clinical assessment, the scales used in people with cognitive impairment are, in this order: Mini Mental State Examination (MMSE) [27], Barthel Scale [28], Geriatric Depression Scale Yesavage (GDS) [29], Lawton Instrumental Activities of Daily Living questionnaire (IADL) [30], Cambridge Cognition Examination (CAMCOG) [31], Clock Drawing Test (CDT) [32] and Trail Making Test (TMT) [33] (Fig. 4).

Treatment management

The Treatment Management is a key function. Here the therapist can design personalized treatment plans based on the information of the user's cognitive profile as stored in the Clinical History Management, unmet needs and preferences. The therapist can schedule trials, select exercises by cognitive sub-modalities, establish levels of

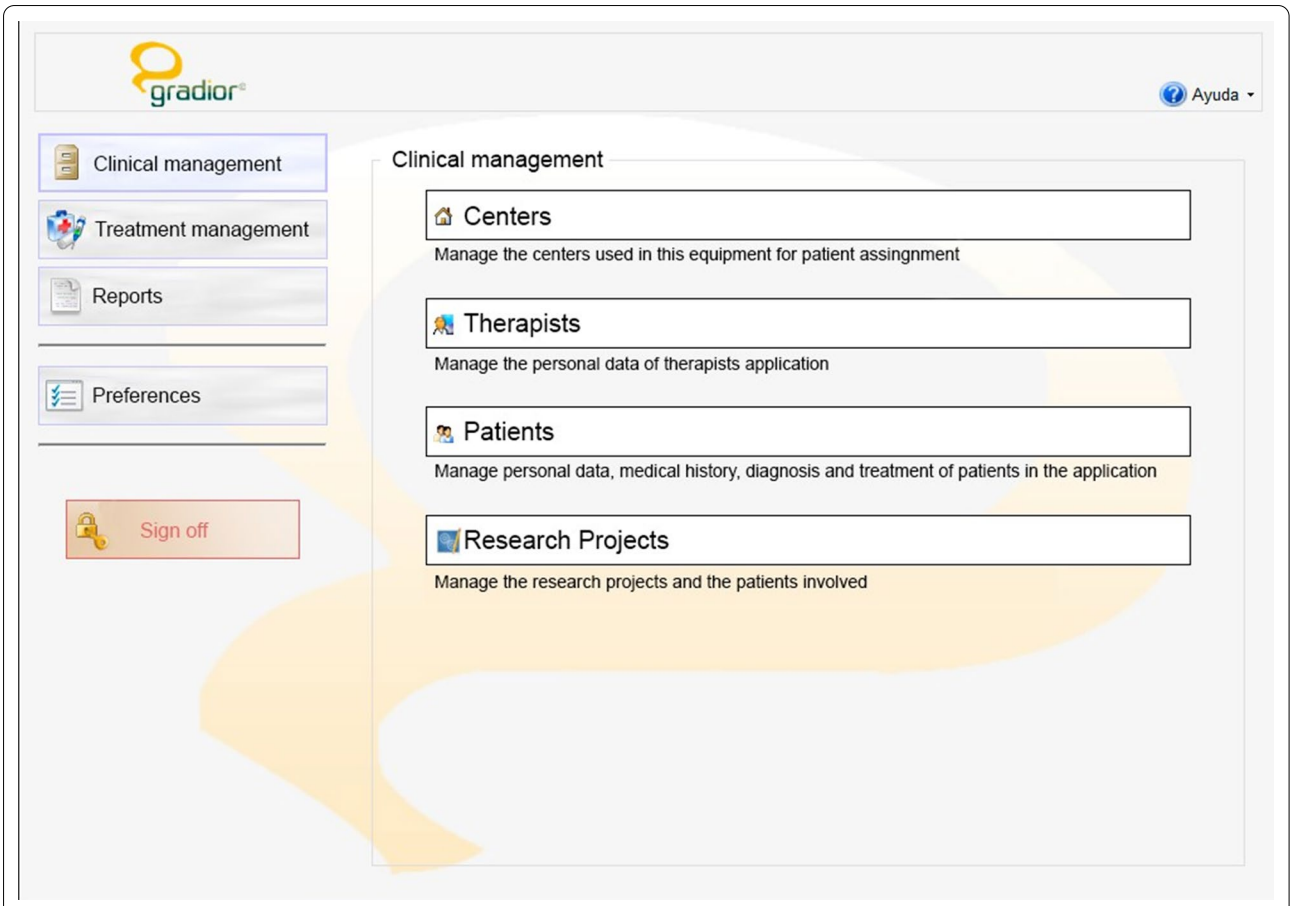

Fig. 2 Clinical management in software GRADIOR

difficulty for each exercise and define the duration of the individualized cognitive rehabilitation plan.

In most cases, the therapist designs a one-week trial rehabilitation training plan, which is subsequently fine-tuned to a suitable personalized cognitive rehabilitation treatment according to the patient's performance. Training can be adjusted at any time during the course of the program, depending on the follow-up and performance of the patient. The program contemplates no automatic changes in treatment plan, so that any alteration always requires the intervention of a therapist (Fig. 5).

Report manager

The Report Manager stores the performance data obtained from every user trial separately. It allows the tracking of patient improvement over time for all cognitive functions. This is essential for patient monitoring and to adapt the cognitive rehabilitation intervention to the user's needs. The therapist can obtain different types of patient report, e.g. report by modality and sub-modality at a general level or level-specific reports. This last report helps the therapist to modify the levels according to individual patient performance (Fig. 6).

Modalities, sub-modalities and exercise/task description

GRADIOR includes exercises aimed at stimulating a variety of cognitive functions (modality): orientation, attention, calculus, executive function, language, memory, perception, reasoning, and different sub-modalities of every function (Fig. 7). Every sub-modality includes different performance levels and different types of exercises (Table 1). Some examples can be found on the GRADIOR website https://www.intras.es/nos-hacemos-mayores (See additional file 1). For instance, the different sub-modalities of the memory modality are: long-term graphic memory, immediate verbal memory, short-term verbal memory, short-term verbal memory compound, long-term verbal memory, implicit memory, location memory, semantic memory and span memory direct.

A special *module called* "INTRAS" permits access to the GRADIOR content database that contains the material used for the exercises (pictures, words, voices, recordings etc.) and allows the addition of new content.

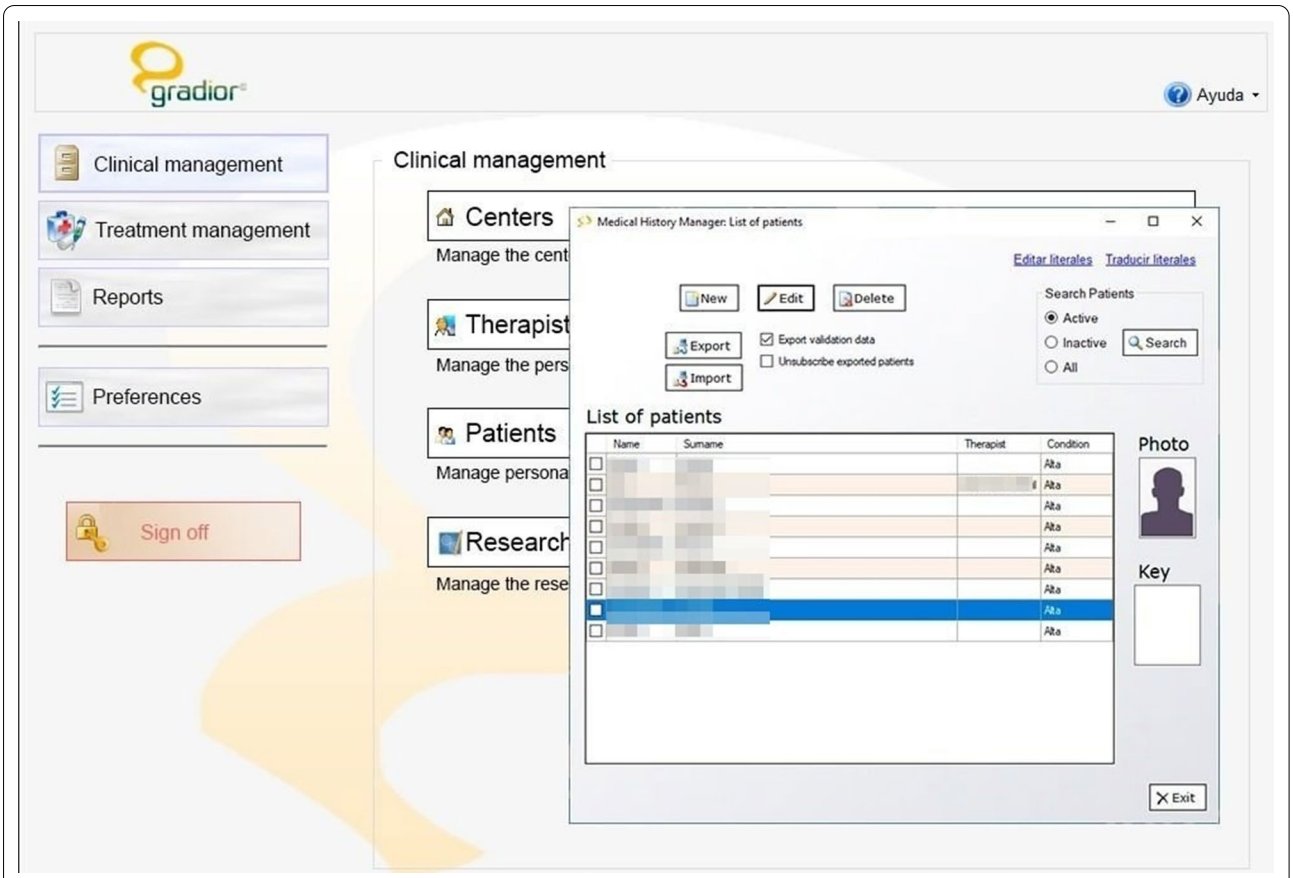

Fig. 3 Medical history manager: list of patients in software GRADIOR

The therapist can add new or specific content to the database that meets the preferences of the patient, takes into account the cultural environment or follows a stimuli ontology. Such new content can even be of personal significance to the individual patient, including family pictures or familiar voices. The module enables the description and categorization of all the stimuli that are required to develop new exercises or to automatically translate the system into other languages.

The INTRAS module is key to the high flexibility and personalized training plans provided by GRADIOR. Therefore this is essential to maximize the benefits patients can obtain from the cognitive rehabilitation program. This module is where the difficulty level for each cognitive sub-modality can be defined, according to the complexity of the stimulus, the number of stimuli, the speed of presentation, the perceptual modalities, familiarity with the stimuli or the number of confusion stimuli. Although GRADIOR's open functioning and flexibility involve many advantages, these could also be a barrier.

Due to the large number of possibilities, defining a therapeutic plan can be very time consuming for therapists. To avoid this, the INTRAS module is optional and therapists can use all the exercises previously developed by default in the GRADIOR 4-basic. The program contains 12,601 exercises (attention-1533, perception-1104, memory-4674, calculus-1500, language-452, reasoning-404, and executive function-2934). This means that the variability of exercise and task is wide enough to avoid repetition during a cognitive rehabilitation program.

Users personalize their treatment by selecting a personal identifier (photo/name) and the traditional password is replaced by a picture chosen by the patient. At the beginning of every session, patients select their personal image and then their password out of 9 pictures by touching the screen. Thus, many users can follow their personalized cognitive rehabilitation program on the same computer without the need to remember a password.

How does it work? GRADIOR-based cognitive rehabilitation treatment steps.

GRADIOR-based cognitive rehabilitation follows a five-step protocol that is implemented in the following order:

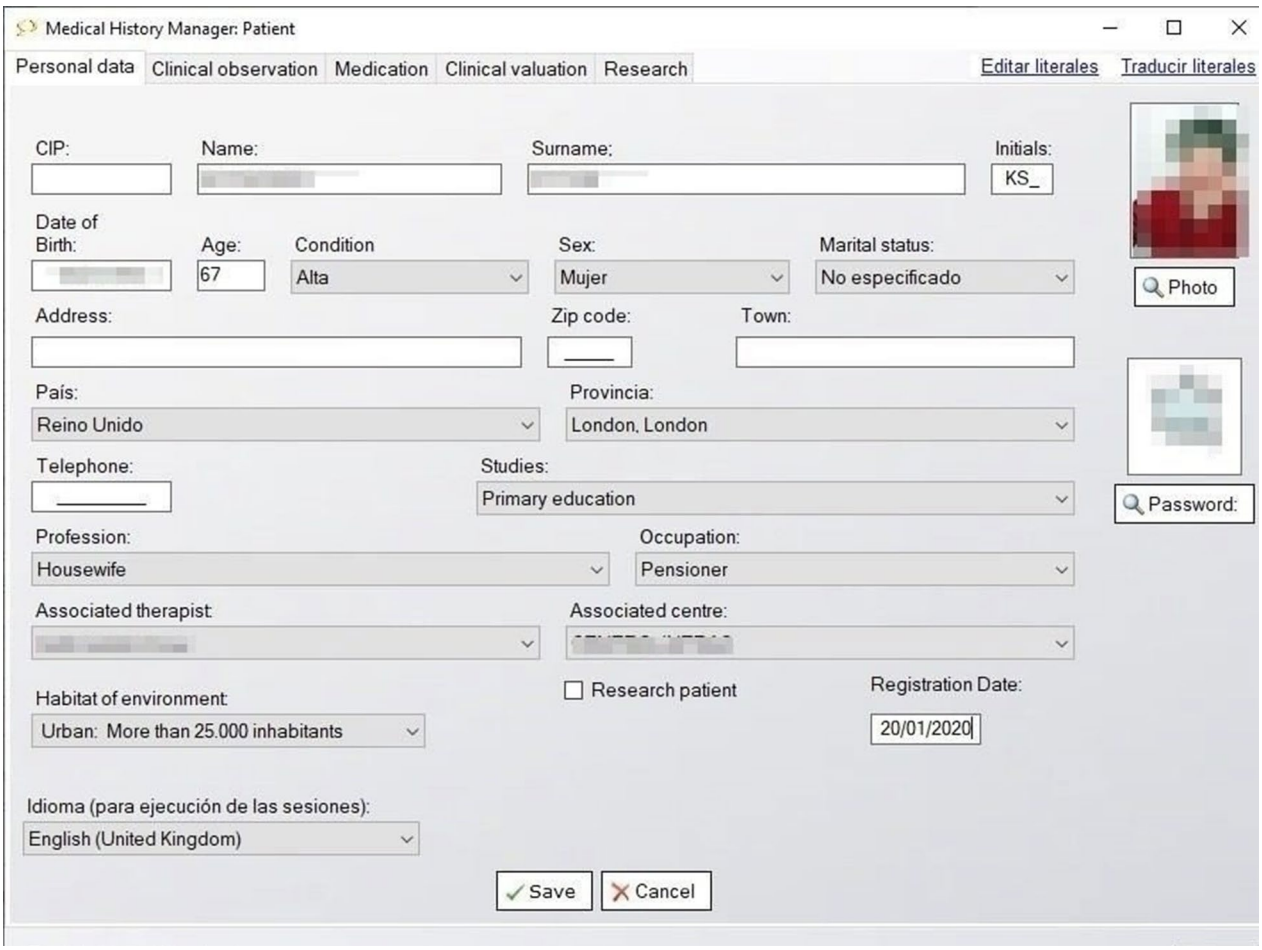

Fig. 4 Medical history manager: patients in software GRADIOR

(1) Preliminary neuropsychological assessment and baseline definition.

Before starting cognitive rehabilitation, it is necessary to obtain the user's cognitive profile in order to personalize the approach. Therefore, the first step is to apply a traditional comprehensive neuropsychological assessment by means of a test battery in GRADIOR.

(2) Trial using baseline treatment.

GRADIOR offers standard treatments for people with similar cognitive capacity. Based on the cognitive assessment results, the user will receive a standard one-week training schedule. This trial week allows the therapist to acquire a thorough insight of the user's cognitive skills, computer skills and motivation to use GRADIOR.

(3) Designing personalized cognitive rehabilitation.

The trial provides the therapist with the appropriate knowledge of the patient's skills and preferences to design a personalized treatment plan. The therapist chooses the exercises to be included in the cognitive rehabilitation treatment plan, their difficulty level, establishes session frequency and duration. The therapist controls all the cognitive rehabilitation variables.

(4) Providing personalized cognitive rehabilitation.

After these three steps, the user starts the actual personalized intervention. Training sessions are completed at home or at a convenient location (e.g. hospital, community center) according to a pre-fixed schedule. While performing the exercises, users can receive feedback on their scores and skills at the end of every session. Although this is optional, it might increase motivation to follow the sessions.

(5) Fitting treatment regularity (levels of difficulty, frequency of tasks).

Depending on the user, the plan can be adapted every month. The therapist checks the patient's outcomes over

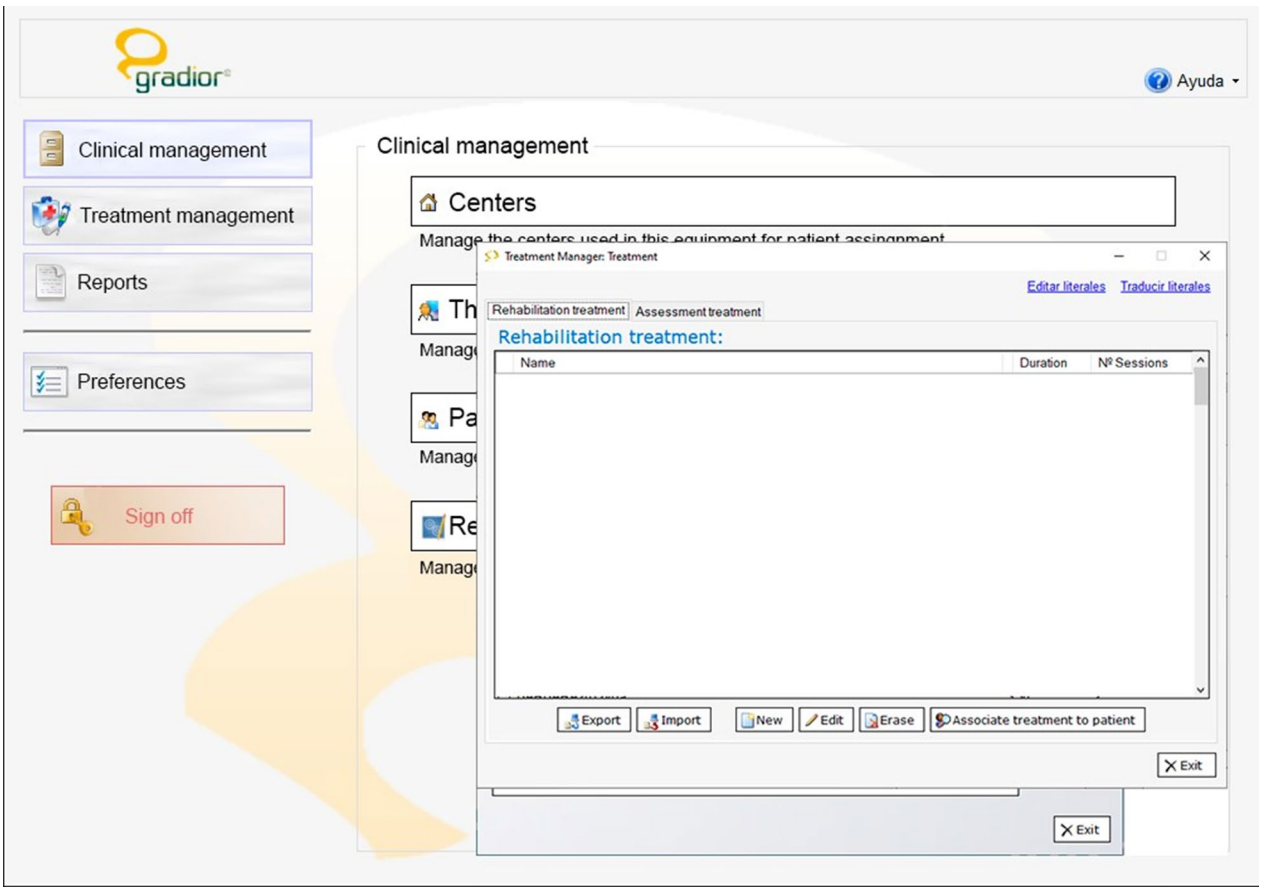

Fig. 5 Treatment management in software GRADIOR

the last period and makes the necessary changes in order to adapt the cognitive rehabilitation plan according to new unmet needs or improved cognitive skills. The client's feelings and motivation regarding GRADIOR are discussed. In the case of patients living in faraway locations, this is discussed via a videoconference embedded in GRADIOR.

GRADIOR usability and usefulness. Preliminary data

From its earliest versions, the GRADIOR program has reached high levels of user satisfaction and usability, contributing to the alleviation of neurocognitive symptoms in people with different pathologies [34]. GRADIOR also provides support for therapists in their daily work, since they report satisfaction with its usefulness and consider it a good psychostimulation tool [35].

The usability characteristics: easy learning, effectiveness/efficiency, memory capacity, low error rate and satisfaction were measured through a "satisfaction evaluation of the GRADIOR centers". It was conducted by Zoto, leader of a Technology Research Group at the Polytechnic University of Madrid. In terms of usability, GRADIOR was considered [34]:

- Highly acceptable, due to its flexibility and simplicity;
- Highly user-friendly, due to its welcoming and approachable interface;
- Highly satisfactory for therapists and users in terms of contents.

Therapists pointed out that it was necessary to continue developing content on cognitive modalities, especially on execution skills. And even though GRADIOR was initially created for people with no technological skills; already in the first version, therapists sometimes felt that certain technical capabilities were required to use the program [34].

Despite these findings, the overall data proved GRADIOR to be highly acceptable. Even among people with schizophrenia, 83.1% of its schizophrenic users enjoyed working with GRADIOR [35], whereas only 22.9% of them reported difficulties in using the program. Most of

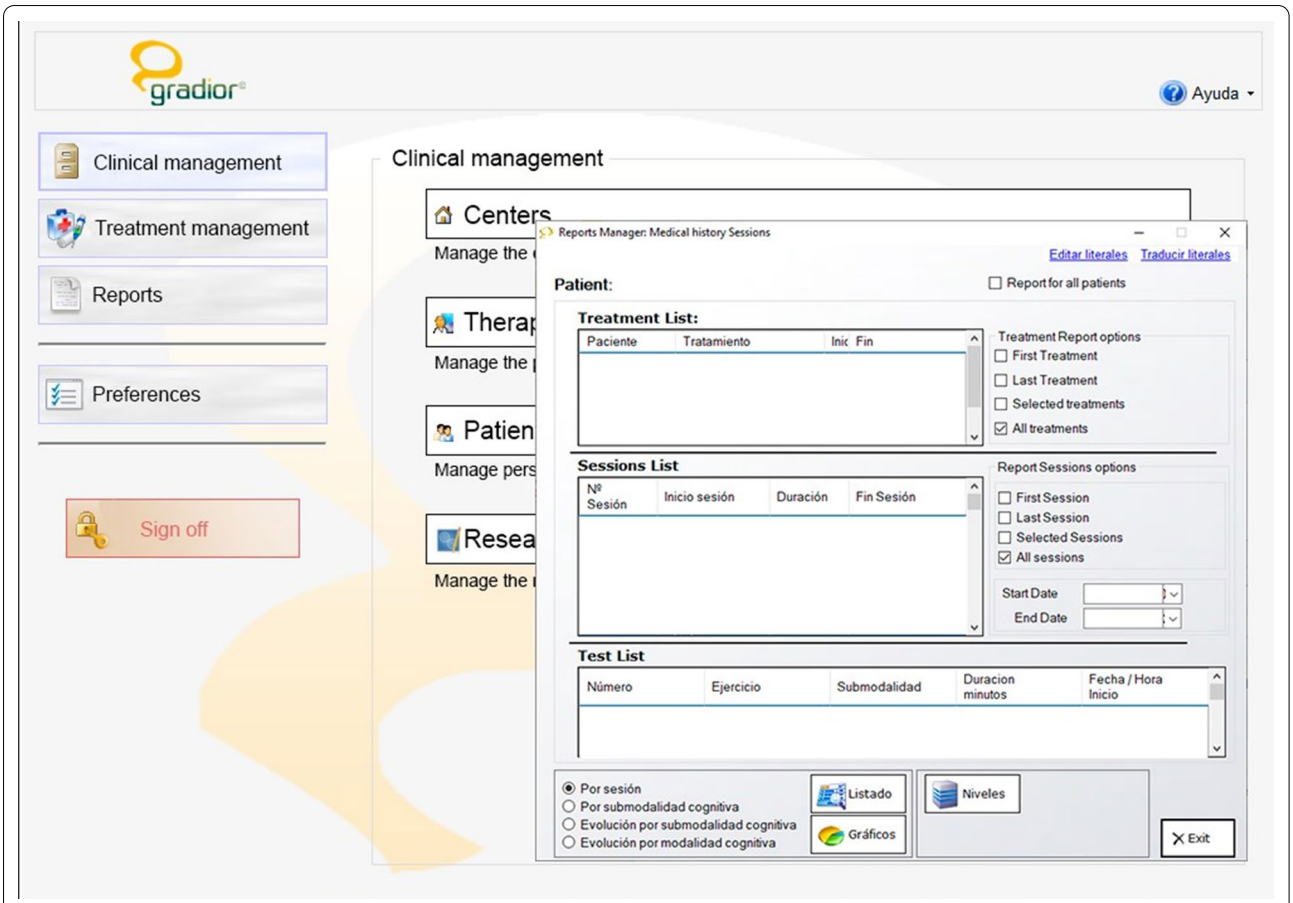

Fig. 6 Report manager: medical history sessions in software GRADIOR

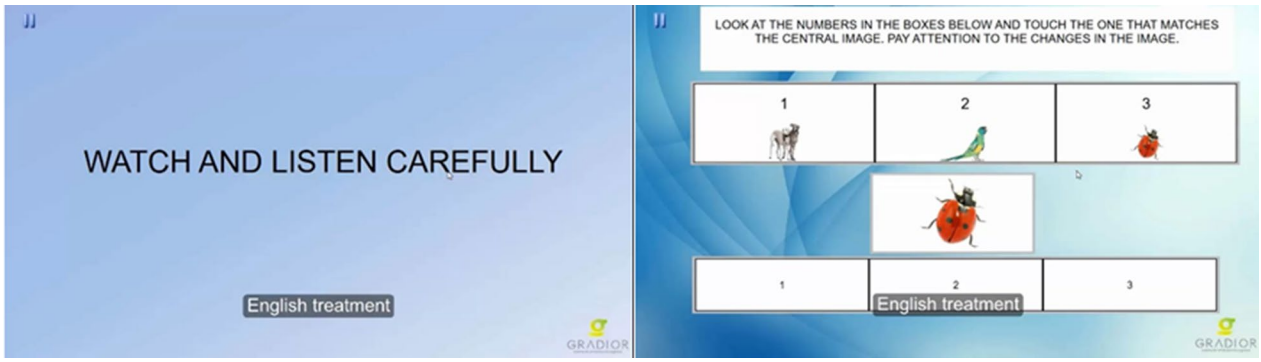

Fig. 7 Attention exercise in software GRADIOR

the respondents considered that GRADIOR had a welcoming interface and that it was pleasant to use.

Not only aspects of usability were defined, aspects associated with effectiveness were also evaluated. GRADIOR proved effective in treating behavioral and cognitive symptoms. In total, 61.8% of patients reported an improvement in their quality of life and independence, and 77.1% of the people described GRADIOR as a useful tool for the provision of individualized treatment according to their needs [35]. Also, other studies found that GRADIOR allowed maintenance of cognitive functions and improvement of emotional and behavioral aspects in people with mild dementia and MCI [36].

Table 1 Cognitive modalities and sub-modalities addressed by GRADIOR 4

Cognitive modalities	Cognitive sub-modalities (levels)	Cognitive modalities	Cognitive sub-modalities (levels)
Orientation	Temporary orientation [3]	Memory	Associative memory face-name [6], associative memory image-word [6], associative memory word-word [6], auditory memory (like verbal memory), immediate graphic memory [7], short-term graphic memory [7]), short-term graphic memory compound [7], long-term graphic memory [7], immediate verbal memory [7], short-term verbal memory [7], short-term verbal memory compound [7], long-term verbal memory [7]), implicit memory [1], location memory [6], semantic memory [1], span memory direct [8], span memory reverse letters [8], span memory direct numbers [8], span memory reverse numbers [8], direct object span memory [8], span reverse object [8]
Attention	Sequential visual selective attention [7], simultaneous visual selective attention [3], attention vigilance color [7], attention vigilance flashes [7], sustained attention color [2], sustained attention sparkles [2], sustained attention figures [2]		
Calculus	Quantitative calculation counting [5], calculus identification of numbers [3], calculus arithmetic problems [12]		
Executive function	Change rules [2], key task [6], auditory inhibition [4], visual inhibition [9], interference [7], numbers and letters [7], ordination stories [4], puzzles [10]	Perception	Perception colors auditory [11], perception colors graph [11], perception colors text [11], visual perception figures [4], visual perception faces [3], visual perception sizes [3]
Language	Language comprehension of words [2], language identification of written letters [3], oral letters identification language [3], word recognition language [2]	Reasoning	Reasoning sorting graphics [2], reasoning sorting texts [2]

Latest development: GRADIOR 4

Drawing from the results of the first studies, new features were proposed in order to improve GRADIOR's efficiency and usefulness. Suggested improvements included: development of a telematics network for easy understanding of instructions, variety of exercises and levels of difficulty, use of good color contrast aided visibility, changes in software programming to avoid interruptions [34] and the inclusion of real images in the exercises would help them to be more familiar and real for the patient [37]. All these features were introduced in the latest version, GRADIOR 4.

The development of GRADIOR was oriented in a user-centered design. In this way, GRADIOR responded to the needs and characteristics of the target population, generating greater usability [38, 39].

Considering the above, subsequent usability studies were carried out with the latest version of GRADIOR. The first studies reported that 81.2% of patients generated an acceptance of the program [40]. Moreover, 91.1% of the patients reported that they enjoyed the sessions, 63.3% of the patients mentioned that the instructions were clear and understandable and 70% of the patients reported that the program met their expectations [41].

Toribio Guzmán [42] proposed a study on aspects of usability and user experience of version 4 of GRADIOR combined with a physical program (Long Lasting Memories Program). For this objective, this study took into account different steps: (1) screening the population by applying the MMSE and the GDS, (2) phase of adaptation and learning to the program, (3) intervention for 3 months: 3–5 days a week for 40 min of cognitive training and 3 times a week for 1 h of physical training, (4) supervision during the sessions, (5) usability evaluation through the design and use of a questionnaire consisting of 5 dimensions: affective evaluation, usability, satisfaction, sustainability, independent life and social integration.

The results of the previous study are presented below. In the dimension on affective evaluation, the patients generated positive feelings and reactions to the use of this program, 79% of patients expressed that the program was fun and 78.9% of patients did not show feelings of boredom [43].

In the usability dimension, a good usability was highlighted through values that exceeded 87% in each evaluated usability criterion (attractive design, images, features in the physical-mental exercises, the main menu and exercises adapted to physical and mental abilities) [44]. A total of 60.1% of the people with MCI established that it was easy to use. In contrast, 40.1% of the people with mild dementia expressed difficulty in its use, requiring help or support during training sessions [43].

In the dimension of satisfaction, a clear predisposition to use the program was highlighted [44]. A quantity of 83.7% of patients believed that it was beneficial to their health. A total of 73% of the participants indicated that the program met expectations. And in 66.9% of the patients, there were feelings of security regarding the use of a technological device [43].

In the dimension of sustainability, 84% of the patients expressed interest in continuing to use the program [44], 96.1% of the patients would recommend the program and 78.1% of the participants would pay for the program [43].

In the last dimension, the patients noted the increase in their social interaction [43]. A total of 37.4% of patients thought they could use it independently at home [44] and a representative score in independent and social life was highlighted for the group with MCI compared to healthy participants.

However, an analysis of the usability of the alpha-version of GRADIOR 4 revealed that, while 46.5% of its users could work easily, it depended on age and on the severity of the impairment suffered [37].Therefore, the user-centered design of any program associated with cognitive training should take into account the characteristics of cognitive decline (type, level, and deficits) of people with dementia.

In this way, the program will be more usable and more widely adopted to the target population [39] As mentioned above, GRADIOR has different exercises per submodality for each modality and at the same time, these exercises have different levels of difficulty, which allows the program to be adapted to the type and level of cognitive decline of the patients.

Additionally, physical disability was found to seriously limit access to GRADIOR. In other words, people with impaired mobility may have difficulties moving to centers where the program is taught. Hence, the GRADIOR version for tablet has been developed; in this way, people can access the program from their own home without having to move to a center.

While context should be taken into account in the design of any technology, not all technologies are applicable to rural environments [38]. Nevertheless, the latest GRADIOR version is applicable in different environments and accessible to people living in rural areas [45]. Indeed, the possibility of using GRADIOR at home through remote monitoring was defined as a priority for future developments [42].

Finally, different professionals who had used version 4 of GRADIOR combined with a physical program mentioned the following: 100% of professionals thought that patients enjoyed the sessions, 60% of them indicated GRADIOR as an easy-to-use program and 100% of professionals rated GRADIOR as a beneficial program [43].

Discussion

After 20 years of development, GRADIOR has become an easy to use and implement computer-based cognitive rehabilitation program, particularly in clinical settings.

Over the last decade, several computer-based cognitive rehabilitation programs have been developed, targeting people at risk for cognitive decline [46, 47]. Many of them have shown positive effects on cognition in different user groups, for instance in preventing cognitive decline in healthy older adults [48] and people with Alzheimer's disease [49]. These programs improve cognitive skills or delay impairment caused by MCI or dementia [50–53].

The common benefits of these computer-based training programs as compared to 'traditional' cognitive rehabilitation programs are the high accessibility of the treatment and its flexibility to adapt the training according to the user's needs, cognitive capacities and motivation [54, 55]. Additional aims of these programs can be to stimulate some of the limited or impaired physical skills of their users (e.g. grasping, arm movement, etc.) [56] or to relieve caregivers' burden [57].

The main advantage of GRADIOR as compared to other computer-based cognitive rehabilitation programs is its flexibility, which allows complete personalization of the training according to users cognitive skills, needs and familiarity with the content [39]. Exercises are based on real pictures, drawings, 3D-virtual objects, sounds, voices, videos and a wealth of multimedia resources aimed at maintaining a high level of attention throughout the sessions. Because of their large number, exercises can be randomly applied avoiding repetition in a same training program and, thus, reducing user boredom. The additional INTRAS module allows therapists to design more exercises.

In general, technological applications are well-accepted by young people, but older or disabled people (target users) might find difficulties or barriers in their use, which makes them reluctant to adopt new technology. To optimize the use of GRADIOR, we used the interface of existing mainstream technology: a touch screen. When touchscreen devices appeared, the computer–human interaction became more intuitive [58] and such devices can be used easily without prior experience, even by people with dementia or MCI [59, 60]. To avoid rejection of the GRADIOR interface, the computer was converted into a TV, an object that is very familiar to elderly people. Not needing to use keyboards contributes to the high usability of GRADIOR. To support this arrangement, usability studies were conducted with old people and schizophrenic patients [61].

Patients identified GRADIOR as an easy-to-use program [43] and generated an acceptance level, especially in people who have never used a computer [40]. GRADIOR noted for its high level of usability by meeting the parameters associated with this construct [44]. Designated as a program that generated positive health benefits [43] and met patient expectations [41]. GRADIOR not only generated the maintenance of cognitive functions, but also increased in social interactions and mood [43]. These

contributed to increase predisposition in patients to continue using GRADIOR [43, 44], due to the positive experience of enjoyment in its use by the user/patient.

GRADIOR has also proved to be cost-effective as the Report Manager Module helps therapists save a lot of time when analyzing patient performance data. The monitoring of clients is very easy and the outcomes can be used as feedback for patients.

In general, GRADIOR provides most of the advantages of using technologies for cognitive rehabilitation. Recently, Zokaei, MacKellar [62] proposed some recommendations for computer-based cognitive training programs in order to increase their success. Their recommendations are that the program (a) targets specific cognitive functions (e.g. memory, attention, etc.); (b) this can be continuously adapted based on participant performance; (c) this will be very immersive and entertaining; (d) this includes immediate quantitative feedback; (e) this is highly accessible from portable digital devices.

GRADIOR meets all of the above: (a) GRADIOR allows stimulation and training for each of the cognitive functions: memory, attention, language; (b) GRADIOR is adaptable to patient performance, because each of its exercises has different levels of difficulty that the therapist can adjust to prevent boredom or frustration caused by their being too easy or too difficult, respectively; (c) GRADIOR includes images associated with the patient's real life to enhance user entertainment; (d) GRADIOR issues a feedback message informing whether the patient has been right or wrong; (e) GRADIOR can be used on digital devices (touchscreen computers or tablets).

In recent decades, significant improvements in memory, perception and attention have been reported in dementia, as well as improvements in working memory and psychomotor learning in people with MCI through computer-based cognitive training [63]. Other studies support the efficacy of computer-based cognitive rehabilitation for people with cognitive impairment [52].

In a meta-analysis of 17 randomized clinical trials, Hill, Mowszowski [64] found statistically significant moderate effect sizes for verbal memory, non-verbal memory, working memory, attention and psychosocial functioning. Other systematic reviews and meta-analyzes also reported similar results, not only for people with cognitive impairment, but also for people with depression and anxiety [23].

Studies on the effectiveness of GRADIOR highlighted the improvement of auditory memory, verbal learning and concentration [65]. As well as, an improvement in the perception of functional capacities, increasing independence and social interaction [44].

Although GRADIOR yielded good results in different types of patients, more robust results are needed [65]. In order to study the effectiveness of the new "GRADIOR" version, from 2018 to the present, a randomized clinical trial framed within Initial Training Network (ITN) action, H2020-MSCA-ITN-2015, under grant agreement number 676265 is being carried out. Through this randomized clinical trial, we intend to evaluate the effectiveness of the GRADIOR rehabilitation program on cognitive functioning and social, emotional and functional aspects in people with MCI and mild dementia [66].

GRADIOR 4 is specific software for cognitive rehabilitation that uses the latest technology and takes into account the preferences of end-users and therapists. The involvement of end-users, therapists and other stakeholders [67] in the development of GRADIOR has led to the creation of a tool that is highly suitable and convenient for clinical settings, while also contributing towards the acceptability of GRADIOR by people with dementia.

We currently consider GRADIOR to be a highly usable tool in clinical practice for people with cognitive impairment caused by a broad range of pathologies. And because it allows distance therapy, it is accessible to people who are usually excluded from regular treatment because of the area they live in or mobility problems. GRADIOR's flexibility makes the tool useful for many different pathologies.

Computer-based cognitive rehabilitation programs like GRADIOR can be provided as part of a comprehensive treatment, yielding good results in different modalities when combined the cognitive stimulation with physical training (LLM project[1] involved GRADIOR 4) [68]. However, accurate software definition is essential, since this marks large differences. Consequently, to deem a computer program useful or not requires a thorough explanation of its features and the results of one software should not be deployed to all of them.

Conclusions

In recent years, the number of older people with dementia in Europe has been growing, and it is estimated that approximately 30% of the population will suffer from some form of dementia by 2060 [1]. This has led to the development, improvement and implementation of different types of treatment, among which are non-pharmacological therapies involving psychosocial approaches and the use of new technologies such as GRADIOR.

GRADIOR is a computer-based cognitive rehabilitation program that allows the stimulation and training of cognitive functions in people with different neurological pathologies, including people with dementia. GRADIOR

[1] Long Lasting Memories Project is partially funded under the ICT Policy Support Programme (ICT PSP) as part of the Competitiveness and Innovation Framework Programme by the European. Project number: 238904.

adjusts and responds to the characteristics and needs of people with dementia, producing greater usability of the software.

In this order of ideas, different studies on user experience, usability and effectiveness have been conducted. Users report a high degree of satisfaction with the use of the program, which turns out to be user-friendly and effective in helping to improve cognitive functions [36, 37, 40, 41, 43, 44]. Currently, new studies of user experience, usability and effectiveness for the new GRADIOR version continue to be carried out, pending the publication of their findings. These new studies will help to contrast and support the data already obtained in previous studies, providing more evidence to support the use of the program in a clinical or rural context with patients with cognitive impairment, which has been positive so far.

The version of GRADIOR in tablet is being developed with the aim that this program can be applied different contexts. For example, in the case of people with physical alterations, which could influence their displacement to specialized centers.

Finally, the development of a computer-based cognitive training program like GRADIOR contributes to the field of cognitive rehabilitation in people with cognitive impairment. This field characterized by pencil and paper stimulation has grown in recent years with the development of new programs that contribute to and help maintain cognitive performance in people with impaired cognitive functions. And therefore, to produce positive effects on the quality of life of the patient; for example, increasing their mood and even the social interaction with other people [43]. This type of treatment is contrary to pharmacological, the latter is usually the most used, but not always the most suitable for the rehabilitation of cognitive deficits.

Supplementary information

Supplementary information accompanies this paper at https://doi.org/10.1186/s12911-020-01293-w.

Additional file 1. GRADIOR PROGRAM.

Abbreviations

CAMCOG: Cambridge Cognition Examination; CDT: Clock Drawing Test; CIE-10: International Diagnosis of Diseases; GDS: Geriatric Depression Scale Yesavage; IADL: Lawton Instrumental Activities of Daily Living questionnaire; ICT: Information and Communications Technology; MCI: Mild cognitive impairment.; MMSE: Mini Mental State Examination; TMT: Trail Making Test.

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Authors' contributions

MAFM and AADB contributed to the design, content and writing of the manuscript. HVDR helped to review and write the paper taking into account the general rules for the use of technology for elderly people and people with dementia. ITD reviewed and added text about the technology. MVPB reviewed and contributed with the architecture of the theoretical framework associated with the problem center that justifies the development of rehabilitation programs. YBA and MTCB are developers of the GRADIOR and, they with EPV added text about the specific features of the software. All authors have read and approved the manuscript.

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Not applicable.

Consent for publication

We confirm that we have written consent to reproduce Fig. 1. Figures 4 and 5 do not require consent.

Competing interests

We declare the following interests: Angie A. Diaz-Baquero (AADB) is a paid member of the INTRAS Foundation responsible for the development and distribution of the GRADIOR software. Manuel A. Franco-Martín (MAFM) was the initial designer of GRADIOR. Yolanda Bueno-Aguado (YBA), María T. Cid-Bartolomé (MTCB) and Esther Parra Vidales (EPV) are former members of the INTRAS Foundation. María V. Perea Bartolomé (MVPB), Isabel de la Torre Díez (ITD) and Henriëtte van der Roest (HVDR) have not interests to declare.

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Publisher's Note

Artículo 2

Diseños Metodológicos Aplicados en el Desarrollo de Programas de Entrenamiento por Computadora para la Rehabilitación Cognitiva en Personas con Deterioro Cognitivo Leve (DCL) y Demencia Leve. Revisión sistemática.

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Resumen

En los últimos años se han desarrollado diferentes programas de entrenamiento cognitivo (EC) basados en ordenador para personas con demencia siguiendo un enfoque psicosocial. **Objetivo:** Esta revisión sistemática tiene como objetivo identificar los diseños

metodológicos aplicados en el desarrollo de programas de entrenamiento cognitivo basado en computadora (ECC) para la rehabilitación del funcionamiento cognitivo en personas con deterioro cognitivo leve (DCL) o demencia leve.

Métodos: Se realizó una revisión sistemática utilizando las bases de datos PubMed y PsycINFO. El período de búsqueda fue entre 2000 y 2019. Los procesos de selección de estudios y extracción de datos fueron realizados por dos revisores independientes. El protocolo fue registrado en el International Prospective Register of Systematic Reviews (PROSPERO) con el número de registro CRD42020159027.

Resultados: Trece estudios cumplieron los criterios de inclusión. El diseño metodológico más utilizado en el desarrollo de programas de ECC para personas con DCL o demencia leve fue el diseño centrado en el usuario (DCU). Este diseño involucra un sistema interactivo caracterizado por la inclusión de los usuarios finales desde las etapas iniciales de su desarrollo, durante el establecimiento de los requisitos funcionales y en la evaluación de la usabilidad y la experiencia de usuario (UX) del programa.

Conclusión: DCU fue el diseño metodológico más utilizado para el desarrollo de programas de ECC, aunque hubo bastante variación en la forma en que se aplicó este diseño. Se dan recomendaciones para estudios futuros sobre el desarrollo de programas de ECC para personas con DCL y demencia leve. El enfoque central debería ser la inclusión y participación de los usuarios finales desde las etapas iniciales de desarrollo.

Palabras clave: demencia; programa basado en computadora; diseño de desarrollo; entrenamiento cognitivo.

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Review

Methodological Designs Applied in the Development of Computer-Based Training Programs for the Cognitive Rehabilitation in People with Mild Cognitive Impairment (MCI) and Mild Dementia. Systematic Review

Angie A. Diaz Baquero [1,2,*], Rose-Marie Dröes [3], María V. Perea Bartolomé [4], Eider Irazoki [2,5], José Miguel Toribio-Guzmán [2], Manuel A. Franco-Martín [1,6,7] and Henriëtte van der Roest [8]

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Abstract: In recent years, different computer-based cognitive training (CT) programs for people with dementia (PwD) have been developed following a psychosocial approach. Aim: This systematic review aims to identify the methodological designs applied in the development of computer-based training (CCT) programs for the rehabilitation of cognitive functioning in people with mild cognitive impairment (MCI) or mild dementia. Methods: A systematic review was conducted using the databases PubMed and PsycINFO. The search period was between 2000–2019. The study selection and data extraction processes were carried out by two independent reviewers. The protocol was registered in International Prospective Register of Systematic Reviews (PROSPERO) under registration number CRD42020159027. Results: Thirteen studies met the inclusion criteria. The most frequently used methodological design in the development of CCT programs for people with MCI or mild dementia was the user-centered design (UCD). This design involves an interactive system characterized by the inclusion of end users from the initial stages of its development, throughout the establishment of functional requirements, and in the evaluation of the program's usability and user-experience (UX). Conclusion: UCD was the most used methodological design for the development of CCT programs although there was quite some variation in how this design was applied. Recommendations for future studies about the development of CCT programs for people with MCI and mild dementia are given. Central focus should be the inclusion and active participation of end users from the initial stages of development.

Keywords: dementia; computer-based program; development design; cognitive training

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1. Introduction

Dementia is a neurodegenerative disease characterized by cognitive, emotional, and social deficits. Cognitive functional impairments generally involve problems with orientation, memory, attention, language, reasoning, calculation, and executive functioning.

Emotional alterations, for example, are associated with symptoms like anxiety, depression and apathy. As a result of these cognitive and emotional alterations, people suffering from dementia may have social problems, such as difficulties participating in their social network and, consequently, loss of social contacts. Currently, it is estimated that there are more than 50 million people with dementia (PwD) in the world, and, by 2050, this number is expected to have increased to 152 million PwD [1].

Pharmacological therapy is the most common treatment for this disease. A large number of clinical trials are being carried out continuously to test the effectiveness of different drugs that help counteract some of the symptoms of the disease in the short term [2–4]. However, as long as there is no cure for dementia, pharmacological therapy will only be part of the care and treatment for PwD.

In recent years, from a psychosocial–technological approach, different cognitive rehabilitation programs have been used with PwD as a complement to medication. Some existing computer-based cognitive training (CCT) programs for people with mild cognitive impairment (MCI) and mild dementia have been flagged by systematic reviews [5,6]. However, when reviewing the studies focusing on them, we found that they failed to provide a detailed description of the methodological design used in the development of these CCT programs for people with MCI and mild dementia. Some of the studies [7–9], including those associated with the BRAINER; CogMed; SOCIABLE; Kitchen and Cooking programs; and the websites of the CogMed, CogniPlus, FesKits programs, and SOCIABLE, only reported the participation of an interdisciplinary group (neuropsychologists and game designers) in the development of the programs, providing no further details. Some of them, such as CogMed, had even been originally developed with people affected by other disorders [10].

Consequently, studies have been conducted to investigate the usability [11–13] and effectiveness of such programs in terms of maintaining cognitive performance and delaying cognitive decline in PwD [14–17]. Nevertheless, many of these programs have never been implemented in clinical practice.

Because of its impact on use, design plays an important role in the development of any computer program and should therefore consider parameters like user-friendliness, being simple, clear, and easy to use [18]. Usability is one of the main criteria that must be fulfilled by a program [19], which should be challenging and useful to motivate the user, poor usability being a demotivating factor [20].

ISO9241–210 [21] proposes a series of standards that should be taken into consideration when developing a human-centered design (HCD) program. These standards are as follows: (1) defining the context (CTX), (2) specifying user requirements, (3) designing, and (4) evaluating the design. The design should start from and respond to users' current needs, involving them in its methodology by means of, among other things, observation (OB), interviews/questionnaires (Q), and field tests [22].

The design of any computer-based program should take into account the characteristics and needs of the target population [23,24]. Older adults may present sensory disturbances associated with hearing and visual impairments, which make it difficult to carry out certain perceptual activities. They may also have physical difficulties affecting their mobility and, more specifically, their fine motor skills. The type of deterioration and its severity vary from one person to another, which also applies to people diagnosed with dementia [25].

In response to these needs, the design of cognitive rehabilitation programs should include the use of appropriate colors, size and text font, background style and sounds [18], touch screens [26,27], and different exercises and cognitive levels [28] to enhance usability and so that the program may be accessible for older adults. Moreover, it is necessary to involve PwD in the design process [29] to know how users experience the computer-based program [30] since a positive or negative impact could determine whether the technology is adopted or not.

In line with the mentioned principles, this systematic review aims to identify the methodological designs used in the development of CCT programs for the rehabilitation of cognitive functioning in people with MCI and people with mild dementia and to describe the ISO9241-210 [21] standards that were followed in the different studies for the development of the computer-based programs.

2. Materials and Methods

2.1. Systematic Literature Review

A systematic review was conducted using the PubMed and PsycINFO databases. The protocol was based on the Preferred Reporting Items for Systematic Review and Meta-Analysis-PRISMA statements [31] and registered in International Prospective Register of Systematic Reviews (PROSPERO) under registration number CRD42020159027 or EC626091945 in April 2020 and updated in October 2020 [32].

2.2. Search Strategies

The databases were searched from inception onwards by the first author under the supervision of a medical information specialist of the VU University Medical Center, on 5 November, 2019. The search terms used were: dementia-MCI AND computer-based program AND development or design AND cognitive. The search period ranged from January, 2000 to October, 2019.

2.3. Eligibility Criteria

Papers targeting people with MCI or mild dementia (Alzheimer's, vascular, frontotemporal dementia) and describing the development process, design, use and/or results of a pilot study, or effect of a study associated with CCT programs were selected, and only papers published in peer-reviewed journals between January, 2000–October, 2019 and written in English or Spanish were accepted.

The review focused on the most prevalent types of dementia (Alzheimer's disease (AD), vascular dementia (VD), mixed AD-VD), excluding those that are less common, such as Lewy bodies, Pick's disease, Huntington, or Parkinson's. Studies that did not include the development of CCT programs and whose main and only topic was the effectiveness or usability of a CCT program were also excluded.

Systematic reviews and meta-analyses were considered for review with the purpose of finding studies that met the inclusion criteria and had not been identified by the initial search strategy.

2.4. Selection Process

The search results from the two databases were uploaded into EndNote X7. Duplicate studies were identified and removed according to the digital guidelines of the VU University Library Amsterdam, the Netherlands [33]

After the process of removing duplicates, two independent reviewers (AADB, EI, MAFM, and HVDR) assessed the titles and abstracts of every study to identify potential studies that met the inclusion criteria. The reviewers considered the additional information, consulting the studies online. Any disagreements between the reviewers regarding the included and excluded studies were discussed until consensus was reached.

The full texts of the included studies were obtained in order to perform a critical reading and extract the relevant information. This process was carried out by AADB. Some systematic reviews were selected for review based on the references included, leading to the addition of new studies that had not been tracked by the initial search strategy. The list of references of these systematic reviews or meta-analyses was examined by one independent reviewer (AADB).

2.5. Data Synthesis

A critical analysis was conducted to identify the methodological designs applied in the development of CCT programs for cognitive function rehabilitation in people with MCI and mild dementia.

First, we extracted information associated with the characteristics of the rehabilitation programs (name of the program), characterization of the sample (sample size, sample distribution by sex, study groups, and diagnosis), country where the data collection was carried out, and dropouts (number and main reasons).

Subsequently, the following information was extracted: (a) type of methodological design applied by each study for the development of the CCT programs in people with MCI and mild dementia and (b) how the ISO9241-210 (21) standards were followed throughout the development of the programs, i.e.,: (1) understanding and specifying the CTX of use, (2) specifying user requirements, (3) producing design solutions, and (4) evaluating the design. The baseline study requirements, measurement instruments, and main results were also extracted.

2.6. Study Selection

The study selection process is presented according to the PRISMA Flow Chart [31] (Figure 1). The search strategy yielded 190 studies (63 studies in PubMed and 127 studies in PsycINFO). Four papers tracked from two publications were added. After removing duplicates, 182 studies were reviewed for their title, abstract, and additional information obtained online.

One hundred and fifty-two studies were excluded due to not meeting the inclusion criteria (the reasons for exclusion are detailed in the PRISMA Flow chart, Figure 1), leaving 30 eligible studies. After reviewing the full text of these 30 studies, 17 were excluded on the following grounds: 10 did not fulfill the inclusion criteria, the full text of six was not available, even though we contacted the main author (who did not respond to our request), and one study was a systematic review. This systematic review was checked against its reference list to find potential papers, and six possible studies were identified and discarded after reviewing their abstracts.

Finally, only 13 studies met the inclusion criteria and were included in the systematic review. Of these 13 studies, the paper by Haesner, Steinert [34] appeared to be a continuation of a study that was reported in another selected paper by Haesner, O'Sullivan [35]. Three studies, Ben-Sadoun, Sacco [36], Benveniste, Jouvelot [37] and Boulay, Benveniste [38], were identified from the study of Ben-Sadoun, Manera [39]. Particularly, the study by Boulay, Benveniste [38] was the continuation of the study by Benveniste, Jouvelot [37]; this latter talks about the user requirements and initial development phases while the first study talks about the evaluation of the final prototype of MinWii, respectively.

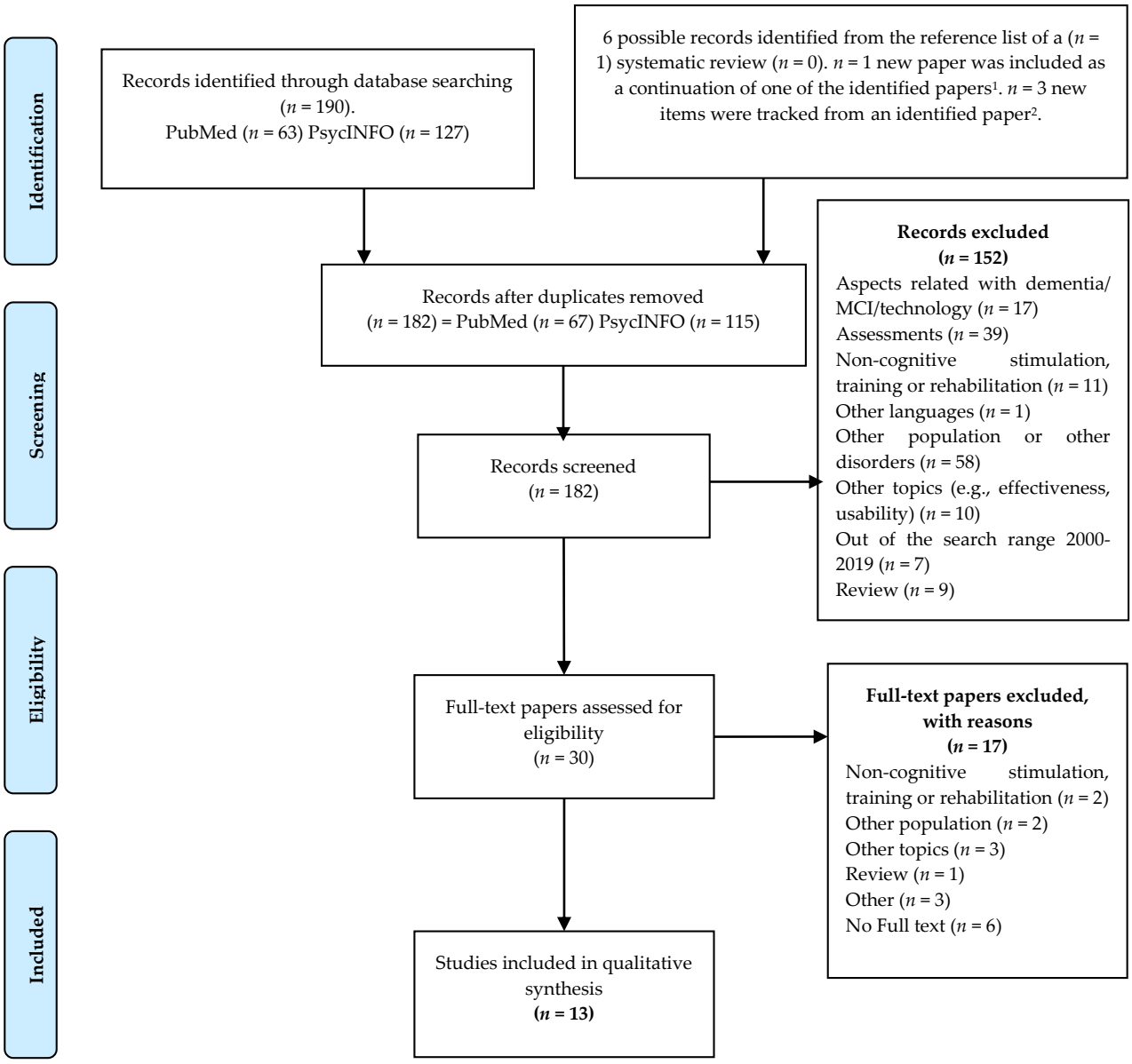

Figure 1. PRISMA Flow Chart. Selection process of the systematic review (From: Moher, Liberati [31]). [1] Haesner, O'Sullivan [35]. [2] Ben-Sadoun, Manera [39].

3. Results.

3.1. Study Aims

A total of 11 CCT programs described in 13 different studies were identified (Table 1). The aim of the studies identified in this review was to develop CCT programs or games for people with MCI or mild dementia, including the user from the initial stages of their development, design, and prototype assessment, and conducting usability and user-experience (UX) assessments throughout the development of each of the prototypes.

Table 1. Sample characteristics for each study.

Program	Study	Participants/Diagnosis	Settings	Drop-Outs
MinWii	Benveniste, Jouvelot [37]	*N* = 9. Dx: AD (MMSE: 10–25).	Geriatrics Unit of Hospital Saint-Maurice (France).	None.
MinWii	Boulay, Benveniste [38]	*N*= 7. 3 males. Mean age: 88.5. Dx: AD (MMSE 12–30).	Long Term Care Unit at La Collégiale Hospital (Paris, France).	*n* = 2. 1 medical problems. 1 refused to continue.
COGWEB	Cruz, Pais J. [40]	*N* = 48/80. 21/48 females. Mean age: 60 ± 13.3. Mean education: 6 ± 4.3. Dx: 25%: subjective memory complaints. 25%: TBI. 25%: stroke and other static brain lesions. 25%: mild AD.	Outpatient memory clinic (Portugal).	*n* = 32 (not able to attend the assessment session at the hospital).
USMART	Han, Oh [41]	*N* = 10. 1 males/9 females. Dx: n= 4 aMCI single-domain type, *n*= 2 aMCI multiple-domain type, *n*= 1 naMCI single-domain type.	KLOSCAD. Dementia Clinic of the Seoul National University Bundang Hospital (South Korea).	*n* = 3: 1 difficulty learning how to use the iPad. 1 felt the inter-retrieval activities were childish. 1 developed an acute physical illness.
LeVer learning platform	Haesner, O'Sullivan [35]	HOP Group: *N*= 6. 3 males. Age: 60–70 years. Education: n = 1: < 9 years; *n* = 2: 10–13 years; *n* = 3: university degree. MCI Group: *N*= 6. 3 males. Age: over 80 years old. Education: *n* = 3: < 9 years; *n*= 2: 10–13 years; *n* = 1: university degree.	Geriatric hospital (Charité Berlin).	None.
LeVer learning platform	Haesner, Steinert [34]	*N* = 80. 44 females. Mean age: 70 years. Dx. *n* = 39 HOP. *n*= 41 MCI.	Senior University, Berlin (Germany).	None.
Software "Atama-no-dojo".	Otsuka, Tanemura [42]	*N*= 19 females. Mean age: 82.2 ± 2.9. Mean education: 10.5 ± 1.7. Dx: MCI (MMSE ≥ 24).	A day-service center in Hyogo Prefecture (Japan).	*n* = 5: 1 vision problem due to macula degeneration, 1 hospitalized with lung cancer, 3 who attended less than 80% of our program sessions.
X-Top	Ben-Sadoun, Sacco [36]	MCI and AD Group: *N* = 10. 6 males. Mean age: 82.3 ± 6.4. HOP Group: *N*= 8. 3 males. Mean age: 71.4 ± 10.1.	Memory Center in Nice (France).	None.

Table 1. *Cont.*

Program	Study	Participants/Diagnosis	Settings	Drop-Outs
Music ePartner	Peeters, Harbers [43]	*N* = 5: 1 male; Age: 60 years. Dx: MCI. 1 male; Age: 70 years; Dx: PwD Moderate–severe. 1 male; Age: 80 years; Dx: PwD Severe. 1 male; Age: 70 years; Dx: PwD Moderate. 1 male; Age: 50 years; Dx: MCI.	Care Organization Pieter van Foreest, Zuid-Holland, (the Netherlands).	None.
Games. (WoZ) interface	Dethlefs, Milders [44]	*N* = 23. HOP Group: *N* = 13. 9 males/4 females. Mean age: 84.33 years. PwD Group: *N*= 10. 8 males/2 females. Mean age: 78.20 years. Dx: *n* = 7 AD, *n* = 2 early onset dementia, *n* = 1 LBD.	Department of Geriatric Medicine (University of Edinburgh). SDCRN (UK).	None.
Gamified environment (DOREMI)	Scase, Marandure [45]	Sample 1: *N* = 18: 1° FG: *N* = 9. 5 males. Mean age: 77.0 ± 7.47. Dx: MMSE (29.3 ± 1.00). 2° FG: *N* = 5. 1 male. Mean Age: 74.6 ± 5.46. Dx: MoCA (22.8 ± 1.64). 3° FG: *N* = 4. 1 males. Mean age: 78.5 ± 1.91. Dx: MoCA (22.0 ± 2.45). Sample 2: *N* = 24: Retirement village: *N* = 11. 1 male. Mean age: 75.4 ± 5.14. Dx: MoCA (26.0 ± 2.28). Living separately in a large city: *N* = 13. 1 male. Mean age: 74.9 ± 3.68. Dx: MoCA (24.4 ± 1.19).	Retirement village and city.	None.
Cognitive Games (DOREMI)	Scase, Kreiner [46]	Sample 1: *N* = 18: 1° FG: *N* = 9. 5 males. Mean age: 77.0 ± 7.47. Dx: MMSE (29.3 ± 1.00). 2° FG: *N* = 5. 1male. Mean age: 74.6 ± 5.46. Dx: MoCA (22.8 ± 1.64). 3° FG: *N* = 4. 1 males. Mean age: 78.5 ± 1.91. Dx: MoCA (22.0 ± 2.45). Sample 2: N = 25: 3 males. Mean age: 75.0 ± 4.28. Dx: MoCA (24.2 ± 1.71).	Does not specify.	None.
Puzzle game design	Gao [22]	*N* = 52: EG: 26. CG: 26. Dx: AD.	Nursing home in a community in Nanjing (China).	None.

Note: AD, Alzheimer's disease; aMCI, amnestic mild cognitive impairment; CG, control group; DOREMI, Decrease of cOgnitive decline, malnutRition, and sedEntariness by elderly empowerment in lifestyle Management and social Inclusion; Dx; diagnostic; EG, experimental group; FG, focus group; HOP, healthy old people; KLOSCAD, Korean Longitudinal Study on Cognitive Aging and Dementia; LBD, Lewy body dementia; MCI, mild cognitive impairment; MMSE, Mini Mental State Examination; MoCA, Montreal Cognitive Assessment; N; number; naMCI, non-amnestic mild cognitive Impairment; PwD, people with dementia; SDCRN, Scottish Dementia Clinical Research Network; TBI, traumatic brain injury; UK, United Kingdom; USMART, The Ubiquitous Spaced Retrieval-based Memory Advancement and Rehabilitation Training; WoZ, Wizard-of-Oz.

3.2. Participants, Settings, and End Users

Participant characteristics and settings are presented in Table 1. Two (15.4%) studies included two samples with different purposes: Scase, Kreiner [46] included a sample of 18 people with the objective of evaluating the UX of a pre-prototype of the games and a second sample of 25 people to evaluate the UX of the final prototype of the games. The use

of two samples had similar purposes in the study carried out by Scase, Marandure [45]; although, this study included a sample of 18 people to evaluate the pre-prototype and 24 people to evaluate the UX of the final prototype and adherence to the games. On the other hand, four (30.8%) studies associated with two programs (LeVer learning platform and MinWii) also used different samples. Specifically, Haesner, O'Sullivan [35] recruited 12 people to investigate the requirements that should be considered in the development of an online platform for cognitive training (CT). These requirements were taken into consideration in a second study carried out by Haesner, Steinert [34], which included 80 people to assess the usability and UX of the final LeVer learning platform. Equally, the Benveniste, Jouvelot [37] study recruited nine people to indicate user requirements, and Boulay, Benveniste [38] recruited seven people for the evaluation of the final MinWii prototype. Sample sizes varied from study to study. In general, the studies of Cruz; Pais J. [40]; Gao [22]; Haesner, Steinert [34]; Scase, Kreiner [46]; and Scase, Marandure [45] used a large sample size ($\geq$30) while the others used a small sample size ($\leq$30).

Regarding the diagnosis of the sample population of the studies included in this review, seven (53.9%) studies recruited people diagnosed with MCI [34,35,41–43,45,46], four (30.8%) studies worked with people diagnosed with mild dementia [22,37,38,44], and two (15.4%) studies included a pooled sample of people diagnosed with MCI and mild dementia [36,40]. Four (30.8%) studies included healthy comparison subjects [34–36,44], two (15.4%) studies included people with other types of diagnoses in their sample (e.g., traumatic brain injury (TBI) or Lewy body dementia (LBD)) [40,44], and one (7.7%) study worked with people with moderate and severe stage dementia [43] (Table 1).

The 13 studies selected for this systematic review included a total of 400 people, of whom 45.8% (n = 183) were people with MCI, 24.3% (n = 97) were people with mild dementia, 16.5% (n = 66) were healthy people, 2.5% (n = 10) were people with MCI or mild dementia, 0.8% (n = 3) were people diagnosed with moderate dementia, and 10.3% (n = 41) were people with other disorders (e.g., TBI). Of the 13 included studies, 30.8% (n = 4) reported dropouts in their samples. The study by Cruz, Pais J. [40] had a dropout rate of 40%; Han, Oh [41] reported a 30% dropout rate; Otsuka, Tanemura [42] reported 26.3% dropout; and Boulay, Benveniste [38] had a 28.6% dropout rate. The main reasons for dropout were failure to regularly attend the training sessions, difficulty in using the device, development of psychiatric disorders, visual impairment, and hospitalization (Table 1).

The people diagnosed with MCI or mild dementia included in the studies were between 50–88 years old. The healthy people were between 60–85 years old. However, some of the studies failed to mention the mean age and/or standard deviation of their sample [22,34,35,37,38,41,43] (Table 1).

Of the 13 studies included in this review, four (30.8%) recruited their sample from hospitals [35,37,38,41], two (15.4%) from memory clinics [36,40], two (15.4%) from day centers or care centers [42,43], one (7.7%) from nursing homes [22], two (15.4%) from medical centers or institutions associated with universities [34,44], and two (15.4%) from other centers [45,46] (Table 1).

3.3. Methodological Design Used for the Development

Table 2 describes the specification of the methodological design used by each of the studies in accordance with the international standards proposed by ISO9241-210 [21] for the development of programs: (1) understanding and specifying the CTX of use (type, characteristics and tasks of users, and physical or social environment), (2) specifying the user requirements, (3) producing design solutions, and (4) evaluating the design.

Of the 13 studies included in this systematic review, 11 (84.6%) used a user-centered design (UCD) [34–38,41,42,44–46] or HCD [43] for the development of the cognitive rehabilitation programs or games. According to ISO9241-210 [21], UCD and HCD are equivalent terms. On the other hand, one study (7.7%) used a human–computer interaction design (HCI) [22], and one study used an end-user interaction design [40] (Table 3).

Table 2. Methodological design in the development of CCT programs for people with MCI and mild dementia according to ISO9241-210 (21) criteria.

Program/Game	Study	Context of Use				Design/Use of the Pre-Prototype	Specify User Requirements			Needs and Requirements Identified	Produce Design Solutions	Design Evaluation				
		Gained Understanding		Specified			Pre-Prototype Evaluation				Development of the Final Prototype	Methods			Aspects Evaluated	
		OB	Literature Review	Users	CTX		Interviews	Q	OB			OB	Interviews	Q	Usability	UX
MinWii	Benveniste, Jouvelot [37]	X	X	X	X	X	-	-	X	X	NA	NA	NA	NA	NA	NA
MinWii	Boulay, Benveniste [38]	X	X	X	X	NA	NA	NA	NA	NA	X	X	-	X	X	X
COGWEB	Cruz, Pais J. [40]	-	X	X	X	NS	NS	NS	NS	NS	X	-	-	X	X	X
USMART	Han, Oh [41]	-	X	X	X	X	NS	NS	NS	X	X	-	-	X	X	X
LeVer learning platform	Haesner, O'Sullivan [35]	-	X	X	X	X	X	X	-	X	NA	NA	NA	NA	NA	NA
LeVer learning platform	Haesner, Steinert [34]	-	X	X	X	NA	NA	NA	NA	NA	X	-	-	X	X	X
Software "Atama-no-dojo".	Otsuka, Tanemura [42]	X	X	X	X	NS	NS	NS	NS	NS	X	-	-	X	-	X
X-Top	Ben-Sadoun, Sacco [36]	X	X	X	X	NS	NS	NS	NS	NS	X	-	-	X	X	X
Music ePartner	Peeters, Harbers [43]	-	X	X	X	X	-	X	-	X	X	-	X	-	X	X
Games. WoZ interface	Dethlefs, Milders [44]	-	X	X	X	NS	NS	NS	NS	NS	X	X	X	-	X	X
Gamified environment (DOREMI)	Scase, Marandure [45]	-	X	X	X	X	X	-	-	X	X	-	X	-	-	X
Cognitive Games (DOREMI)	Scase, Kreiner [46]	-	X	X	X	X	X	-	-	X	X	-	X	-	-	X
Puzzle game design.	Gao [22]	-	X	X	X	NS	NS	NS	NS	NS	X	NS	NS	NS	NS	NS

Note: CTX, context; DOREMI, Decrease of cOgnitive decline, malnutRition, and sedEntariness by elderly empowerment in lifestyle Management and social Inclusion; OB, observation; Q, questionnaire; UX, user-experience; NA, did not apply; NS, did not specify; USMART, The Ubiquitous Spaced Retrieval-based Memory Advancement and Rehabilitation Training; WoZ, Wizard-of-Oz.

Table 3. User requirements baseline and main outcome measures.

Program	Study	Methodological Design	Instruments for Assessment	Requirements Baseline	Instruments for Assessment of the Final Program	Outcomes Measures
MinWii	Benveniste, Jouvelot [37]	UCD.	OB (interactions between user-computer, user-other users, user-caregiver).	Low cognitive and motor requirements. A rewarding UX and hardware. Software and operational simplicity UX.	NA.	NA.
MinWii	Boulay, Benveniste [38]	UCD.	NA.	NA.	PSQ.	UX, Usability.
COGWEB	Cruz, Pais J. [40]	End-User Interaction Study Design.	NS.	NS.	OQ.	UX. Usability
USMART	Han, Oh [41]	UCD.	Evaluation and limitations of a previous program.	Limitations of a previous version: Dispensable presence of the professional and modification in the treatment.	17-item PSQ.	UX. Usability
LeVer learning platform	Haesner, O'Sullivan [35]	UCD.	Semi-structured QI. Q	8 factors should be considered when developing an interactive web-based platform for CT. Web design, training, initial evaluation, exercises, feedback, improvement of cognitive performance, communication between users, self-training.	NA.	NA.
LeVer learning platform	Haesner, Steinert [34]	UCD.	NA.	NA.	Questions regarding sociodemographic data, computer and tablet use, HB, QoL, technology commitment and, in terms of personality-related characteristics, self-efficacy.	UX. Usability
Software "Atama-no-dojo".	Otsuka, Tanemura [42]	UCD.	NS.	NS.	IQ.	UX.
X-Top	Ben-Sadoun, Sacco [36]	UCD.	NS.	NS.	Q.	UX. Usability
Music ePartner	Peeters, Harbers [43]	HCD or UCD.	Q to customize the program.	Users preferences. Identification of baseline requirements associated with the role of music in the person's life, frequency with which they listened to music, if they had played any musical instruments, familiarity with music.	Interview.	UX. Usability

Table 3. *Cont.*

Program	Study	Methodological Design	Instruments for Assessment	Requirements Baseline	Instruments for Assessment of the Final Program	Outcomes Measures
Games. WoZ interface	Dethlefs, Milders [44]	UCD.	NS.	NS.	Interview. OB of every session's interaction between the users and the program (Video recording).	UX. Usability
Gamified environment (DOREMI)	Scase, Marandure [45]	UCD.	FG Interviews.	Previous knowledge. Physical characteristics. Customization. Social interaction. Ease of use and understanding. Types of games.	FG Interviews.	UX.
Cognitive Games (DOREMI)	Scase, Kreiner [46]	UCD.	FG Interview.	Previous knowledge. Physical characteristics. Customization. Social interaction. Ease of use and understanding. Types of games.	FG Interviews.	UX.
Puzzle game design	Gao [22]	HCI.	NS.	NS.	NS.	NS.

Note: CT, cognitive training; DOREMI, Decrease of cOgnitive decline, malnutRition, and sedEntariness by elderly empowerment in lifestyle Management and social Inclusion; FG, focus group; HCD, human-centered design; HCI, human–computer interaction design; IQ, impression questionnaire; NA, did not apply; NS, not specified; OB, observation; OQ, opinion questionnaire; PSQ, patient satisfaction questionnaire; Q, questionnaire; QI, qualitative interview; QoL, quality of life; SMART, Spaced Retrieval-based Memory Advancement and Rehabilitation Training; UCD, user-centered design; UX, user-experience; USMART, The Ubiquitous Spaced Retrieval-based Memory Advancement and Rehabilitation Training; WoZ, Wizard-of-Oz.

3.3.1. Understanding and Specifying the CTX of Use

Four (30.8%) studies were based on observation of their users [36–38,42] and all the studies (N = 13) reviewed the literature as a means to understand the CTX of use (Table 2) in terms of type, user characteristics (or needs and deficits) and tasks, and physical or social environment of people with MCI or mild dementia. Accordingly, all studies specified the characteristics of the users or target population and the CTX of use of the program or game to be developed, i.e., the application environment and tasks (Table 1).

3.3.2. Specification of User Requirements

Six (54.5%) studies designed or used a pre-prototype of the program in order to specify target population requirements [35,37,41,43,45,46], in contrast with five (45.5%) studies that did not specify them and did not use a pre-prototype of the program [22,36,40,42,44] (Table 2).

Pre-prototypes were evaluated through interviews in two (33.3%) studies [45,46], based on questionnaires in one study (16.6%) [43], using a combination of interviews and questionnaires in one study (16.6%) [35], and through OB in one study (16.6%) [37], one study (16.6%) failing to specify the method used [41] (Table 2).

Scase, Marandure [45] and Scase, Kreiner [46] conducted focus group (FG) interviews with people with MCI using a pre-prototype of their games and gamified environment in the Decrease of cOgnitive decline, malnutRition, and sedEntariness by elderly empowerment in lifestyle Management and social Inclusion (DOREMI) Project. This study identified the following baseline requirements: prior knowledge of computer use; preferences for games such as puzzles, cards, and quizzes; the importance of adapting the interface design according to physical problems; the use of clear instructions; and the inclusion of challenging games (Table 3).

Haesner, O'Sullivan [35] used a semi-structured interview and a questionnaire, alongside existing programs on the web to identify the baseline requirements. In other words, they did not build a pre-prototype but built their own prototype from existing prototypes. Thus, they reported the following baseline requirements: (1) attractive looking design, (2) face-to-face training course, (3) pretest followed by progress assessments, (4) exercises should include tasks and challenges associated with the real life of the people and be of interest to them, (5) inclusion of personal comments/feedback in real time, (6) the training situation should help improve the person's performance, (7) possibility of communication through audio-video between people, and (8) additional information for self-training (Table 3).

The starting point of Han, Oh [41] was the limitations found in an existing program: Spaced Retrieval-based Memory Advancement and Rehabilitation Training (SMART). These limitations, which included the need for the constant presence of a professional during the sessions, entailing high costs and, therefore, the impossibility of increasing treatment intensity, became the main focus for the design and development of a new program: The Ubiquitous Spaced Retrieval-based Memory Advancement and Rehabilitation Training (USMART) (Table 3).

The purpose of Peeters, Harbers [43] was to develop a Music ePartner for the rehabilitation of episodic memory in people with MCI. Hence, a questionnaire was used to evaluate people's musical preferences so that the authors could customize the design to users' preferences and needs (Table 3).

Benveniste, Jouvelot [37] found different baseline requirements for the development of the MinWii: (a) the use of a Wiimote system to allow greater accessibility for people with motor problems; (b) the use of a graphical interface to counteract visual problems; (c) the use of simple games to reduce feelings of frustration; (d) simplicity of design and the use of familiar devices such as a TV or computer (Table 3).

3.3.3. Development of Final Prototype

Eleven (84.6%) studies developed a final prototype of the program [22,34,36,38,40–46]. Of these, 10 (90.9%) studies used qualitative methods aimed at evaluating the final prototype of the program, and one study (9.1%) did not report an evaluation of the usability or UX aspects of the final prototype [22] (Table 2).

3.3.4. Evaluation Methods

From the studies (n = 10) that evaluated the final prototype of the program, three studies evaluated UX [42,45,46] and seven evaluated usability and UX [34,36,38,40,41,43,44]. Three studies evaluated the intervention through interviews [43,45,46], one used a combination of OB and interviews [44], one used a combination of OB and a questionnaire [38], and five used questionnaires [34,36,40–42] (Tables 2 and 3).

3.3.5. Usability

Music ePartner's intuitive interface used touch screens that made it easy to use, and the inclusion of personalized settings in the interface [43] expresses the preferences of the end user [36].

Particular aspects of the interface of each program that were highlighted by users were, for example, the clarity of the instructions in COGWEB [40] and the use of plain and straightforward language in the games Wizard-of-Oz (WoZ) interface, which facilitated better understanding [44].

Haesner, Steinert [34] also took different aspects of usability into consideration, administering a questionnaire to end users, who had the opportunity to interact with the LeVer learning Platform. The exercises achieved high acceptance rates (97.3%): 90% of the people rated the graphic design and content positively, 97.4% rated usability positively, and 36.9% considered the platform very useful. The content (12.7 $\pm$ 3.1 out of 20 points), accuracy (7.4 $\pm$ 1.5 out of 10 points), layout (7.3 $\pm$ 1.5 out of 10 points), ease of use (7.1 $\pm$ 1.7 out of 10 points), timeliness (6.6 $\pm$ 2.0 out of 10 points), and program speed (9.4 $\pm$ 2.9 out of 15 points) on USMART also received positive ratings [41].

3.3.6. User-Experience

People with MCI [43,45,46] and PwD [36,38,44] rated their experience positively regarding the use of the final program. Users found the exercises included in the program COGWEB [40], DOREMI project [45], and Music ePartner [43] interesting. Eleven out of thirteen healthy old people (HOP) and 8/10 PwD enjoyed the activities in the games of WoZ interface [44]. Likewise, people with MCI who used Atama-no-dojo [42] and Music ePartner [43] enjoyed the exercises of each program, respectively. Additionally, the USMART program received a satisfaction score of 8/10 from people with MCI [41].

The "Find it", "Match it", and "Solve it" games in the DOREMI Project [46], Quiz and Prover tasks in the WoZ interface [44] and the X-Top games [36] were all highly appreciated by users, who regarded them as challenging and interesting. However, the "Complete it" game in the DOREMI Project [46] and the sorting activity in the WoZ interface [44] received negative feedback from users, who reported that their low difficulty levels generated feelings of boredom.

In addition, the people with MCI participating in the studies selected for this review pointed out that using these programs had benefited their cognitive performance [34,42,45,46], specifically their memory (71.4%) [41]. They also indicated the physical [45], emotional, and social benefits obtained, among which were that they contributed to promote interaction with their caregivers [43] and other people [38,45].

Peeters, Harbers [43] differentiated between people with different levels of cognitive impairment, noting that people in the early stage of dementia often gained more benefits from using CT programs than people in advanced stages of the disease. Boulay, Benveniste [38] also mentioned that the level of cognitive impairment influenced the use of the Wiimote, even though users were able to learn how to use it.

People with MCI expressed interest in purchasing and continuing to use the USMART program autonomously at home [41]. In the Haesner, Steinert [34] study, 89.2% of the people mentioned that they would continue using the LeVer learning platform.

3.4. Risk of Bias in Outcome Assessment

We consider that the PRISMA "risk of bias outcome assessment" item is not applicable to this review, because our objective was to identify the methodological designs and methods applied in the development of CCT programs for the rehabilitation of cognitive functioning in people with MCI and mild dementia, and not to evaluate the effectiveness of these methodological designs or the developed products.

4. Discussion

In the past years, different CCT programs have been developed [47,48], targeting people with different pathologies, including MCI and mild dementia [49]. These programs aim to preserve or improve cognitive abilities [50–52]. However, to promote their implementation, dissemination, and successful adoption by their target users, it is important that such users be involved throughout the development process. To gain insight into the extent to which this has been so in the development of CCT programs for people with MCI and mild dementia, we conducted this systematic review aimed at identifying the designs and methods applied in the development of these CCT programs.

We identified 13 studies on the development of CCT programs, which described 11 different CCT programs. All the studies included for this systematic review used some variant of end-user centered methodological design. Likewise, most studies fulfilled most or all of the criteria of the International Standards for HCD for Interactive Systems [21]. These standards provide an approach to the development of interactive systems that are usable, efficient, ergonomic, accessible, sustainable, and safe for the end-user.

Understanding and specifying the CTX of use is one of the main standards proposed by the ISO9241-210 [21]. The studies included in this systematic review used OB and literature review as a source to understand the CTX of use. All of them specified the CTX by reporting the characteristics and needs of the program's target population, as well as the environment in which it would be applied and the tasks the users were to perform.

Specification of user requirements. Only half of the studies took this standard into account. The use of a qualitative methodology was predominant, as was the development or use of pre-prototypes to define user requirements. Previous knowledge or use of the computer in the elderly was a factor that was taken into account in the development of CCT programs [45,46]. This requirement stems from the little familiarity that older people have with technology, as indicated in previous studies [53]. Therefore, interfaces need to fulfill at least some minimum requirements, such as an intuitive, graphical, simple, familiar [37], and attractive interface [35]. Nevertheless, despite these findings, Góngora Alonso, Toribio Guzmán [13] pointed out that lack of experience in the use of technology does not necessarily have to influence its use.

Our study also demonstrates the need to adapt and develop a CCT program involving end users from the initial stages, taking into consideration their physical or motor difficulties [45,46], which could be one of the main reasons for a person to stop using the CCT program [41,42]. The importance of considering this need in the development of CCT programs was also pointed out in and consistent with other studies, such as the study of Góngora Alonso, Toribio Guzmán [13]. In addition, our review also demonstrated the importance of taking into account cognitive problems, including those related to language [54], for example, by using simple and clear instructions, as noted by Scase, Marandure [45]; and Scase, Kreiner [46].

Furthermore, our findings pointed out some of the specific requirements that CCT program exercises should have. Although some approaches seem contradictory, this does not mean that they are not valid and necessary, an example being how Benveniste, Jouvelot [37] states that the exercises should be easy to avoid frustration, whereas Scase, Marandure [45]

posed challenging exercises to maintain motivation. The right answer probably lies somewhere in between: the programs should include conservative approaches associated with exercises that can be adapted to users' cognitive level without them finding them too easy or too difficult. Another important requirement, brought forward by Han, Oh [41], is the capacity of modifying treatment intensity according to the person's performance. This is an important finding that has also been pointed out in other studies, such as that by Franco-Martin, Diaz-Baquero [55].

Other studies extensively discussed the ecological validity of the exercises. Djabelkhir, Wu [56] suggested that people with MCI integrate a technological device (Tablet–PC) into their daily lives. Although the concept of ecological validity is not very recent, it is still little applied in CCT programs. Nevertheless, the study by Haesner, O'Sullivan [35] does mention its relevance. Ecological validity encourages thought and reflection throughout the early stages of development on how the exercises included in a CCT program could contribute or transfer to users' real life, i.e., that exercises have a practical application for people.

Another requirement was the importance of including real-time feedback [35]. Feedback has also been described by other studies as a basic training principle that helps maximize the benefit of a CCT program [57].

In general, the specification of user requirements mentioned by the studies included in this systematic review took into account the needs, experience, and knowledge of the end users [58], which positively contributed to the design of the final programs. In particular, these requirements were associated with the changes and characteristics (physiological, neuropsychological, social, and physical changes) of older PwD mentioned by Guisado-Fernández, Giunti [18] in his systematic review. However, our review also shows that 45.5% of the studies did not report such baseline requirements. We consider that the establishment of user requirements based on end-user participation from the early stages of the development is of great importance in the development of any CCT program because this will allow the creation and development of more usable and personalized CCT programs [29]. Ideally, the interface should be adjustable to the specific functional and cognitive impairments of the older adults with MCI and mild dementia who are to use it [28,59].

Design evaluation. Overall, most of the identified studies took usability and UX evaluations into account from the use of the same sample. However, the Scase, Marandure [45] and Scase, Kreiner [46] studies considered the use of a parallel or second sample for this phase. Undoubtedly, the above represents a methodological advantage because it provides greater objectivity and eliminates biases. In this order of ideas, usability mainly focused on the concepts of familiarity and ease of use. Lack of usability has been considered one of the most important demotivating factors in the use of CCT programs [20]. Usability is regarded as a fundamental and predisposing factor for the use and adoption of a CCT program, and most of the studies included in this systematic review used a touch screen navigation system, which turned out to be more intuitive and usable for people with MCI and mild dementia with few technological skills.

The COGWEB [40] and WoZ Interface [44] programs stood out for their use of clear instructions and simple and straightforward language. These findings are in line with the approach of Tziraki, Berenbaum [60], who point out the importance of using a clear semantic structure for instructions. In general, usability aspects should also encompass the interface's graphic design, as well as the content and exercises [34]. Additional aspects are accuracy, ease of use, timeliness, and program speed [41].

Furthermore, 90% of the studies included UX evaluations of their final program. UX is a subjective aspect that influences the acceptance of a CCT program by its end users. In general, our review shows that people with MCI and mild dementia positively evaluated the exercises included in each program. However, levels of satisfaction and interest in the DOREMI project [45,46], WoZ Interface [44], and X-top [36] programs depended on the

level of difficulty of the exercises. The inclusion of challenging activities has also been identified as one of the motivational factors for the use of CCT programs [20].

People with MCI and mild dementia mentioned that they benefited from the CCT programs at the cognitive, emotional, physical, and social levels [34,38,41–43,45,46]. Expectations regarding the use of a CCT program are often associated with the benefits and support they can potentially provide in relation to specific aspects of cognitive functioning [61]. The estimated potential benefit is a key aspect, since it influences the motivation to continue using the program [62]. However, sometimes these expectations are unrealistic and extreme; therefore, the person must be well informed about the scope and limitations of a CCT [18].

Boulay, Benveniste [38] and Peeters, Harbers [43] both pointed out that the level of deterioration suffered by the people influenced the benefits they perceived from the use of the CCT program. This was confirmed in other studies, which reported that PwD with higher levels of impairment could find difficulties in using technology and therefore required closer supervision and continuous repetition of instructions [62]. This may impact their self-efficacy [63,64] and cause lower motivation to continue using a certain program. On the other hand, Hofmann, Hock [65] showed that, after three weeks of training, people with AD became faster in executing the tasks and needed less and less help using the computer. This last finding was similar to that reported in the approach of Boulay, Benveniste [38].

4.1. Limitations

Some studies that fulfilled the inclusion criteria may not have been detected due to limitations in our search strategy or the small number of databases used for this review. However, taking into account our objective, we consider the databases used the most appropriate due to their clinical orientation. Therefore, we did not use additional specific technological databases as these are generally more oriented to the advancement of the technology from an engineering point of view and not so much from a clinical perspective. Nevertheless, Future studies are recommended to expand the search strategy by using additional databases. Another limitation of our study was that we were unable to retrieve the full text of six studies that met the criteria after reading the abstract, because the full text was not accessible from various databases or via the corresponding author. It is also possible that some recent publications have not (yet) been included in the selected databases.

Furthermore, gray literature was not included in the search because we considered the topic of methodological design in the development of the program to be complex and relatively new, especially when applied to people with MCI and mild dementia.

4.2. Recommendations

Whereas the definition of CTX of use is important as a first phase, it is clearly not enough to design a CCT program, which requires the creation and assessment of a pre-prototype that involves end users from the initial stages of development to find out their requirements. Identifying these requirements does not only tackle most of the methodological problems, but also those associated with the quality and use of the final program, while also avoiding future additional costs resulting from subsequent necessary adaptations. It is therefore strongly recommended that future studies use an interactive and participatory design, including end users from the beginning of the pre-prototype development, carrying out evaluations in order to identify user requirements and, in turn, including them in the final development of the prototype.

Regarding the methodological phase of the evaluation of the final prototype, usability and UX tests generally added quality to the programs, described the user's adaptation, and determined the impact, use, and significance of the CCT program. It is recommended that future studies include both types of evaluations (usability and UX), as both provide complementary and important data to consider in the development of a CCT program for people with MCI and mild dementia.

The wide heterogeneity in the application of the user- or human-centered methodological design for the development of CCT programs in people with MCI and mild dementia was evident. Therefore, our findings indicate the need to apply this methodology in a more standardized way in the design of CCT programs, based on a series of clear rules that this field of research can follow, such as ISO9241-210 [21].

The scientific value of this review is that it summarizes the evidence regarding the methodological designs used in the development of CCT programs in people with MCI and mild dementia and the ways in which different studies followed the ISO9241-210 (2019) standards [21] for the development of CCT programs. We propose that better descriptions of the used methodological design are included in future publications, as well as a critical reflection regarding the design and development process of CCT programs. Few studies have been carried out on this topic in this field of study, and most systematic reviews focus on the evaluation of the effectiveness of CCT programs.

This systematic review also has practical value for developers because it provides recommendations related to the different standards proposed by the ISO9241-210 [21] for the development of programs from a UCD. These recommendations and findings should be taken into consideration in future research or projects that seek to develop a CCT program for people with MCI and mild dementia, with the aim of minimizing errors in program development, thus avoiding higher long-term costs and generating maximum effectiveness of the intervention.

Finally, following these recommendations in the development of CCT programs will also provide value in the clinical field. That is, the clinical field of Neuropsychology will have more usable CCT programs and, in turn, more effective programs according to their therapeutic objective, for example, to maintain cognitive functioning and delay cognitive deterioration. Above all, this field will have CCT programs designed and developed from and for people with MCI and mild dementia. The target population should be the central and starting point of any CCT program.

5. Conclusions

Taking into consideration the objective of this systematic review, we conclude that UCD was the most used methodological design for the development of CCT programs. However, we found variations in its use and application across studies. Some of these variations suggested possible flaws in the design and might have led to problems associated with the usability and UX of these programs.

We propose the use of a user-centered methodology for the development of CCT programs for people with MCI or mild dementia. This methodology is to be regarded as an interactive process where the inclusion and active participation of the end-user from the initial stages of design is the central focus [66]. This will lead to higher usability and better UX, avoiding additional costs for future adaptations and increasing the likelihood of adaptation of the program and opportunities on the technology market. Any study that intends to develop a CCT program for people with MCI or mild dementia should take UCD standards into account.

Finally, we underline some key points and/or objectives that should be taken into account for the development of a CCT program for people with MCI and mild dementia for each of the criteria established by the ISO9241-210 [21]:

(a) Understand and specify the CTX to use:
- Describe and characterize the target population (MCI and mild dementia): sociodemographic (age group, sex, educational level) and clinical (diagnosis, physical, psychological, cognitive symptoms) aspects.
- Define the CTX of use: day center, nursing home, clinic, home, etc.

(b) Specify user requirements:
- Involve end users from this stage.
- Develop a pre-prototype CCT program.

- Use of qualitative methodology: OB, interviews, questionnaires, etc.
- Inquire about the physical and sensory (visual or auditory disturbances), social (social red), and cognitive (orientation, attention, memory, language, executive function, calculation alterations) needs of the user and their impact on the use of the CCT program.
- Inquire about previous knowledge about the use of technological devices and the preferences of the elderly.
- Define and propose the program requirements with respect to design (device type and navigation method) and content (type of exercises, difficulty levels, type of instructions and feedback) so that these adjust to those specific needs.

(c) Program design and evaluation:

- Involve end users.
- Use of qualitative methodology.
- Evaluation of usability regarding the design (intuitive, graphical, simple, familiar) and content of the CCT program.
- Evaluation of the UX regarding the level of satisfaction, experience (positive or negative), and expectations of the people with MCI and mild dementia.

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Abbreviations

AD	Alzheimer's disease;
aMCI	Amnestic mild cognitive impairment;
CG	Control group;
CT	Cognitive training;
CTX	Context;
DOREMI	Decrease of cOgnitive decline, malnutRition, and sedEntariness by elderly empowerment in lifestyle Management and social Inclusion;
EG	Experimental group;
FG	Focus group;
HCD	Human-centered design;
HCI	Human–computer interaction design;
HOP	Healthy old people;
IQ	Impression questionnaire;
KLOSCAD	Korean Longitudinal Study on Cognitive Aging and Dementia;
LBD	Lewy body dementia;
MCI	Mild cognitive impairment;
MMSE	Mini mental state examination;
MoCA	Montreal Cognitive Assessment;
N	Number;
naMCI	Non-amnestic mild cognitive impairment;
OB	Observation;
OQ	Opinion questionnaire;
PC	Computer;
PSQ	Patient satisfaction questionnaire;
PwD	People with dementia;
Q	Questionnaire;
QI	Qualitative interview;
QoL	Quality of life;
SDCRN	Scottish Dementia Clinical Research Network;
SMART	Spaced Retrieval-based Memory Advancement and Rehabilitation Training;
TBI	Traumatic brain injury;
UCD	User-centered design;
USMART	The Ubiquitous Spaced Retrieval-based Memory Advancement and Rehabilitation Training;
UX	User-experience.

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Artículo 3

La efectividad de GRADIOR: un programa de rehabilitación neuropsicológica para personas con deterioro cognitivo leve (DCL) y demencia leve. Resultados de un ensayo controlado aleatorio después de 4 y 12 meses de tratamiento.

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Resumen

Antecedentes: Se han desarrollado programas de entrenamiento cognitivo basados en computadora (ECC), con resultados prometedores en el mantenimiento/mejora del rendimiento cognitivo en personas con demencia. **Objetivo:** El objetivo fue evaluar la efectividad del programa de rehabilitación cognitiva "GRADIOR" en personas con deterioro cognitivo leve (DCL) y demencia leve.

Método: Este estudio fue un ensayo clínico aleatorizado (ECA) multicéntrico simple ciego. Los participantes fueron reclutados de hospitales/centros de día. El grupo experimental (GE) y el grupo de control (GC) recibieron ECC y cuidado diario, respectivamente. Las medidas de resultado obtenidas durante T_0: línea base, T_1: a los 4 meses, T_2: a los 12 meses se compararon inter e intra- grupos.

Resultados: Se detectaron diferencias significativas y/o tamaños del efecto importantes a nivel intragrupo e inter-grupo para la mayoría de las variables, observándose una tendencia de mejora y/o mantenimiento para el GE a los 4 meses en Razonamiento visual del Cambridge Cognitive Examination (CAMCOG), Dígitos y Aritmética del WAIS-III, FVS, Mini-Examen del Estado Mental (MMSE), Trail Making Test (TMT)-A-Errores y, a los 12 meses en Razonamiento Visual de CAMCOG, Dígitos y símbolos del WAIS-III, TMT-B-Errores, Memoria Visual de Rivermead Behavioral Test de Memoria, Fluidez Lexical Verbal-P, Escala de Depresión Geriátrica (GDS) de Yesavage, TMT-A-tiempo, cuyo objetivo fue evaluar algunas funciones ejecutivas y/o la memoria. El GC presentó una tendencia de empeoramiento en la mayoría de las escalas hacia los 12 meses. También hubo una interacción significativa entre "tiempo y grupo" para el MMSE ($F = 8.971$; $p = 0.03$; $\eta2 = 0.019$) y el GDS ($F = 3.414$; $p = 0.04$; $\eta2 = 0.041$), como también, tamaños del efecto pequeño para TMT-A-time ($F = 1.641$; $p = 0.21$; $\eta2 = 0.021$) y TMT-A-Errores ($F = 0.908$; $p = 0.41$; $\eta2 = 0.019$).

Conclusión: se ha demostrado que ECC con GRADIOR produce un beneficio sobre las funciones cognitivas y procesos emocionales (ISRCTN: 15742788).

Palabras Clave: Entrenamiento cognitivo; demencia; defecto cognitivo leve; ensayo controlado aleatorizado; rehabilitación.

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The Effectiveness of GRADIOR: A Neuropsychological Rehabilitation Program for People with Mild Cognitive Impairment and Mild Dementia. Results of a Randomized Controlled Trial After 4 and 12 Months of Treatment

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Abstract.
Background: Computer-based cognitive training programs have been developed with promising results on the maintenance/improvement of cognitive performance in people with dementia.
Objective: The objective was to evaluate the effectiveness of the cognitive rehabilitation program "GRADIOR" in people with mild cognitive impairment and mild dementia.
Method: This study was a single-blind multicenter randomized clinical trial. Participants were recruited from hospitals/day centers. The experimental group (EG) and control group (CG) received computer-based cognitive training (CCT) and routine daily care, respectively. Outcome measures at T_0: baseline, T_1: at 4 months, T_2: at 12 months were compared within and between-groups.

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Results: Significant differences or important effect sizes were detected at the intragroup and intergroup level for most variables, observing a trend of improvement and/or maintenance at 4 months by Visual Reasoning of Cambridge Cognitive Examination (CAMCOG), Digit and Arithmetic of WAIS-III, Semantic Verbal Fluency, Mini-Mental State Exam (MMSE), Trail Making Test (TMT)-A-Mistakes and at 12 months by Visual Reasoning of CAMCOG, Digit Symbol of WAIS-III, TMT-B-mistakes, Visual Memory of Rivermead Behavioural Memory Test, Lexical Verbal Fluency-P, Yesavage's Geriatric Depression Scale (GDS), TMT-A-time scales whose objective was to evaluate some executive functions and/or the memory. The CG presented a worsening trend for most of the measures towards 12 months. There was also a significant interaction between "time and group" for MMSE ($F = 8.971$; $p = 0.03$; $\eta^2 = 0.019$) and the GDS ($F = 3.414$; $p = 0.04$; $\eta^2 = 0.041$), as well as small effect sizes for TMT-A-time ($F = 1.641$; $p = 0.21$; $\eta^2 = 0.021$) and TMT-A-mistakes ($F = 0.908$; $p = 0.41$; $\eta^2 = 0.019$).
Conclusion: CCT with GRADIOR has been proved to benefit cognitive functions (ISRCTN:15742788).

Keywords: Cognitive training, dementia, mild cognitive impairment, randomized controlled trial, rehabilitation

INTRODUCTION

Dementia is a neurodegenerative disease that is characterized by a series of cognitive [1, 2], emotional [3], physical [4], and social [5] deficits, which gain visibility as the disease progresses through its various stages. Mild cognitive impairment (MCI) has been regarded as an early stage of dementia, although it not always evolves in such direction. An individual with MCI could develop dementia if several risk factors converge [6, 7]. Hence, an early diagnosis of MCI is essential [8] to start therapy, which, although it cannot revert the symptoms, some of them can help preserve cognitive condition and/or delay cognitive decline.

People with dementia (PwD) can be treated with pharmacological therapy [9] and also with psychosocial therapies, the latter of which are aimed at physical, cognitive, social, and emotional, or even family unit rehabilitation [10].

One of the challenges of these psychosocial interventions is that they are difficult to implement, both because of their cost and because of the expertise these require. In this regard, new technologies offer the possibility of changing and improving such interventions so that these might be more accessible [11]. Examples of this are the e-Salud interventions, aimed at providing support for activities of daily living (ADL) [12, 13] or at improving the cognitive and emotional condition of PwD [14].

The improvements observed involve cognitive functions such as attention [15–17], memory [16, 18, 19] and executive function (EF) [15, 20] in people with MCI and dementia. Likewise, other studies have mentioned improvements in social and emotional aspects, such as anxiety levels [15] and depression [21].

Although the scientific literature includes a broad variety of studies on the effectiveness of computer-based cognitive training (CCT) programs [21, 22], it is necessary to strengthen the evidence base of the usefulness of this type of intervention. The lack of methodological rigor associated with limitations such as sample size [23] and short CCT periods [24, 25] hinders the gathering of solid evidence [26]. Therefore, it is necessary to further assess the "effectiveness" of these interventions using randomized controlled trials (RCT).

The aim of this study is to evaluate the effectiveness of a CCT program (GRADIOR) on cognition and emotional condition in people with MCI and mild dementia by conducting an RCT [27]. This study will only present the effectiveness results associated with the GRADIOR intervention up to 4 and 12 months. The follow-up period at 16 and 24 months, as well as the results associated with some secondary measures, will be published later.

METHODS

Study design

The design used was a simple-blind, multicenter, RCT (ISRCTN:15742788) [28]. Our design initially included four parallel groups [27]. However, the development of the ehcoBUTLER platform was initially part of a European project that failed to become ready for our RCT. Therefore, we decided not to include it. This led to a change in the number of parallel groups, the allocation ratio, and the sample size.

The sample population was recruited between June 2018 and December 2019. The participants

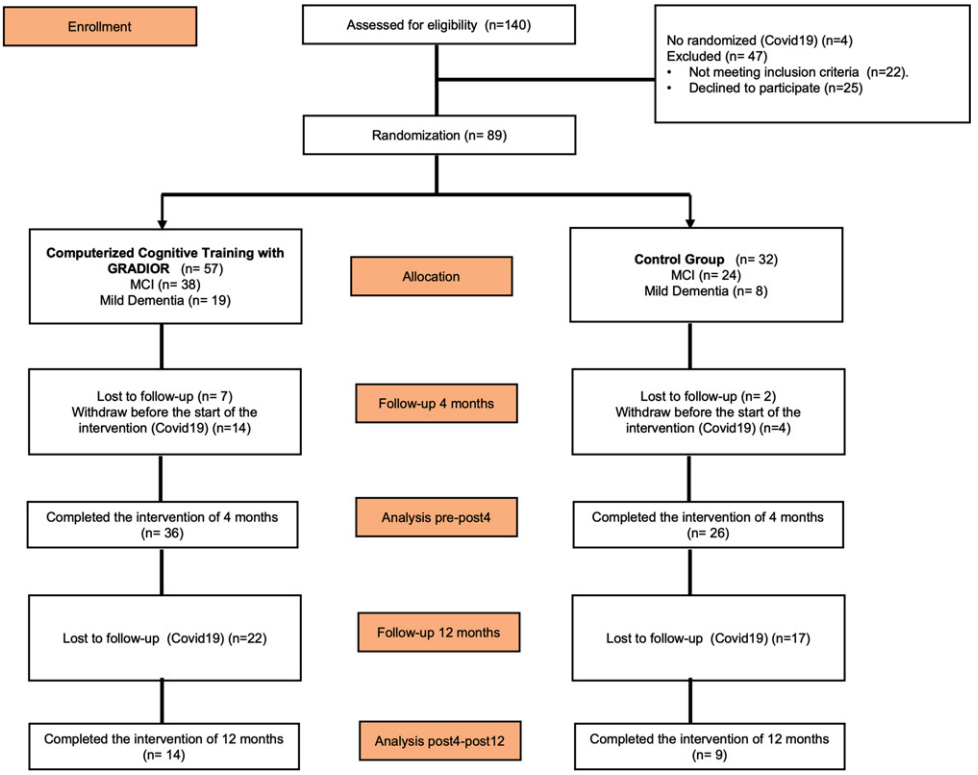

Fig. 1. Recruitment and randomization process.

were randomized (1:2) to one of the two study groups by a simple random assignment (Fig. 1). We used a computer-generated random number sequence through the Epidat 4.1 program. An independent researcher generated the assignment. The evaluators were neuropsychologists who were blinded. The inter-rater reliability was ($\alpha = 99.1\%$). The therapists who supervised each session and the participants were not blinded. Participants agreed to participate prior to randomization and without knowing which group they would be assigned. The individuals in the experimental group (EG) attended two or three weekly CCT sessions (depended on each center) using GRADIOR over a 12-month period, whereas those in the control group (CG) received usual care.

This study was multicenter because it involved daycare centers, memory clinics, and hospitals in the Spanish regions of Castile and León, and Galicia. The study was approved on May 17, 2017, by the Medication Research Ethics Committee of health-care area of Zamora (Number:387-E.C). Informed consent was obtained from all the participants and caregivers.

Participants

Eighty-nine people participated in this study. These were randomly assigned to the experimental ($n = 57$) and control ($n = 32$) group. The dropout rate for this study before 4 months was 10%, although 20% of the participants did not start the intervention due to the onset of the COVID-19 pandemic. The final sample consisted of 62 participants who completed 4-months of intervention. Only 23 participants completed the scheduled 12 months, which could not be completed by the rest of participants because of the outbreak of the COVID-19 pandemic (Fig. 1).

Participants were aged 60–90 and were clinically diagnosed with MCI according to Petersen [29] and with mild dementia according to the Diagnostic and Statistical Manual of Mental Disorders (DSM-V) [30]. A psychogeriatrician and neurologist made the diagnosis according to the criteria mentioned above and considering the patient's medical history. The MCI types were amnestic, and types of dementia included were as follows: Alzheimer's disease, vascular dementia, mixed and frontotemporal dementia. Scores obtained on the Mini-Mental State Exam

(MMSE) were additional: MMSE ≤ 27 for MCI, and MMSE: $20 \leq x \leq 25$ for mild dementia, adjusting each score according to the participant's age and level of education [31]. A score of ≤ 5 on Yesavage's Geriatric Depression Scale (GDS) was required, each participant should participate voluntarily, have a reference caregiver, and be fluent in speaking and understanding Spanish.

On the other hand, the participants were excluded when they had severe physical comorbidities, significant sensory disturbances (hearing-visual), neurological disorders (Huntington's disease, traumatic brain injury, Parkinson's disease), clinically significant psychopathological disorders (depression, anxiety, bipolar disorder, psychosis), and/or a history of psychoactive substance use (alcohol, tobacco).

Neuropsychological assessment

The participants of both groups were assessed at three different moments throughout the intervention (T_0: at baseline, T_1: at 4 months, and at T_2: 12 months of intervention). The cognitive scales used for the main outcome measurements were the MMSE [32], the cognitive subscale of the Alzheimer's Disease Assessment Scale [33], TMT-A-B [34], the Clock Drawing Test [35], Digit Symbol, Arithmetic and Digits of the Wechsler Adult Intelligence Scale (WAIS-III) [36], Visual Memory of the Rivermead Behavioural Memory Test (RBMT) [37], Visual Reasoning of the Cambridge Cognitive Examination (CAMCOG) [38], and Verbal Fluency Test [39, 40]. Secondary result measurements were associated with GDS [41]. These instruments have been described in greater detail in the protocol published on the RCT [27].

Computer-based cognitive training with GRADIOR

GRADIOR is a computer-based cognitive training program. It is a program that provides good usability and user experience [42–49]. This program includes a wealth of orientation, memory, attention, perception, EF, reasoning, and calculation exercises. It allows the design and customization of intervention plans according to the type and level of the patient's cognitive disorder [45, 50]. The cognitive intervention plan for this RCT was designed according to the cognitive profile (Supplementary Figure 1) and the level of difficulty for each exercise was adjusted to the cognitive level of each people. The participants attended two or three weekly 30-min sessions over a 12-month period. The sessions were carried out in specialized rooms with computers in daycare centers, memory clinics, and hospitals.

Statistical analysis

The statistical analysis was conducted using the Statistical Package for the Social Sciences software package (SPSS) [51]. The Shapiro-Wilk Test of normality was used, taking sample size into account to identify the type of distribution of each of the variables. The comparison between the EG-CG was performed using the Mann-Whitney U Test for two independent samples to check whether there were significant differences between both groups regarding at each of the times T_0–T_1–T_2 (intergroup). The Wilcoxon signed-Rank Test was used to compare the cognitive performance between times T_0–T_1 and T_1–T_2 for each of the groups, which allowed the identification of changes over time (intragroup). The significance threshold set for each of the analyses was ≤ 0.05.

To run the repeated measures ANOVA Test, it was necessary to verify the assumptions of homoscedasticity ($p \geq 0.05$) and sphericity ($p \geq 0.05$). The Greenhouse-Geisser correction was used in those cases where homoscedasticity was not met. The assumption of sphericity was tested using Mauchly's Test of Sphericity. The repeated measures ANOVA analysis allowed us to see the time factor (changes over time in the sample in general) and the interaction between factors "time versus study group" (differences between the two groups over time) and "time, clinical group, and study group" (differences over time with respect to the study group and the clinical group).

RESULTS

Sample characteristics

The sample that completed 4 months of intervention consisted of 62 individuals. The mean age was 74.73 ± 6.63 and 27.4% were men. The mean number of years of education was 9.36 ± 2.68, and 66.1% ($n = 41$) of the individuals had a diagnosis of MCI, and 33.9% ($n = 21$) of mild dementia. The final sample comprised a total of 23 individuals who completed the 12 months of CCT. Of these, 26.1% were men. The mean age was 76.30 ± 7.69 and the mean number of years of education was 9.96 ± 3.11. Of the sample,

60.9% ($n = 14$) and 39.1% ($n = 9$) of the individuals were diagnosed with MCI and with mild dementia, respectively. However, there were no significant differences between EG-CG regarding age, years of education, sex, or clinic group at 4 or 12 months (Table 1).

Comparison between groups for each condition (T_0–T_1–T_2) (intergroup)

The Shapiro-Wilk Test revealed that most of the variables were not normally distributed, which led to the use of the Mann-Whitney U Test. There were no significant differences between the two groups as to T_0, T_1, and T_2. However, a medium-moderate effect size (d = 0.460) was found for Visual Reasoning of CAMCOG in T_1 ($n = 23$), the EG performing better than the CG (2.07 ± 1.14 and 2.00 ± 1.50, respectively). Small effect sizes in T_1 were found for TMT-B-Time (d = 0.317) and Arithmetic of WAIS-III (d = –0.302), and in T_2 for Visual Memory of RBMT (d = –0.317) and Digit Symbol of WAIS-III (d = 0.302) (Table 2).

Evolution of cognitive-psychological performance for each group (intragroup)

The Shapiro-Wilk Test revealed that most of the variables were not normally distributed for either group during T_0–T_1 and T_1–T_2. Based on this and on sample size within each group, the Wilcoxon signed-rank Test was conducted (Table 3).

Regarding the changes seen between T_0 and T_1 for EG, we highlight an improvement trend of EG during T_1. In this way, we find a small effect sizes for Visual Reasoning of CAMCOG (d = –0.172), WAIS-III Digits (d = –0.123), WAIS-III Arithmetic (d = –0.244), and Semantic Verbal Fluency (SVF) (d = –0.273), and medium-moderate for Lexical Verbal Fluency M (d = –0.310), MMSE (d = –0.439), and TMT-A-Mistakes (d = 0.436). However, a worsening trend was only detected in TMT-B-Time with a medium-moderate effect size (d = 0.362)

On the other hand, we observed that for the T_1–T_2 condition in EG, there was a trend of improvement with small effect sizes for CAMCOG-Visual Reasoning (d = –0.111) and WAIS-III Digit Symbol (d = –0.200), medium-moderate for TMT-B-mistakes (d = 0.359) and RBMT-Visual Memory (d = –0.364), moderate for Lexical Verbal Fluency (LVF-P) (d = –0.489) and GDS (d = 0.538), and there were significant differences ($p = 0.02$) and a large

Table 1
Characterization of the sample in the experimental group (EG) and control group (CG)

Variable		Test T ($n = 62$)			CG		EG		Test W ($n = 23$)			CG		EG	
		T/χ^2	p	Cohen's d	N	M±SD	N	M±SD	W/χ^2	p	Cohen's d	N	M±SD	N	M±SD
Age		1.54	0.13	0.395	26	76.23 ± 6.56	36	73.64 ± 6.56	79.50	0.31	0.262	9	79.22 ± 6.98	14	74.43 ± 7.78
Education		0.01	0.99	0.003	25	9.36 ± 2.86	34	9.35 ± 2.60	66.00	0.85	0.048	9	10.44 ± 3.68	14	9.64 ± 2.79
Sex	Women	3.259	0.07		22 (84.6%)		23 (63.9%)		0.115	0.74		7 (77.8%)		10 (71.4%)	
	Men				4 (15.4%)		13 (36.1%)					2 (22.2%)		4 (28.6%)	
Clinic Group	MCI	0.965	0.33		19 (73.1%)		22 (61.1%)		0.175	0.68		5 (55.6%)		9 (64.3%)	
	Dementia				7 (26.9%)		14 (38.9%)					4 (44.4%)		5 (35.7%)	

*$p \leq 0.05$; **$p \leq 0.01$; CG, control group; EG, experimental group; MCI, mild cognitive impairment.

Table 2
Mann-Whitney U test. Intergroup comparison (EG and CG) during each time (T_0, T_1, T_2)

Test	T_0			T_1			T_1			T_2		
	$N=62$						$N=23$					
	W	*p*	Cohen's d	W	*p*	Cohen's d	W	*p*	Cohen's d	W	*p*	Cohen's d
MMSE	509	0.56	0.088	482	0.85	0.030	56.500	0.70	–0.103	69.000	0.73	0.095
ADAS-Cog	456	0.87	–0.026	425.5	0.55	–0.091	66.000	0.87	0.048	66.000	0.87	0.048
TMT A Time	400	0.28	–0.145	527	0.37	0.126	73.500	0.41	0.167	69.000	0.71	0.095
TMT-A Mistakes	480	0.83	0.026	522	0.33	0.115	70.500	0.65	0.119	68.000	0.67	0.079
TMT B Time	456.5	0.85	–0.025	485.5	0.78	0.037	83.000	0.16	**0.317**	76.000	0.33	0.206
TMT-B Mistakes	477.5	0.90	0.020	414.5	0.44	–0.114	64.000	0.97	0.016	72.000	0.59	0.143
WAIS-III: Digits	483.5	0.83	0.033	416.5	0.46	–0.110	79.000	0.32	0.254	58.500	0.80	–0.071
WAIS-III: Digit Symbol	540	0.30	0.154	481	0.85	0.028	59.000	0.82	–0.063	82.000	0.24	**0.302**
WAIS III: Arithmetic	553	0.22	0.182	501	0.38	0.133	44.000	0.24	**–0.302**	67.000	0.82	0.063
CAMCOG: Visual Reasoning	428	0.56	–0.085	538.5	0.31	0.151	92.000	0.07	**0.460**	52.000	0.50	–0.175
RBMT: Visual Memory	396	0.30	–0.154	462.5	0.94	–0.012	63.500	1.000	0.008	43.000	0.20	**–0.317**
CDT Order	451.5	0.97	–0.008	552.5	0.22	0.181	79.500	0.29	0.262	56.000	0.68	–0.111
CDT Copy	473.5	0.94	0.012	468.5	0.70	0.060	74.500	0.48	0.183	68.500	0.74	0.087
SVF	510.5	0.31	0.155	482	0.55	0.090	50.500	0.83	–0.065	54.500	0.61	–0.135
LVF-P	478.5	0.59	0.083	528.5	0.19	0.196	65.000	0.45	0.204	62.500	1.000	–0.008
LVF-M	474.5	0.63	0.074	427	0.56	–0.088	62.000	0.59	0.148	73.000	0.54	0.159
LVF-R	502.5	0.37	0.137	482	0.85	0.030	52.500	0.94	–0.028	53.000	0.55	–0.159
GDS	444	0.74	–0.051	425.5	0.55	–0.091	58.000	0.77	–0.079	74.000	0.50	0.175

$^{*}p \leq 0.05$; $^{**}p \leq 0.01$; ADASCog, Alzheimer's disease Assessment Scale: cognitive subscale; CAMCOG, Cambridge Cognition Examination; CDT, Clock Drawing Test; GDS, Geriatric Depression Scale; LVF, Lexical Verbal Fluency; MMSE, Mini-Mental State Examination; RBMT, Rivermead Behavioural Memory Test; SVF, Semantic Verbal Fluency; T_0, baseline; T_1, at 4 months of intervention; T_2, at 12 months of intervention; TMT, Trail Making Test; WAIS-III, Wechsler Adult Intelligence Scale.

effect size (d = –1000) for TMT-A-time. However, slight worsening tendencies were also detected for the WAIS-III Arithmetic with moderate effect sizes (d = 0.636) and, a high effect size with a significant difference for the MMSE ($p = 0.01$; d = 0.868) and LVF-M ($p = 0.03$; d = 1000).

Regarding the CG, this exhibited an improvement trend during T_1 and had small effect sizes for Digit Symbol (WAIS-III) (d = –0.281), LVF-M (d = –0.289), LVF-R (d = –0.294), WAIS-III Arithmetic (d = –0.327), medium-moderate for TMT-B-mistakes (d = 0.382), moderate for TMT-A-Time (d = –0.552) and WAIS-III Digits (d = –0.636), this last variable with significant differences ($p = 0.01$). And this group showed a worsening tendency for TMT-A-mistakes (d = –0.258).

On the other hand, the CG also showed an improvement trend in T_2 with moderate effect sizes for RBMT-Visual Memory (d = –0.500), medium-high for TMT-A-mistakes (d = 0.700), and a large for TMT-B-Time (d = –1000). However, CG showed a worsening trend during T_2 with small effect sizes for WAIS-III Digit Symbol (d = 0.200), LVF-M (d = 0.267), and GDS (d = –0.286), medium-moderate for SVF (d = 0.429), moderate for CAMCOG-Visual Reasoning (d = 0.500), WAIS-III Arithmetic (d = 0.583), and Clock Drawing Test (CDT)-Copy (d = 0.600), medium-high for WAIS-III Digits (d = 0.694) and CDT-Order (d = 0.667).

Repeated measures ANOVA

Most of the variables met the assumption of homoscedasticity. For the cases in which this principle was not fulfilled, we applied the Greenhouse-Geisser correction [52]. Thus, variance in the CG and in the EG in each of the variables for T_0–T_1–T_2 was the same. Most of the variables also met the assumption of sphericity, except for AdasCog-total, TMT-B-Time-Mistakes, and WAIS-III Digit-Symbol. After running the repeated measures ANOVA, the effect of the time factor (T_0, T_1, T_2) was significant on the cognitive performance associated with the tests: Digits ($F = 3.632$; $p = 0.04$; $\eta^2 = 0.030$) and Arithmetic of WAIS-III ($F = 4.372$; $p = 0.02$; $\eta^2 = 0.038$) (Table 4). Therefore, cognitive performance was not the same in the three times recorded and we identified an increase in cognitive performance at 4 months and a slight decrease at 12 months in the general sample. Although, we can say that they remained around the average, so their performance was not low (Fig. 2).

There was a statistically significant interaction between time and study group (experimental and

Table 3
Wilcoxon signed-rank test. Intragroup comparison (EG-CG) with respect to cognitive performance between T_0–T_1 and T_1–T_2

Test	Group	p	Cohen's d	T_0		T_1		p	Cohen's d	T_1		T_2	
				($n = 62$)						($n = 23$)			
				N	$\bar{x} \pm$ SD	N	$\bar{x} \pm$ SD			N	$\bar{x} \pm$ SD	N	$\bar{x} \pm$ SD
MMSE	Control	0.20	**–0.337**	26	24.15 ± 4.16	26	24.81 ± 4.06	1.000	–0.048	9	24.11 ± 4.46	9	24.22 ± 4.97
	Experimental	0.05*	**–0.439**	36	24.28 ± 2.54	36	24.97 ± 2.91	0.01**	**0.868**	14	25.21 ± 2.33	14	23.43 ± 2.56
ADAS-Cog	Control	0.58	0.134	26	14.88 ± 7.75	26	14.31 ± 7.29	0.57	**0.250**	9	17.11 ± 10.52	9	16.44 ± 13.14
	Experimental	0.62	–0.103	35	14.00 ± 4.99	35	14.43 ± 6.48	0.40	–0.275	13	12.69 ± 4.03	14	14.29 ± 4.01
TMT A Time	Control	0.07	**–0.552**	25	7.80 ± 5.61	22	9.09 ± 6.66	0.89	–0.133	7	10.71 ± 10.97	8	13.75 ± 14.33
	Experimental	1.00	–0.007	33	11.21 ± 11.32	35	13.43 ± 16.21	0.03*	**–1.000**	14	9.29 ± 10.72	14	11.79 ± 11.87
TMT-A Mistakes	Control	0.47	**–0.258**	26	0.54 ± 1.07	25	0.64 ± 1.19	0.27	**0.700**	9	0.89 ± 1.54	9	0.22 ± 0.44
	Experimental	0.17	**0.436**	36	0.42 ± 0.77	36	0.25 ± 0.44	1.000	–	14	0.21 ± 0.43	14	0.14 ± 0.36
TMT B Time	Control	0.79	0.106	9	14.44 ± 11.02	10	15.00 ± 9.13	0.37	**–1.000**	3	15.00 ± 13.23	2	25.00 ± 7.07
	Experimental	0.25	**0.362**	11	15.91 ± 18.68	15	15.33 ± 11.26	1.000	0.333	5	14.00 ± 9.62	5	10.00 ± 6.12
TMT-B Mistakes	Control	0.19	**0.382**	17	1.59 ± 1.42	20	1.40 ± 1.31	0.53	0.333	5	1.20 ± 1.79	7	2.14 ± 1.77
	Experimental	0.34	0.214	28	2.14 ± 1.46	31	2.23 ± 1.52	0.29	**0.359**	12	2.25 ± 1.66	12	1.83 ± 1.53
WAIS-III: Digits	Control	0.01**	**–0.636**	26	10.65 ± 2.17	25	11.48 ± 2.20	0.09	**0.694**	9	11.44 ± 2.46	9	10.11 ± 3.14
	Experimental	0.59	–0.123	36	10.47 ± 2.61	36	10.58 ± 2.95	0.96	0.036	14	10.57 ± 2.14	14	10.57 ± 2.74
WAIS-III: Digit Symbol	Control	0.25	**–0.281**	23	10.17 ± 2.06	23	10.35 ± 2.21	0.85	0.200	8	11.00 ± 2.45	8	10.75 ± 2.66
	Experimental	0.76	–0.081	36	9.83 ± 2.87	35	10.11 ± 2.41	0.62	**–0.200**	14	9.57 ± 2.28	14	9.79 ± 1.72
WAIS III: Arithmetic	Control	0.24	**–0.327**	26	10.50 ± 2.34	25	10.68 ± 2.67	0.15	**0.583**	9	10.44 ± 2.92	9	9.00 ± 3.74
	Experimental	0.25	**–0.244**	36	9.75 ± 3.08	36	10.22 ± 2.82	0.08	**0.636**	14	10.36 ± 2.10	14	9.00 ± 3.11
CAMCOG: Visual Reasoning	Control	0.75	–0.100	26	2.00 ± 1.10	25	1.96 ± 1.06	0.59	**0.500**	9	2.00 ± 1.50	9	1.78 ± 1.56
	Experimental	0.45	**–0.172**	36	2.22 ± 1.42	35	2.43 ± 1.20	0.80	–0.111	14	2.07 ± 1.14	14	2.14 ± 1.29
RBMT. Visual Memory	Control	0.84	–0.058	26	7.00 ± 3.02	25	6.84 ± 3.01	0.26	**–0.500**	9	6.11 ± 3.18	9	6.78 ± 3.03
	Experimental	0.70	0.089	36	7.94 ± 2.10	36	7.78 ± 2.38	0.33	**–0.364**	14	7.71 ± 2.09	14	8.43 ± 2.41
CDT-Order	Control	0.40	–0.212	26	7.25 ± 2.74	25	7.56 ± 2.07	0.22	**0.667**	9	7.56 ± .2.78	9	6.72 ± 3.09
	Experimental	0.62	–0.117	34	7.35 ± 2.24	36	7.60 ± 2.38	0.88	–0.073	14	7.57 ± 2.70	14	7.64 ± 2.06
CDT-Copy	Control	0.81	–0.068	26	8.81 ± 1.86	25	8.76 ± 1.93	0.35	**0.600**	9	8.44 ± 2.86	9	8.00 ± 3.43
	Experimental	0.58	0.133	36	9.10 ± 1.14	36	8.99 ± 1.50	0.88	0.073	14	9.00 ± 1.51	14	9.00 ± 1.00
SVF	Control	1.00	0.000	25	7.80 ± 3.28	25	7.56 ± 3.37	0.37	**0.429**	9	7.67 ± 3.97	9	7.33 ± 4.00
	Experimental	0.21	**–0.273**	34	7.03 ± 2.88	34	7.62 ± 3.59	0.80	0.109	12	8.75 ± 3.86	14	8.43 ± 2.82
LVF-P	Control	0.51	–0.162	25	7.72 ± 3.55	25	8.16 ± 3.22	1.000	–0.067	9	8.00 ± 4.30	9	7.67 ± 4.12
	Experimental	0.55	–0.129	34	7.56 ± 3.04	34	7.82 ± 2.76	0.21	**–0.489**	12	7.33 ± 2.77	14	8.29 ± 3.02
LVF-M	Control	0.24	**–0.289**	25	7.48 ± 3.66	25	8.28 ± 3.69	0.68	**0.267**	9	8.78 ± 4.27	9	8.44 ± 3.88
	Experimental	0.18	**–0.310**	34	7.68 ± 3.44	34	8.26 ± 3.42	0.03*	**1.000**	12	8.25 ± 4.11	14	7.71 ± 4.03
LVF-R	Control	0.24	**–0.294**	25	8.84 ± 2.53	25	9.40 ± 2.90	0.78	0.200	9	8.89 ± 3.66	9	8.00 ± 3.39
	Experimental	0.38	–0.200	34	8.50 ± 2.57	34	8.97 ± 2.58	0.89	0.061	12	8.83 ± 2.52	14	8.93 ± 2.92
GDS	Control	0.69	–0.105	26	3.42 ± 3.23	25	3.32 ± 3.09	0.59	**–0.286**	9	2.89 ± 2.20	9	3.22 ± 2.17
	Experimental	0.49	–0.153	36	3.86 ± 3.66	36	4.19 ± 3.81	0.10	**0.538**	14	4.14 ± 3.98	14	3.07 ± 3.27

*$p \leq 0.05$; **$p \leq 0.01$; ADASCog, Alzheimer's disease Assessment Scale: cognitive subscale; CAMCOG, Cambridge Cognition Examination; CDT, Clock Drawing Test; GDS, Geriatric Depression Scale; LVF, Lexical Verbal Fluency; MMSE, Mini-Mental State Examination; RBMT, Rivermead Behavioural Memory Test; SVF, Semantic Verbal Fluency; TMT, Trail Making Test; T_0, baseline; T_1, at 4 months of intervention; T_2, at 12 months of intervention; WAIS-III, Wechsler Adult Intelligence Scale.

Table 4
Levene's test, sphericity, and ANOVA. Comparison of cognitive performance between T_0, T_1–T_2 ($n = 23$)

Test	LEVENE'S TEST						SPHERICITY		ANOVA					
	T_0		T_1		T_2				T_0–T_1–T_2			T_0–T_2 Group		
	F	p	F	p	F	p	χ^2	p	F	p	η^2	F	p	η^2
MMSE	22.402	<0.00	5.943	0.02	8.983	0.01	4.965	0.08*	2.165	0.13	0.011	8.971	0.03*	0.019
ADAS-Cog	2.543	0.13*	2.562	0.12*	13.533	0.00	152.552	<0.00	0.630	0.44	0.010	0.610	0.44	0.009
TMT A Time	0.402	0.55*	27.517	<0.00	7.713	0.01	5.567	0.06*	0.532	0.59	0.007	1.641	0.21	**0.021**
TMT-A Mistakes	0.703	0.41*	11.803	0.00	0.863	0.36*	1.844	0.40*	2.424	0.10	0.050	0.908	0.41	**0.019**
TMT B Time	1.292	0.27*	0.055	0.82*	2.228	0.15*	12.752	0.00	0.535	0.52	0.004	1.564	0.23	0.012
TMT-B Mistakes	0.301	0.59*	0.299	0.59*	0.861	0.36*	59.117	<0.00	2.504	0.13	0.035	0.206	0.66	0.003
WAIS-III: Digits	0.316	0.58*	0.021	0.58*	0.394	0.54*	0.911	0.63*	3.632	0.04*	0.030	3.285	0.18	0.014
WAIS-III: Digit Symbol	28.398	<0.00	8.209	0.01	8.241	0.01	181.195	<0.00	1.590	0.22	0.012	1.584	0.22	0.012
WAIS III: Arithmetic	0.364	0.55*	0.505	0.49*	0.304	0.59*	2.321	0.31*	4.372	0.02*	0.038	0.380	0.69	0.003
CAMCOG: Visual Reasoning	0.003	0.96*	0.270	0.61*	0.072	0.79*	1.833	0.40*	0.156	0.86	0.002	0.307	0.74	0.003
RBMT: Visual Memory	2.996	0.10*	2.155	0.16*	1.510	0.23*	2.996	0.22*	2.308	0.11	0.018	0.002	1.0	<0.001
CDT Order	0.0435	0.52*	0.007	0.93*	3.685	0.07*	0.601	0.74*	0.938	0.40	0.010	1.009	0.97	0.011
CDT Copy	4.436	0.05	5.510	0.03	7.100	0.02	0.385	0.83*	0.394	0.68	0.002	0.598	0.55	0.003
SVF	4.221	0.05*	0.394	0.54*	3.342	0.08*	1.062	0.59*	0.655	0.53	0.005	0.920	0.41	0.007
LVF-P	0.546	0.47*	5.239	0.03	2.978	0.10*	5.544	0.06*	1.821	0.18	0.019	0.334	0.72	0.003
LVF-M	0.064	0.80*	0.193	0.67*	0.115	0.74*	1.111	0.60*	1.572	0.22	0.010	0.535	0.59	0.003
LVF-R	0.682	0.42*	2.490	0.13*	0.263	0.61*	5.684	0.06*	0.547	0.58	0.006	0.344	0.71	0.004
GDS	0.236	0.63*	4.104	0.06*	1.386	0.25*	5.368	0.07*	1.697	0.20	0.020	3.414	0.04*	0.041

$n = 23$. Test of Levene $p \geq 0.05$*; Sphericity $p \geq 0.05$*; ANOVA $p \leq 0.05$*; CAMCOG, Cambridge Cognition Examination; CDT, Clock Drawing Test; LVF, Lexical Verbal Fluency; MMSE, Mini-Mental State Examination; RBMT, Rivermead Behavioural Memory Test; SVF, Semantic Verbal Fluency; TMT, Trail Making Test; WAIS-III, Wechsler Adult Intelligence Scale; GDS, Geriatric Depression Scale.

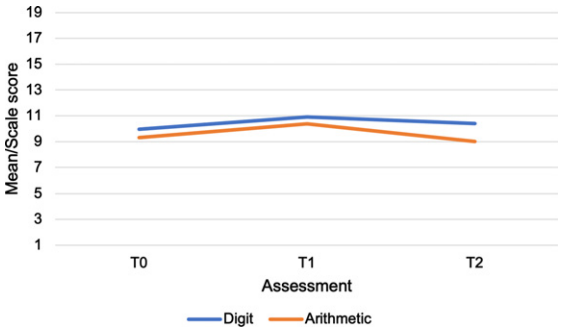

Fig. 2. Analysis with ANOVA. Time factor for Digits and Arithmetic of the Wechsler Adult Intelligence Scale (WAIS-III).

control) in patient performance on the following tests: MMSE ($F = 8.971$; $p = 0.03$; $\eta^2 = 0.019$) and the GDS ($F = 3.414$; $p = 0.04$; $\eta^2 = 0.041$) (Table 4). This analysis showed that the cognitive performance of EG patients was less positively influenced by training than CG patients at the 12-month evaluation in MMSE. While the opposite occurred for the GDS (Fig. 3). Also, small effect sizes were found between time- study group interactions for the following variables: TMT-A-time ($F = 1.641$; $p = 0.21$; $\eta^2 = 0.021$) and TMT-A-mistakes ($F = 0.908$; $p = 0.41$; $\eta^2 = 0.019$) (Table 4, Fig. 3).

Also, we found a significant interaction and a low-medium effect size between time, study group, and clinical group for the variable CDT Order ($F = 3.455$; $p = 0.04$; $\eta^2 = 0.033$) (Table 5). This analysis showed that people with MCI in the EG maintained their cognitive performance over a long time and even improved in the case of people with mild dementia, while people with MCI and mild dementia in the CG tended to decrease their performance with relation to time (Fig. 4).

On the other hand, a low-medium effect size was found for CAMCOG visual reasoning ($F = 2.753$; $p = 0.08$; $\eta^2 = 0.030$) and medium for TMT-B-Mistakes ($F = 1.731$; $p = 0.20$; $\eta^2 = 0.068$) (Table 5). So, people with MCI and mild dementia of the EG improved their performance in TMT-B-Mistakes over time compared to the CG that decreased in the case of people with MCI or was maintained in the case of people with mild dementia. With respect to Visual Reasoning of CAMCOG, people with EG MCI improved their performance over time compared to CG, contrary to what happened with people with mild dementia (Fig. 4). No adverse effects of GRADIOR were reported in people with MCI and mild dementia.

DISCUSSION

The purpose of this RCT was to find out the effects of a GRADIOR CCT program on cognitive

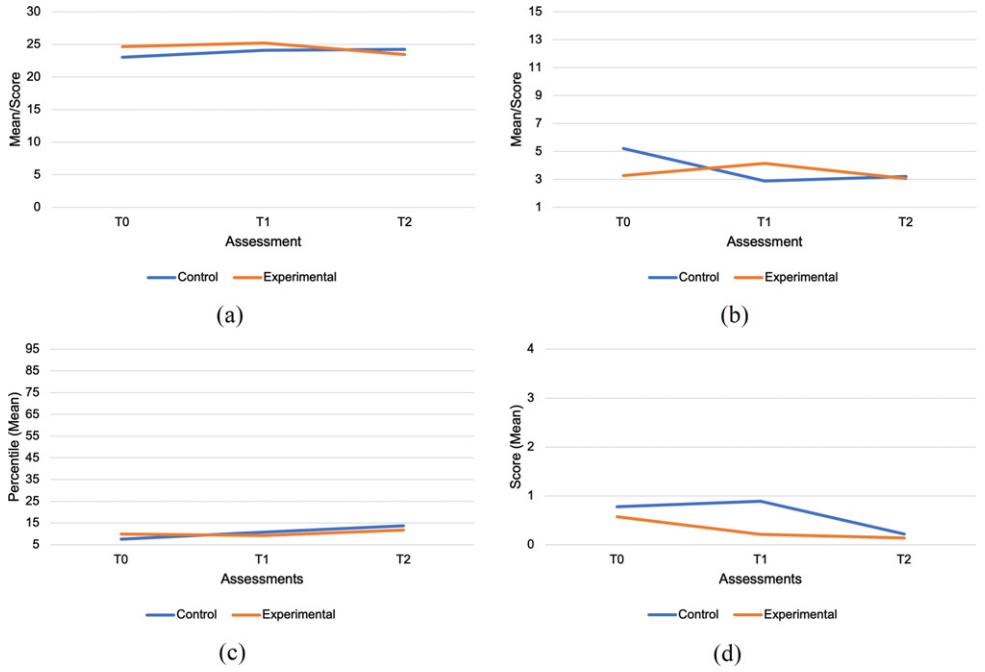

Fig. 3. Analysis with ANOVA. Time and group study (Experimental and Control) interaction for a) Mini-Mental State Examination (MMSE), b) Geriatric Depression Scale (GDS), c) Trail Making Test (TMT) A Time, and d) TMT A mistakes.

Table 5
Levene's test, sphericity, and ANOVA. Comparison of cognitive performance between T_0, T_1–T_2 ($n = 23$) according to the clinical group (MCI and mild dementia) with respect to the study group (experimental and control)

Test	Levene's Test						Sphericity		ANOVA		
	T_0		T_1		T_2				T_0–T_2* Study Group* Clinic Group		
	F	p	F	p	F	p	χ^2	p	F	p	η^2
MMSE	1.377	0.28*	2.923	0.06*	1.533	0.24*	3.129	0.21*	1.758	0.19	0.008
ADAS-Cog	2.202	0.12*	1.640	0.22*	1.903	0.17*	5.798	0.06*	0.725	0.49	0.003
TMT A Time	1.477	0.26*	2.574	0.09*	1.981	0.16*	17.127	<0.001	0.597	0.56	0.011
TMT-A Mistakes	3.244	0.06*	3.145	0.06*	87.750	<0.001	2.000	0.37*	0.714	0.50	0.015
TMT B Time	–	–	–	–	–	–	–	–	–	–	–
TMT-B Mistakes	6.304	0.01	6.299	0.01	7.231	0.01	1.292	0.52*	1.731	0.20	**0.068**
WAIS-III: Digits	0.026	0.99*	1.322	0.30*	0.830	0.49*	2.430	0.30*	1.087	0.34	0.008
WAIS-III: Digit Symbol	0.940	0.44*	3.362	0.04	4.378	0.02	0.406	0.81*	1.566	0.22	0.009
WAIS III: Arithmetic	1.267	0.31*	2.270	0.11*	0.602	0.62*	1.437	0.49*	1.891	0.17	0.017
CAMCOG: Visual Reasoning	0.891	0.46*	0.909	0.45*	0.367	0.78*	1.024	0.60*	2.753	0.08	**0.030**
RBMT: Visual Memory	1.026	0.40*	0.308	0.82*	0.911	0.45*	3.737	0.15*	0.543	0.59	0.004
CDT Order	0.163	0.92*	4.251	0.02	0.585	0.63*	1.411	0.49*	3.455	0.04*	**0.033**
CDT Copy	2.113	0.13*	3.444	0.04	6.063	0.00	0.572	0.75*	1.175	0.32	0.006
SVF	1.612	0.22*	0.568	0.64*	1.783	0.19*	1.188	0.55*	0.192	0.83	0.001
LVF-P	2.377	0.10*	2.589	0.09*	2.793	0.07*	5.601	0.06*	0.958	0.39	0.010
LVF-M	1.665	0.21*	4.235	0.02	0.670	0.58*	0.316	0.85*	0.039	0.96	<0.001
LVF-R	0.675	0.58*	2.265	0.11*	0.776	0.52*	4.855	0.09*	1.017	0.37	0.011
GDS	0.149	0.92*	1.391	0.28*	0.887	0.47*	5.000	0.08*	0.175	0.84	0.002

$n = 23$. Test of Levene $p \geq 0.05$*; Sphericity $p \geq 0.005$*; ANOVA $p \leq 0.05$*; CAMCOG, Cambridge Cognition Examination; CDT, Clock Drawing Test; LVF, Lexical Verbal Fluency; MMSE, Mini-Mental State Examination; RBMT, Rivermead Behavioural Memory Test; SVF, Semantic Verbal Fluency; TMT, Trail Making Test; WAIS-III, Wechsler Adult Intelligence Scale; GDS, Geriatric Depression Scale.

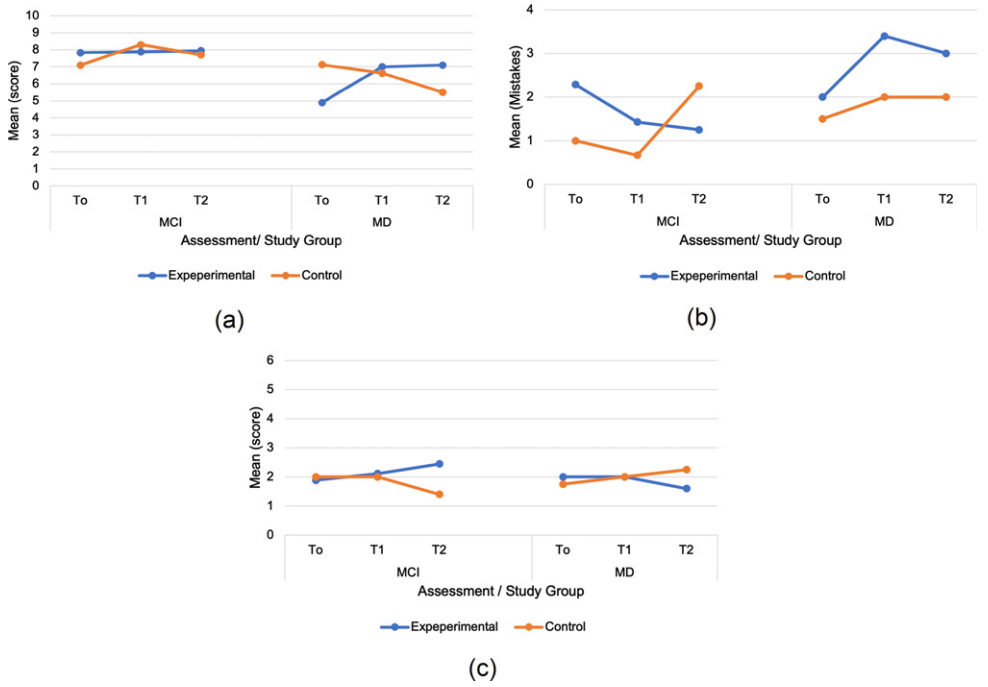

Fig. 4. Analysis with ANOVA. Time, Clinical Group (MCI and Mild dementia), and Study Group (Experimental and Control) interaction for a) Clock Drawing Test (CDT) Order, b) Trail Making Test (TMT) B mistakes, and c) Visual Reasoning of Cambridge Cognition Examination (CAMCOG).

and emotional aspects in people with MCI or mild dementia. Regarding the general cognitive performance obtained from the MMSE, an instrument used for the selection and during the follow-up evaluations in the sample, we observe an improvement trend at 4 months with respect to the baseline and a worsening trend at 12 months with respect to 4 months in the EG. Although this seems to underestimate the effect of CCT at first, it was important for us to evaluate cognitive functions and processes by using different specific tests for this objective.

One of the cognitive functions most evaluated was EF. In this order of ideas, both groups exhibited alterations in *visual reasoning* (CAMCOG) at the beginning of the study, which could be attributed to the sample's low educational level. However, the EG had a better performance than the CG in visual reasoning (CAMCOG) at 4 months (intergroup). Also, we saw longitudinal changes in cognitive performance within each group (intragroup). The CG showed a deterioration trend towards 12 months compared to 4 months, while the EG slightly improved at 4–12 months of CCT. Likewise, with respect to the EG, we found that people with MCI improved their performance while people with mild dementia worsened over time compared to the CG.

This could be explained because the GRADIOR cognitive training plan included activities such as puzzles; possibly this allowed training this EF. This means that the treatment contributed to a slight improvement in this process, preventing an even greater deterioration in the EG.

Our results suggesting an improvement trend in selective-sustained attention (evaluated by TMT-A-mistakes) at 4 months with respect to baseline and thereafter in processing speed (evaluated by TMT-A-time) at 12 months with respect to 4 months in people attending the GRADIOR sessions. Also, the results showed an interaction between "time and study group"; in this way, the EG slightly worsens its performance in TMT-A-time at 4 months, but makes fewer errors at 12 months, compared to CG, where the opposite happens. This means that these people found "doing it well" more important than "doing it fast" and therefore prioritized and intensified their attention capacity while performing the task. The improvement in attentional processing has also been noted in other studies such as that by Hagovská et al. [17] after 10 weeks of CCT and González-Palau et al. [16] after 12 weeks of combined (cognitive and physical) training delivered to healthy older adults and older adults with MCI.

The improvement in processing speed has been explained as the result of stimulation associated with social interaction in people with MCI [20]. According to our study, the improvement in processing speed after 12 months with respect to 4 months in the EG could have been due to the increase in social interaction during the CCT. The way in which GRADIOR was applied, in a shared room where users worked with their customized programs [50], probably favored the increase in social interaction among the people with MCI and mild dementia that attended the CCT [44, 53]. Further research is required to define the relationship between processing speed and social interaction.

The EG showed an improvement in *selective-divided attention, alternation, cognitive flexibility, inhibitory control*, and *cognitive flexibility* (evaluating processes by the TMT-B-mistakes) after 12 months of CCT with respect to 4 months (intragroup). Likewise, the results highlighted that the group of people with MCI and mild dementia associated with the EG improved in these processes over time compared to the CG. Studies also mentioned an enhancement in these processes in people with MCI [20]. This could be explained by the fact that GRADIOR is a CCT program that includes one of the basic training principles: "feedback" [54]. GRADIOR delivers feedback on the individual's performance in each of the activities, which offers the person the chance to "learn" and correct the mistake immediately and/or soon after making it [50].

In the field of neuropsychology, mistakes of omission or commission are a relevant source of qualitative information in the assessment of cognitive processes. People with MCI or mild dementia are often aware of these mistakes and, therefore, probably of their deficits. The purpose of any treatment, CCT or therapeutic process is that the patient, depending on the level of decline, be aware of his/her deficit. If otherwise, we would be dealing with anosognosia [55, 56].

As compared to the TMT-A, the EG took longer in completing the TMT-B at 4 months, which suggests low processing speed, although this decreases with age [57, 58]. The EG probably made more mental checks to avoid mistakes and were more aware of their difficulties, something that could be observed with greater precision during the evaluation at 12 months, which contributed to these results, considering the complex nature of the task of the B-condition of the TMT.

The overall improvement in EF after using a CCT program was also noted by Shatil et al. [59], although these authors only included healthy older adults in their study. In our study, there were also changes associated with EF such as fluency, categorization, and monitoring of performance evaluated by SVF and LVF, although these were observed at two different stages of the intervention. While the EG showed an improvement trend at 4 months in SVF tasks, at 12 months, this same group improved in LVF-P tasks. This was not so in the CG. This is interesting, the form of gradual improvement in verbal fluency, semantic fluency being the first to show improvement and then phonological fluency. The latter being in most cases the most compromised in PwD [60].

Calculation and numerical reasoning (WAIS-III Arithmetic) were one of the best-preserved functions in people with MCI and mild dementia at baseline. Both groups showed an improvement trend at 4 months and a slight worsening at 12 months. In this regard, the improvement was greater in the EG and the worsening in the CG. It is worth noting that one of the reasons why calculation is one of the best-preserved abilities among this population group could be related to their living conditions and, especially, to the need of developing and training this ability due to its multiple uses in various areas of daily living, from activities like shopping to more professional uses. Therefore, activities of daily living contribute to preserving the most frequently used functions.

One of the commonly deteriorated functions in people with MCI and mild dementia is memory [57, 61]. We only managed to perceive an improvement trend at 12 months with respect to 4 months in visual recognition tasks (RMBT) in both groups. Nevertheless, the EG obtained better results than the CG at 12 months. This is in line with the study conducted by Hwang et al. [62], where a significant increase in visual recognition was reported in people with Alzheimer's disease. It is a simple cognitive task that seems to benefit from any psychosocial intervention, both the usual and the more specific using GRADIOR. Moreover, considering that people with MCI accounted for a large percentage of our sample, recognition tasks were often better retained than free-recall ones [63].

Different studies have also reported significant alterations in the working memory (WM) of people with MCI and mild dementia [64, 65]. In our study, WM at 4 months appeared well-preserved in both groups, although the EG improved at 12 months in

Digit-Symbol test of WAIS-III compared to 4 months (intragroup). CG worsened at 12 months with respect to 4 months in two tests (Digit and Digit-Symbol of WAIS-III) (intragroup).

According to Hyer et al. [18], the WM in people with MCI improved after 7 weeks of CCT. Studies based on shorter periods of CCT and focused on WM only report improvements in this function in people with MCI [19, 24]. Other studies noted changes in the two variants of the WAIS-III Digits Test. Cavallo et al. [14] found that performance was better in forward and backwards spans of the Digits test at 12 weeks of CCT and that it was maintained at 6 months in people with Alzheimer's disease. This last finding was not explicit in our study, where the overall score on the WAIS-III Digits Test was considered.

Regarding *Visuoconstructive ability* of CDT, both groups performed similarly at baseline and at 4 months. However, the CG showed a worsening trend at 12 months with respect to 4 months, while the EG maintained similar levels of performance at 4–12 months (although the latter was not significant). However, a significant interaction was found which made it relevant that the EG of people with MCI maintained their performance and the group of people with mild dementia slightly improved at 4 months and maintaining over time compared to people with MCI and mild dementia of CG, this group decreased their performance.

Finally, the EG experienced an improvement in *mood* at 12 months of CCT with respect to 4 months. Also, there was a significance interaction between the CG-EG with a small effect size, where the EG scored better than the CG on the GDS at 12 months. Our findings are even related to meta-analyses such as that by García-Casal et al. [21] who also mentioned a small effect size on the improvement of depression in PwD after a CCT program. Or also, studies that reported an improvement in mood in people with MCI [16], even if others consider that this improvement is not possible [66].

Recommendations and limitations

The results reveal that the functioning and improvement of both groups at 4 months was similar, these data being inconclusive as to the short-term benefits of using this CCT program. Only after 12 months of CCT did the results show slight improvement and/or maintenance trends in certain cognitive processes and mood, with moderate-large effect sizes and, in certain cases, statistical significance in EG. In contrast, the CG showed greater worsening tendencies towards 12 months.

The above might be explained based on how the CCT GRADIOR was implemented: the first 3 months of CCT consisted of a standard plan, after which treatment was tailored to each individual's cognitive level over the 12 months. Such customization could have provided more benefits and effectiveness insofar as it was adjusted to the cognitive needs and characteristics of each participant. GRADIOR suggests and recommends a series of criteria to serve as the basis to make changes in the difficulty level of each task [50].

Flak et al. [67] suggested a comparison between customized and nonadaptive training and their influence on the WM of patients with MCI. Nevertheless, they found no changes after 5 weeks of CCT. By contrast, the study by Peretz et al. [68] proved the effectiveness of a customized CCT plan at 3 months on improving visuospatial WM, visuospatial learning, and sustained attention in older adults. While these studies provide an interesting approach, it would be advisable to consider in any cognitive training, the design of a training plan personalized to the individual's cognitive profile and characteristics.

Another relevant aspect was that the sample consisted of people with MCI, which is sometimes spontaneously reversible, and mild dementia, whose natural progress is not towards rapid decline. The benefits of applying a specific program CCT such as GRADIOR in cases of MCI and mild dementia will be more relevant when applied over long periods of time [24], against what is commonly the case with the implementation of these programs in studies based on few weeks of intervention [26, 69].

Lee et al. [25] recommended studies with longer periods of CCT be undertaken. Nevertheless, it is necessary to be aware of the difficulties involved in completing RCTs with older adults and long CCT programs. Such studies are often challenged by different factors that may be biological (high rates of mortality), physical (mobility alterations), contextual (little understanding of the family about the disease and its treatment), psychological (emotional disturbances that hinder treatment adherence), social (stigma associated with the person's social network), environmental (pandemic outbreak), and economic (lack of funding, high costs of human resources and infrastructures).

The relevance of this RCT is its 12-month length, so that, in addition to customizing the CCT, the purpose was continuity in time with frequent sessions

over an extended period to test whether there were significant changes in cognitive processes and/or if they were maintained over time. If so, the use of a continuous CCT program would be related to the progressive nature of the neurodegenerative process that occurs in dementia, although this process varies among individuals and CCT cannot guarantee full recovery of cognitive processes.

One of the study's limitations is that the sample was small. Although the initial sample was 89 people, only 62 individuals managed to complete the 4 months and our attempt to have the sample complete the 12 months was hampered by the consequences of the outbreak and the extension in time of the COVID-19 pandemic.

The pandemic led to the closure of many public health centers and, therefore, the people undergoing the CCT with GRADIOR stopped attending the sessions. Only 23 individuals managed to complete the 12-months scheduled for the CCT before the pandemic began and therefore, the CG people on the waiting list were unable to start the treatment. This situation helps to redefine its current implementation and strengthens lines of research that are already in progress to consolidate the use of portable devices at home to make these programs more accessible to older adults [70], developing CCT programs based on a user-center methodology [71], and implementing digital literacy programs to bridge the digital divide [72]. Shatil et al. [59] suggested TV-based computer literacy training for older adults. Nevertheless, it will be necessary to develop devices.

We are aware that CCT is not the only treatment option for people with MCI and mild dementia, since the literature includes studies assessing the effectiveness of these cognitive programs combined with physical training programs [73] or other approaches such as reminiscence therapy [74] on different alterations associated with the disease. Dementia is a neurodegenerative disease that causes changes at different functional levels [75], so it would be interesting to engage in future studies to assess the effectiveness of GRADIOR in combination with other types of program [44]. In short, we believe that a multidisciplinary approach could prove more beneficial for this population [10].

GRADIOR can be considered a promising CCT program, it is a 1) flexible program that has not only been developed to be used with people with dementia, but also with people with other neurological and/or psychiatric pathologies; 2) it is easy to use for people with little knowledge in technology; 3) useful, due to its effectiveness, degree of usability [47] and level of user experience [48]. Specifically, it allows the 4) construction of a neuropsychological profile of each user from a neuropsychological evaluation that can be carried out from the same program; 5) design and implementation of a cognitive stimulation plan based on altered processes and the user's cognitive level; 6) adjustment of the treatment plan according to the user's cognitive performance.

Also, and considering our results, the use of GRADIOR is recommended in people with MCI and mild dementia for long periods of time. Cognitive training should be continuous and maintained over time due to the characteristics of the cognitive deterioration that these people present. We consider that its interruption could have a negative impact on the cognitive state of the person.

Implications

This study has important methodological, clinical, and practical implications in the field of neuropsychology, new technologies, and dementias. Methodological implications in terms of trying to imply a representative sample size and with it the multiple factors that could make sample collection difficult, which could be taken into consideration by future studies. Also, the application and implementation of a "GRADIOR" CCT program for long periods of time (12 months) and its positive influence on the maintenance of cognitive processes. Both the sample size and the continuity of treatment are two factors that any clinical trial whose objective is to evaluate the effectiveness should try to incorporate. These are also factors that have constituted part of the limitations of most of the studies currently published on the subject.

Perhaps the scope of this RCT could be questioned due to the changes in the design mentioned in the methodology session and the final size of the sample, but we consider that this RCT maintained its methodological rigor and presented an effort to want to overcome the limitation associated with the short training time proposed in most RCTs. We know that maintaining an RCT of 12 months requires a cost of great magnitude with respect to human, technological, and infrastructure resources. But above all, maintaining the level of sample motivation for them to attend the CCT sessions requires, for example, that the CCT be interesting and personalized to the needs of the people. And although we reported a sample loss around 12 months, this was not due to the nature

of the RCT, but to the impossibility of continuing due to external factors, specifically due to COVID-19.

Regarding the clinical implications, cognitive rehabilitation has proven to be a field that responds to certain needs of people with dementia from the use of pencil and paper to the design and development of CCT programs such as GRADIOR that contribute to training, maintenance, and improvement of cognitive performance and delay of progressive deterioration in people with dementia. GRADIOR is a program that is adapted to the type and level of cognitive impairment, aspects that contribute not only to its effectiveness, but also to its usability. The use of tools such as GRADIOR makes the work of the therapist easier, who could have a session with several patients at the same time.

Likewise, this study indicates a tool, whose practical implication corresponds to its degree of accessibility that prevents these people from starting a cognitive training plan. Although this point is currently being improved, to increase its degree of accessibility. Likewise, this study contributes to future studies on effectiveness with respect to methodological aspects.

Conclusion

Some intergroup differences in cognitive performance were detected with respect to each of the evaluation times, visual reasoning (CAMCOG) being one of them. Likewise, improvement trends were identified at the intragroup level between baseline, 4 months, and 12 months for EG with respect to most of the cognitive processes evaluated by the different tests and although something similar happened for CG at 4 months, this same group showed changes and a tendency to worsen towards 12 months in most of the tests. We also highlight the interaction between "time and group", showing GRADIOR a positive impact on mood (GDS) and sustained attention (TMT-A-mistakes) in EG. And a significant interaction between "time, study group, and clinic group" for the CDT Order, highlighting the positive impact of the GRADIOR sessions in people with MCI and mild dementia of EG.

The effects seem to be more significant in those cases where the 12-month treatment was completed, which is why it is advisable to use this type of programs for long periods to test their effects. Many patients were unable to complete the scheduled sessions because of the COVID-19 pandemic, which also highlights the relevance of implementing these intervention programs through more accessible technologies.

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SUPPLEMENTARY MATERIAL

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Artículo 4

Determinantes de la Adherencia a un Programa de Entrenamiento Cognitivo Basado en Computador "GRADIOR" en Personas con Deterioro Cognitivo Leve (DCL) y Demencia Leve

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Resumen

Antecedentes: Se han venido implementando programas informáticos desde un enfoque psicosocial para la atención a personas con demencia. Sin embargo, diferentes factores podrían determinar la adherencia de las personas mayores a este tipo de tratamiento. El **Objetivo** de este trabajo fue identificar los determinantes sociodemográficos, cognitivos,

psicológicos y de salud física que ayudaron a predecir la adherencia o no a un programa de entrenamiento cognitivo computarizado (ECC) “GRADIOR” en personas con deterioro cognitivo leve (DCL) y demencia leve.

Método: Este estudio fue parte de un ensayo clínico aleatorizado (ECA) (ISRCTN: 15742788). Sin embargo, este estudio sólo se centró en el grupo experimental (n = 43) incluido en el ECA. Este grupo fue dividido en personas adherentes (cumplimiento: ≥60% de las sesiones y persistencia en el tratamiento hasta 4 meses) y no adherentes. Los participantes tenían entre 60 y 90 años y fueron diagnosticados con deterioro cognitivo leve y demencia leve. Seleccionamos desde el protocolo de evaluación del ECA, pruebas que evaluaran aspectos cognitivos (memoria y funcionamiento ejecutivo), psicológicos y de salud física. El ECC con GRADIOR consistió en asistir a 2-3 sesiones semanales durante 4 meses con una duración de 30 minutos. Análisis de datos: Phi y correlaciones biserial-puntual, se obtuvo un análisis de regresión logística múltiple para encontrar el modelo de adherencia y se utilizó U Mann-Whitney.

Resultados: El modelo de adherencia estuvo compuesto por las pruebas Dígito-Símbolo y Aritmética de la Escala Wechsler de Inteligencia para Adultos (WAIS-III) y Fluidez Verbal Léxico (FVL) -R. Este modelo tuvo el 90% de sensibilidad, 50% de especificidad y 75% de precisión. El valor p de bondad de ajuste del modelo fue 0,02.

Conclusiones: un buen funcionamiento ejecutivo en atención, memoria de trabajo (MT), fluidez verbal fonológica y flexibilidad cognitiva, predijeron una mayor probabilidad de que una persona fuera adherente.

Palabras clave: demencia; rehabilitación; software; basado en computadora; cognición; psicología

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Article

Determinants of Adherence to a "GRADIOR" Computer-Based Cognitive Training Program in People with Mild Cognitive Impairment (MCI) and Mild Dementia

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Abstract: Background: Computer-based programs have been implemented from a psychosocial approach for the care of people with dementia (PwD). However, several factors may determine adherence of older PwD to this type of treatment. The aim of this paper was to identify the sociodemographic, cognitive, psychological, and physical-health determinants that helped predict adherence or not to a "GRADIOR" computerized cognitive training (CCT) program in people with mild cognitive impairment (MCI) and mild dementia. Method: This study was part of a randomized clinical trial (RCT) (ISRCTN: 15742788). However, this study will only focus on the experimental group (n = 43) included in the RCT. This group was divided into adherent people (compliance: ≥60% of the sessions and persistence in treatment up to 4 months) and non-adherent. The participants were 60–90 age and diagnosed with MCI and mild dementia. We selected from the evaluation protocol for the RCT, tests that evaluated cognitive aspects (memory and executive functioning), psychological and physical health. The CCT with GRADIOR consisted of attending 2–3 weekly sessions for 4 months with a duration of 30 min *Data analysis:* Phi and Biserial-point correlations, a multiple logical regression analysis was obtained to find the adherence model and U Mann–Whitney was used. Results: The adherence model was made up of the Digit Symbol and Arithmetic of Wechsler Adult Intelligence Scale (WAIS-III) and Lexical Verbal Fluency (LVF) -R tests. This model had 90% sensitivity, 50% specificity and 75% precision. The goodness-of-fit p-value of the model was 0.02. Conclusions: good executive functioning in attention, working memory (WM), phonological verbal fluency and cognitive flexibility predicted a greater probability that a person would be adherent.

Keywords: dementia; rehabilitation; software; computer-based; cognition; psychology

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1. Introduction

The World Alzheimer Report 2019 estimated that there are more than 50 million people with dementia (PwD) in the world, a number that will increase to 152 million by 2050 [1]. In recent years, various investigations have been developed on the effectiveness

of computer-based cognitive training (CCT) programs to help delay decline and maintain cognitive status in people with mild cognitive impairment (MCI) and mild dementia [2,3]. However, it is not only important to study the effectiveness, but it is also necessary to take into consideration the rate and therefore, the possible characteristics that determine adherence to CCT program.

Adherence has been mostly studied in association with the use of drugs [4], there being few studies about adherence to CCT programs in people with MCI and dementia [5]. The WHO defines adherence as the degree to which a person's behavior with respect to a treatment corresponds to the recommendations provided by a healthcare professional [6]. Therapeutic compliance has been used as a synonym for adherence, this refers to the degree to which a patient acts according to a therapeutic regimen [7]. That is, the frequency, duration, and latency of a specific treatment. Recently, the literature emphasized persistence to help complement the definition of adherence, terms often used interchangeably, but differing. Persistence refers to the time of treatment from its beginning to its end; in which, there could be a "grace period". That is, a permitted time interval in which the person temporarily suspends the treatment, but retakes it until its end [8]. Spanish Society of Pharmacy, Clinic, Family and Community (SEFAC) proposes that for a patient to be completely adherent, he/she must be compliant and persistent [9]. However, there will be cases where a person may be compliant, but not necessarily persistent, vice versa or neither [10].

The WHO pointed out the lack of adherence as a public health problem and proposed some factors that could determine it, such as: socioeconomic level, the person, the therapy, different conditions, the health system, and care team [9]. Our research will particularly focus on investigating the determinants of adherence associated with the person.

So, adherence can be predicted and explained from a cognitive, psychological, social, neurocognitive, and even technological point of view. Scase et al. [11] pointed out the mild level of deterioration, social interaction, and the availability of technological support to explain the adherence of a group of people with MCI to computer-based gamified environments. Evers et al. [12] mentioned that poor baseline performance in memory, attention, and semantic verbal fluency (SVF) tests helped to predict greater adherence in older women.

Park et al. [13] tried to associate adherence to virtual reality (VR) training program with the improvement of cognitive functioning. Turunen et al. [14] mentioned good memory performance as one of the variables that helped to predict the adherence to a CCT program in adults at risk of dementia. Han et al. [15] found a correlation between the improvement of memory skills and adherence to The Ubiquitous Spaced Retrieval-based Memory Advancement and Rehabilitation Training (USMART) in people with MCI. On the other hand, when older adults are aware of their cognitive decline, specifically when it affects their executive functioning, there was an increase in their adherence [16]. Similarly, de Wit et al. [17] mentioned that the compensatory strategies offered by a memory support system training in people with MCI could influence adherence. Certain psychological variables such as positive expectations at the beginning of a CCT program were found among the main factors that help predict adherence [14]. On the other hand, it seems that people with cognitive impairment spent more time on web-based CT sessions than people with depressive symptoms or other psychiatric disorders [18].

Moreover, earlier studies have already remarked the difficulties in finding features linked to low adherence to the intervention based on individual Cognitive Stimulation Therapy (iCST) [19]. Consequently, the objective of this study was to identify the sociodemographic, cognitive, psychological, and physical-health determinants that helped predict adherence (therapeutic compliance and persistence) or not to a "GRADIOR" CCT program in people with MCI and mild dementia.

2. Materials and Methods

2.1. Study Design

This study was part of a multicenter simple-blind, randomized clinical trial (RCT) on the effectiveness of the GRADIOR cognitive rehabilitation program in people with MCI and mild dementia [20,21]. This trial was registered at isrctn.com (ISRCTN: 15742788) [22] and was approved by the Drug Research Ethics Committee of the Zamora Health Area (Number: 387-E.C). The recruitment period began in June 2018 and lasted until December 2019. The protocol of this RCT had variations, the main one being related to the design because the ehcoBUTLER platform was excluded. This was not completed on time when the RCT started, which led to modifications in the design with respect to the number of parallel groups, the sample size, and the type of randomization.

The participants included in this RCT were randomly assigned (1:2) to the control or experimental group. Those in the control group (CG) maintained their daily activities, remaining on the waiting list, and those in the experimental group (EG) attended CCT sessions using the GRADIOR program for 4 months. However, the present study focused on the EG. From which, two groups were formed: adherent (compliance-persistent) and non-adherent (those who did not meet any or none of the conditions).

2.2. Participants

The study sample included 43 participants aged 60 to 86, and 72.1% had a basic primary educational level. Participants were selected from day centers, memory clinics and hospitals in the Spanish regions of Castile and León and Galicia. *The inclusion criteria* were as follows: (1) clinical diagnosis of MCI according to Petersen's criteria [23] and mild dementia according to the diagnostic criteria of the Diagnostic and Statistical Manual of Mental Disorders (DSM-V) [24] (this diagnostic was carried out by a psychogeriatrician and neurologist); the types of MCI included were amnestic, and for mild dementia were Alzheimer's disease, vascular dementia, mixed dementia, and frontotemporal dementia; (2) score on the Yesavage Geriatric Depression Scale (GDS) ≤ 5; (3) voluntary participation of each people; (4) participation of a reference caregiver; 5) speaking and understanding Spanish. An additional criterion was the Mini-Mental State Exam (MMSE) scores, the cut-off point for MCI was $\leq$27 and for mild dementia was $20 \geq X \leq 25$. MMSE scores were adjusted according to age and educational level of each people [25].

The exclusion criteria were: (1) severe physical comorbidity; (2) severe sensory alterations (auditory or visual) indicated after clinical evaluation by the psychogeriatrician or neurologist; (3) clinically proven psychopathological disorders (depression, anxiety, bipolar disorder, psychosis); (4) neurological disorders (Huntington's disease, stroke, Parkinson's disease, dementia with Lewy bodies); (5) history of substance use (e.g., alcohol, tobacco).

To make up the group of adherents, the conditions of compliance and persistence were considered. Regarding therapeutic compliance, people who attended at least 66% of the sessions of the maximum number of sessions, for 30–40 min per session. Additionally, to consider a person persistent or not, the person had to attend weekly for 16 weeks (4 months) of intervention, and therefore they should not exceed the only "grace period" or allowed interval of absence from the CCT of two continuous weeks. If the person met only one or neither of the two conditions, they were considered non-adherent.

2.3. Neuropsychological Assessment

Possible predictor variables of adherence were associated with the baseline of RCT. We constructed an evaluation protocol for the RCT, which included several scales that evaluated different aspects. However, we selected the variables for our study, considering the literature and our objectives. Sociodemographic aspects such as age, sex, educational level and years of education were assessed. Appendix A describes each of the test used to specifically measure global cognitive performance, memory and EF: MMSE [26], Memory of words, Word recognition and Total of Alzheimer's Disease Assessment Scale—Cognitive Sub-scale (ADASCog) [27], Trail Making Test (TMT) forms A–B [28], Digits, Arithmetic and

Digit Symbol of Wechsler Adult Intelligence Scale (WAIS-III) [29], Visual Recognition of the Rivermead Behavior Memory Test (RBMT) [30], Visual Reasoning of the Cambridge Cognition Examination (CAMCOG) [31] and Verbal Fluency (Semantic and Lexical) [32].

Affective state, motivation and expectations were also evaluated as part of the psychological dimension (Appendix A). The affective component was evaluated using the GDS [33]. Motivation was valued using the following question: "Do you need someone to encourage you to attend the workshop?" The other questions included in the questionnaire were associated with the following expectations: (1) memory improvement; (2) improvement in quality of life; (3) spending free time in a pleasant way; (4) meeting new people at the workshop. Data on the use of technologies were collected based on the question "Do you usually use any technology?"

Finally, we used the EuroQol (EQ-5D-5L) test [34], which assesses the patients' perception about the physical-health dimension: mobility, self-care, daily activities, pain-discomfort and anxiety-depression, and patients' perception regarding their current health condition (Appendix A).

2.4. Computer-Based Cognitive Training (CCT) and Adherence

GRADIOR is a computer-based cognitive rehabilitation program and allows CCT of different cognitive functions that present a deficit or deterioration based on different etiologies, including dementia [35]. It includes a series of exercises associated with orientation, memory, attention, perception, executive functioning, reasoning, and calculation (Figure 1). Each of these cognitive modalities (cognitive functions) includes various sub-modalities (cognitive processes) to customize CCT to the user's cognitive profile [36]. The RCT was based on a cognitive training plan designed for people with MCI and mild dementia, independently (Table 1). This meant that the type of exercises was a function of diagnosis. However, the plan was personalized for each patient according to his/her cognitive level in each exercise. Participants had to attend two or three weekly sessions (this was determined for each center), each lasting 30–40 min. The interface of GRADIOR uses an intuitive touchscreen system and meets usability standards [37,38], providing good user experience [39] to adapt to the needs of older people.

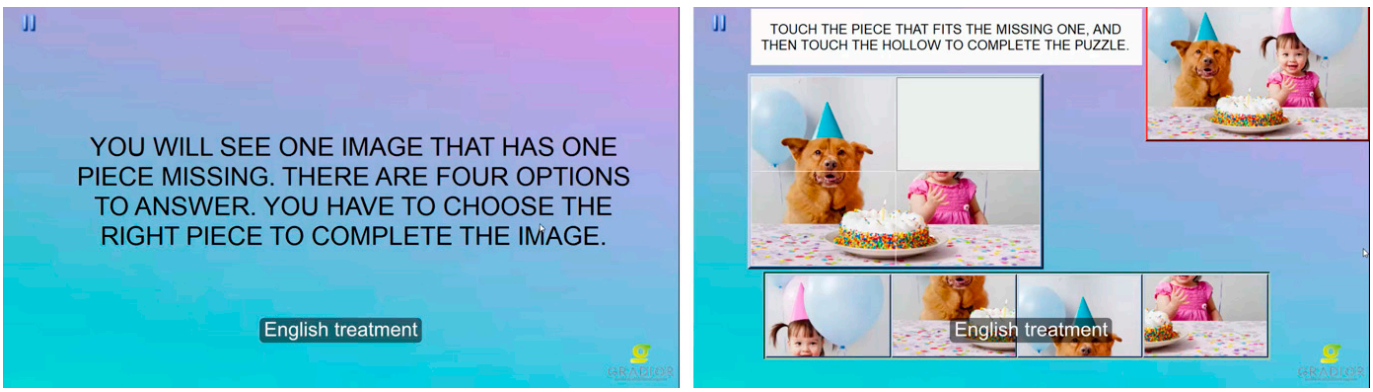

Figure 1. Puzzle exercise. Cognitive modality: executive function. II; software pause.

Table 1. "GRADIOR" computer-based cognitive training (CCT) plan according to modalities and sub-modalities for participants with mild cognitive impairment (MCI) and mild dementia.

Cognitive Function	Mild Dementia	Both	Mild Cognitive Impairment (MCI)
Orientation		Orientation	
Attention		Selective sequential visual	
		Selective visual-simultaneous	
		Vigilance color	
Memory	Span numbers direct	Hearing short term	Word-Word Associative
		Immediate graphic	Associative image-word
		Span numbers inverse	Span direct lyrics
		Location	
		Verbal compound short term	
		Associative face-name	
		Span direct objects	
Executive Function		Puzzles	Numbers and letters
		Keys	Change rules
		Visual inhibition	Ordination stories
		Interference	
Perception	Visual sizes	Graphic colors	Visual figures
	Visual faces	Text colors	
Calculation		Number identification	
		Arithmetic problems	
Reasoning	Sort charts		

To calculate the adherence rate, the number of sessions attended by each person at the CCT during the 4 months was divided by the maximum number of sessions attended, the result was multiplied by one hundred, except for participants who died or dropped out because of medical reasons, for whom the adherence rate was calculated only until the time of drop-out. We consider the cut-off point of 66% for the rate of adherence or therapeutic compliance according to the literature [5,40,41]. Like compliance, persistence or not was considered as a dichotomous variable [42] and was measured taking into account whether or not the person completed the 4 months of intervention, considering the grace period.

2.5. Statistical Analyses

The statistical analysis was performed with the Software Statistical Package for the Social Sciences (SPSS) [43]. We used the punctual biserial correlation to find the degree of association between the dichotomous and dependent variable (adherent and non-adherent) and the quantitative and independent variables (socio-demographic, cognitive, psychological and physical-health). Additionally, the Phi correlation to find the association between dichotomous variables.

The independent variables that were significantly correlated with the dependent variable were taken into consideration as possible predictor variables of adherence and, therefore, were introduced in the analysis with Multiple Logistic Regression. This was used to identify the IVs that helped to predict adherence or not to CCT. We used this analysis because the dependent variable was dichotomous and we had several independent variables, some metric and some qualitative.

Then, we have used a non-parametric analysis for two independent samples (Mann–Whitney) due to the size of the sample and because not all variables followed a normal distribution (Shapiro–Wilk). This analysis allowed us (1) to compare the performance between adherent and non-adherent group, (2) to investigate if there were significant differences between people with MCI and mild dementia in relation to each group (adherent and non-adherent) and, (3) to evaluate if there were significant differences between MCI-adherent vs. MCI-non-adherent and mild dementia-adherent vs. mild dementia-non-adherent with respect to the variables (Digit Symbol and Arithmetic of WAIS-III and LVF-R) that made up the adherence model.

3. Results

3.1. Participant Characteristics

In total, 140 people were contacted to enter the study, and 47 (33.6%) were excluded due to the following reasons: they did not meet the criteria (n = 22) and did not want to participate (n = 25). Additionally, four (2.9%) were not randomized due to the onset of COVID-19. A total of 89 (63.6%) people were randomized. Of these, 57 were assigned to the EG. However, only 75.4% (n = 43) participants managed to initiate the intervention and 24.6% (n = 14) did not start any session due to the start of COVID-19 (Figure 2).

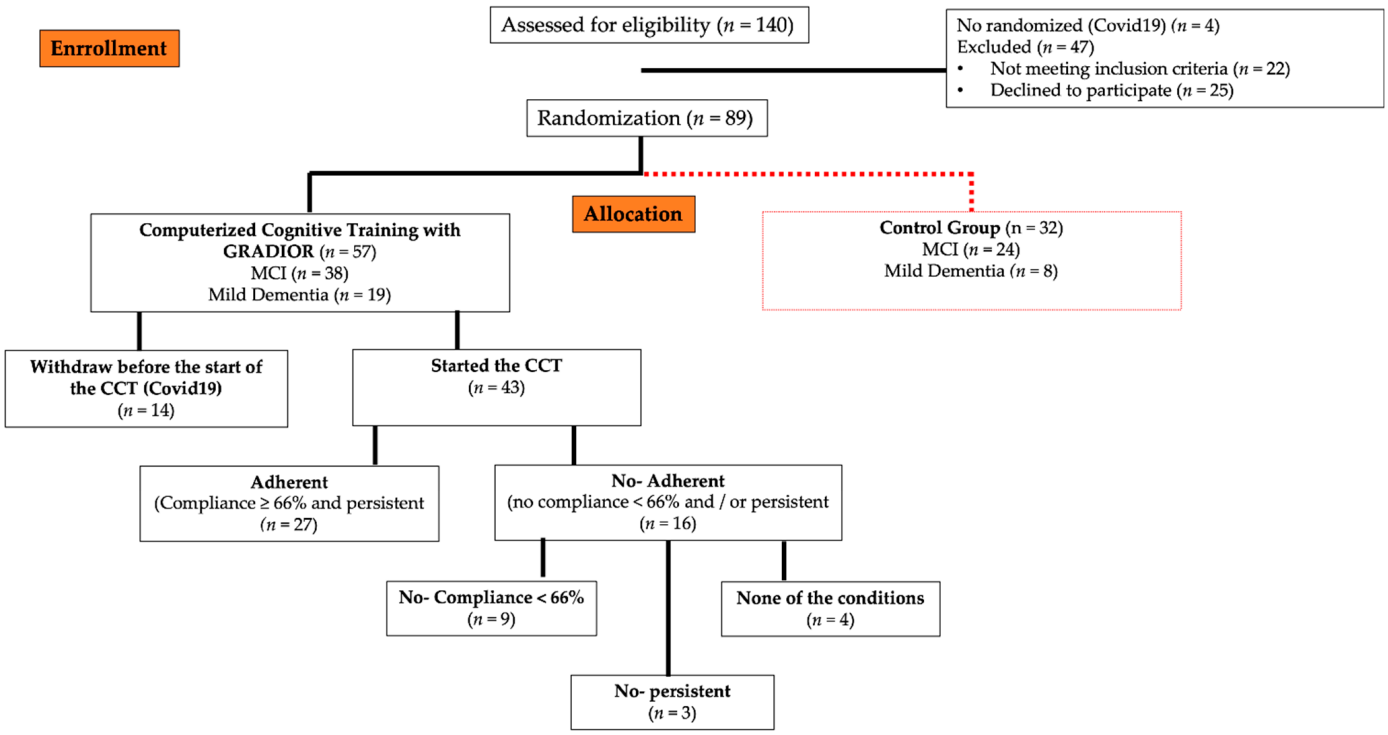

Figure 2. Sample randomization process of randomized clinical trial (RCT). Additionally, conformation of the adherent and non-adherent group in the experimental group (EG). CCT, Computerized cognitive training.

The EG participants were classified into two groups (adherent and non-adherent). Twenty-seven (62.8%) made up the group of adherents. The mean age of this group was 73.6 ± 6.0, and 40.7% were men. The mean years of education were 9.6 ± 2.8. Sixteen (59.3%) participants were diagnosed with MCI and 40.7% (n = 11) with mild dementia. The mean adherence rate of this group was 83.3 ± 8.6. The non-adherent group (n = 16) had a mean of 76.1 ± 7.5 for age and 8.4 ± 1.1 for years of education. Of this group, 37.5% (n = 6) were men, 68.8% (n = 11) were diagnosed with MCI and 31.2% (n = 5) with mild dementia. Additionally, the mean adherence rate was 59.2 ± 16.1. However, there were no significant differences between the two groups (adherent and non-adherent) with respect to age, sex and years of education (Table 2). Of the non-adherent participants, 56% (n = 9) did not comply with 66% of the CCT sessions, 19% (n = 3) were not persistent or dropped-out during the training period (4 months), and 25% (n = 4) did not meet any of the above conditions (Figure 2).

Table 2. Baseline characteristics for the adherent and non-adherent group.

Variable	Sub-Categories	T.Student/ Mann–Whitney/X^2	*p*	*d-cohen*/r_b	Adherent			No-Adherent		
					$\bar{x} \pm$ SD	Number	%	$\bar{x} \pm$ SD	Number	%
Age		−1.185	0.243	−0.374	73.6 ± 6.0			76.1 ± 7.5		
Sex										
	Female	0.044	0.834	0.032		16	61,50%		10	38,50%
	Male					11	64,70%		6	35,30%
Years of education		264.000	0.120	0.222	9.6 ± 2.8			8.4 ± 1.1		
Clinical Group										
	MCI					16	59,30%		11	40,70%
	Mild dementia					11	68,80%		5	31,30%
Adherence Rate					83.3 ± 8.6			59.2 ± 16.1		
MMSE					24.4 ± 2.4			22.6 ± 3.9		
ADAS-Cog: Memory of words					6.1 ± 1.3			6.4 ± 1.5		
ADAS-Cog: word recognition					3.4 ± 1.9			4.6 ± 3.6		
ADAS-Cog: Total					13.7 ± 5.0			17.2 ± 6.7		
TMTA_Mistakes					0.4 ± 0.8			0.4 ± 0.7		
TMTA_Time					12.8 ± 12.0			6.3 ± 2.4		
WAIS-III: Total Digit					10.8 ± 2.6			9.3 ± 2.5		
CAMCOG: Visual Reasoning					2.4 ± 1.4			1.9 ± 1.5		
RBMT: Drawing recognition					7.7 ± 2.2			8.0 ± 2.7		
WAIS-III: Digit Symbol		312.000	0.016 *	**0.444**	10.2 ± 2.7			8.3 ± 2.8		
WAIS-III: Arithmetic		306.500	0.022 *	**0.419**	10.3 ± 2.9			7.7 ± 3.0		
SVF					7.2 ± 3.0			5.6 ± 2.5		
LVF-P					7.7 ± 3.1			6.3 ± 3.2		
LVF-M					8.1 ± 3.8			6.3 ± 3.5		
LVF-R		2.575	0.014 *	**0.812**	8.8 ± 2.5			6.6 ± 3.0		
GDS					4.1 ± 4.0			4.4 ± 2.9		
Health condition					67.0 ± 21.4			76.3 ± 19.6		
Motivation:Attend	Nothing					20	62,50%		12	37,50%
	Somethings					4	66,70%		2	33,30%
	I'm not sure					1	100,00%		0	0,00%
	Quite a lot					2	50,00%		2	50,00%
Expectations: Memory	Nothing					3	60,00%		2	40,00%
	I'm not sure					3	75,00%		1	25,00%
	Quite a lot					13	56,50%		10	43,50%
	A lot					8	72,70%		3	27,30%
Expectations: Quality of life	Nothing					1	33,30%		2	66,70%
	I'm not sure					4	100,00%		0	0,00%
	Quite a lot					14	56,00%		11	44,00%
	A lot					8	72,70%		3	27,30%
Expectations: Free time	I'm not sure					1	100,00%		0	0,00%
	Quite a lot					10	66,70%		5	33,30%
	A lot					16	59,30%		11	40,70%
Expectations: Relating	Nothing					2	100,00%		0	0,00%
	Somethings					2	50,00%		2	50,00%
	I'm not sure					3	100,00%		0	0,00%
	Quite a lot					10	47,60%		11	52,40%
	A lot					10	76,90%		3	23,10%
EQ-5D-5L: Mobility	I have no problem					21	70,00%		9	30,00%
	Minor problems					3	60,00%		2	40,00%
	Moderate problems					2	40,00%		3	60,00%
	serious problems					1	33,30%		2	66,70%
EQ-5D-5L: Self-care	I have no problem					23	63,90%		13	36,10%
	Minor problems					1	33,30%		2	66,70%
	Moderate problems					3	100,00%		0	0,00%
	serious problems					0	0,00%		1	100,00%
EQ-5D-5L: Everyday activities	I have no problem					20	60,60%		13	39,40%
	Minor problems					1	33,30%		2	66,70%
	Moderate problems					5	83,30%		1	16,70%
	serious problems					1	100,00%		0	0,00%
EQ-5D-5L: Pain/discomfort	I have no problem					15	75,00%		5	25,00%
	Minor problems					5	41,70%		7	58,30%
	Moderate problems					3	60,00%		2	40,00%
	serious problems					4	80,00%		1	20,00%
	I can't					0	0,00%		1	100,00%
EQ-5D-5L: Anxiety/depression	I have no problem					18	72,00%		7	28,00%
	Minor problems					2	33,30%		4	66,70%
	Moderate problems					4	57,10%		3	42,90%
	serious problems					2	50,00%		2	50,00%
	I can't					1	100,00%		0	0,00%
Prior use of technology	No					4	66,70%		2	33,30%
	Yes					23	62,20%		14	37,80%

Note: $\bar{x}$, mean; * *p*-value $\leq$ 0.05; CAMCOG, Cambridge Cognition Examination; EQ-5D-5L, EuroQol; GDS, Geriatric Depression Scale; LVF, Lexical Verbal Fluency (forms P, M, R); MCI, mild cognitive impairment; MMSE, Mini-Mental State Examination; RBMT, The Rivermead Behavioural Memory Test; SD, standard deviation; SVF, Semantic Verbal Fluency; TMT, Trail Making Test; WAIS-III, Wechsler Adult Intelligence Scale. Bold Data; significance effect size.

3.2. Adherence Prediction Model to CCT Program

The variables that were directly correlated with the adherent group to the CCT were: Digit Symbol of WAIS-III (p = 0.02), Arithmetic of WAIS-III (p = 0.02) and lexical verbal fluency (LVF)-R (p = 0.03).

These variables were significantly correlated with the dependent variable and were included in a multiple logistic regression model. The final model proposed that the predictors of adherence were associated with performance in Digit Symbol of WAIS-III (OR: 1.06; 95 CI: 0.77–1.47), Arithmetic of WAIS-III (OR: 1.22; 95 CI: 0.90–1.65) and LVF-R (OR: 1.22; 95 CI: 0.91–1.62) (Table 3). Therefore, an increase in performance in these tests predicts an increase in the probability that a person is adherent (compliant and persistent). The adherent group obtained a better performance with moderate-high effect sizes than the non-adherent group in Digit Symbol of WAIS-III (p = 0.016; r_b = 0–444), Arithmetic of WAIS-III (p = 0.022; r_b = 0.419) and LVF-R (p = 0.014; d-cohen = 0.812) (Table 2). The goodness-of-fit p-value of the model was 0.02, with a McFadden R-squared value of 0.174 (Table 3). This model has 90% sensitivity, 50% specificity and 75% precision to correctly identify the adherence group (compliance-persistence). Of the 16 people who were not adherent, the model would only be able to correctly predict 8 subjects.

Table 3. Model of adherence to a CCT program "GRADIOR".

Predictor Variable	McFadden R^2	p-Value	Estimate	Standard Error	OR	z	95% CI
WAIS-III: Digit Symbol	0.174	0.019	0.064	0.164	1.066	0.387	0.773–1.470
WAIS III: Arithmetic			0.203	0.153	1.225	1.329	0.908–1.653
LVF-R			0.200	0.146	1.222	1.368	0.917–1.627

Note: CCT, computer-based cognitive training; CI, confidence interval; LVF-R, Lexical Verbal Fluency; OR, odds ratios; WAIS-III, Wechsler Adult Intelligence Scale.

Regarding the adherent group, there were significant differences with moderate effect sizes between the group of people with MCI and mild dementia with respect to performance in Digit Symbol of WAIS-III (p = 0.010; r_b = −0–591), Arithmetic of WAIS-III (p = 0.005; r_b = −0.642) and LVF-R (p = 0.030; r_b = −0.500). Better performance was seen in people with MCI compared to people with mild dementia (Table 4).

Table 4. Mann–Whitney U test. Comparison between people with MCI and mild dementia in relation to each group (adherent and non-adherent).

Variable	Group	Adherent					No-Adherent				
		Mann–Whitney	p-Value	r_b	N	$\bar{x} \pm$ SD	Mann–Whitney	p-Value	r_b	N	$\bar{x} \pm$ SD
WAIS-III: Digit Symbol	Mild Dementia	36.000	0.010 **	**−0.591**	11	8.7 ± 0.7	11.000	0.065	**−0.600**	5	6.3 ± 1.5
	MCI				16	11.3 ± 0.6				11	9.2 ± 0.6
WAIS III: Arithmetic	Mild Dementia	31.500	0.005 **	**−0.642**	11	8.2 ± 0.7	16.000	0.205	**−0.418**	5	6.4 ± 1.4
	MCI				16	11.7 ± 0.6				11	8.3 ± 0.9
LVF-R	Mild Dementia	44.000	0.030 *	**−0.500**	11	7.5 ± 0.8	10.000	0.052 *	**−0.636**	5	4.2 ± 1.6
	MCI				16	9.7 ± 0.5				11	7.7 ± 0.6

Note: * p-value ≤ 0.05; ** p-value ≤ 0.01; $\bar{x}$, mean; LVF, Lexical Verbal Fluency; r_b, Rank biserial correlation; WAIS-III, Wechsler Adult Intelligence Scale. Bold Data; significance effect size.

On the other hand, we wanted to compare people with MCI-adherents with MCI-non-adherents and the same for people with dementia. Regarding people with MCI, there were low effect sizes between adherents and non-adherents in relation to performance in Digit Symbol and Arithmetic (r_b = −0.358). We observed a better performance of the MCI-adherent group compared to the MCI-non-adherence group. While in the dementia group, there were low–medium effect sizes (r_b = −0.417) for Arithmetic and LVF-R. We found that the mild dementia-adherent group performed better than the mild dementia-non-adherent group (Table 5).

Table 5. Mann–Whitney U test. Comparison between MCI-adherent vs. MCI-non-adherent and mild dementia-adherent vs. dementia-non-adherent.

Variable	Group	Dementia					MCI				
		Mann–Whitney	p	r_b	N	$\bar{x} \pm$ SD	Mann–Whitney	p	r_b	N	$\bar{x} \pm$ SD
WAIS-III: Digit Symbol	No-Adherent	17.500	0.464	−0.271	4	6.6 ± 1.9	52.000	0.137	**−0.358**	9	9.9 ± 0.5
	Adherent				12	8.4 ± 0.7				18	10.7 ± 0.7
WAIS III: Arithmetic	No-Adherent	14.000	0.232	**−0.417**	4	6.0 ± 1.8	52.000	0.139	**−0.358**	9	9.0 ± 0.9
	Adherent				12	8.2 ± 0.6				18	10.9 ± 0.7
LVF-R	No-Adherent	14.000	0.244	**−0.417**	4	4.8 ± 1.9	61.500	0.324	−0.241	9	8.2 ± 0.7
	Adherent				12	7.1 ± 0.9				18	9.2 ± 0.6

Note: $\bar{x}$, mean; LVF, Lexical Verbal Fluency; r_b, Rank biserial correlation; WAIS-III, Wechsler Adult Intelligence Scale. Bold Data; significance effect size.

4. Discussion

It is well known that the recruitment and involvement phase of CCT is the most difficult, due to therapeutic nihilism among families and often general practitioners (GPs), and because of patients' fear of dealing with something new [44]. However, difficulties do not end at the beginning, as patients require motivation to continue the CCT program. In all these stages, we can identify several features that are intrinsic to the person and could intervene and predict adherence to a CCT program. Our purpose was to identify the sociodemographic, cognitive, psychological, and physical-health determinants that helped predict adherence or not to a "GRADIOR" CCT program in people with MCI and mild dementia. It can also be used as guidance to personalize the intervention so that patients might gain more benefits and to improve the sustainability of the care system and take care about the risks of drop-out in specific patients.

4.1. Socio-Demographic Variables and Adherence

We did not find age to be a predictor of adherence to CCT, contrary to some studies such as Maseda et al. [45]. Even so, it is difficult to support that age is the only factor that influences adherence itself, but it is probably associated with other problems or capacities that affect adherence. Indeed, age may also be associated with greater cognitive impairment.

Another sociodemographic factor considered was years of education, and we formally hypothesized that it was going to influence on adherence. However, we did not find any relationship between these variables [14]. In contrast, some studies reported educational level as a predictor of adherence [46,47]. We cannot establish any formal recommendations in this regard since different research conclusions are reached. We consider that future studies should assess this aspect more thoroughly to define its relevance. Moreover, it will probably be necessary to combine educational level with other intellectual activities as reading, work performance, hobbies, etc., to identify the main feature involved in adherence.

As for the variables sex and diagnosis, these were not predictors of adherence. However, it is likely that our results were influenced by the greater number of women and people with MCI that made up our sample. Therefore, it would be interesting for future studies to include more balanced groups in terms of sex and diagnosis to determine their level of influence on adherence.

4.2. Cognitive Profile and Adherence

Different studies support the presence of executive dysfunction associated with alterations in response inhibition and cognitive flexibility in people with MCI [48] and deficits in working memory (WM) [49], inhibition process, sensitivity to interference [50], flexibility and reasoning [51] in people with Alzheimer's. In this order of ideas, our findings indicated how some executive functions (EF) such as attention, WM, numerical reasoning, and verbal fluency, evaluated by Arithmetic, Digit Symbol and LVF-R test are involved in adherence to

a CCT program such as GRADIOR. Additionally, our previous study on the effectiveness of GRADIOR indicated a trend of improvement in these cognitive processes after 4 months of intervention in the EG [21].

Anderson-Hanley, Arciero, Barcelos, Nimon, Rocha, Thurin and Maloney [16] pointed out EF as a motivator of adherence. In turn, poor executive functioning has been identified as an important factor that helps negatively predict the prognosis of dementia [52].

In particular, the role of WM as an adherence factor has been pointed out in studies on the improvement of this cognitive function (WM) after CCT sessions [53,54], while other studies have associated adherence with memory, the latter from a more general level [14,15]. Other studies have pointed out the association between adherence and delayed recall [55]. The functioning of the WM depends on the process of attention for the performance of the tasks associated with the Arithmetic and Digit Symbol scales. In our study, the WM sub-processes involved in performing these tasks were particularly associated with (1) maintaining information for a short time, which allowed for the (2) using, manipulating, or processing of this information. In some cases, this allowed for the activation of more complex cognitive functions such as numerical reasoning (Arithmetic).

It is probable that the attention, maintenance and manipulating of information associated with WM and the phonological verbal fluency are more directly linked to adherence. In fact, there was a significantly better performance at the beginning of the CCT by the adherent group compared to the non-adherent group in these functions. Likewise, when we simplify the comparison by clinical groups, we find that the MCI/dementia adherent group performed better for these functions compared to the MCI/dementia non-adherent group. In accordance with our findings, we suggest paying more attention to those people with a lower cognitive performance in these tests and, therefore, a greater deterioration in these EF, because they may not be as adherent to a CCT program. So, the development of strategies to link and maintain these people in a CCT program will take more effort, from conducting an adequate neuropsychological evaluation to determining the presence and severity of deficits to planning a personalized CCT intervention plan.

4.3. Physical-Health Variables and Adherence

Our findings did not mention any physical-health variable that was able of predicting a person's adherence to a CCT program such as GRADIOR. Most participants agreed that they did not have mobility problems, self-care, ADL, pain and discomfort, anxiety, and depression. Possibly, if we had found greater problems in these dimensions, this could have somehow influenced adherence to the CCT with GRADIOR. However, this did not happen, which could be explained because the sample was made up of people with MCI and mild dementia, and not people in advanced stages of the disease.

In this regard, Tolea et al. [56] pointed out that cognitive deterioration is linked with physical deterioration. In this way, people who progress in their cognitive deterioration also progress in their physical deterioration. These changes can also vary according to the etiology, and per example, people with vascular dementia progress more quickly to physical deterioration than people with Alzheimer's dementia.

Despite our findings, it's necessary that technologies, including CCT programs, should be available and accessible not only in a clinical center, but also at home in order to improve the access people suffering physical limitations to the treatment [57,58].

4.4. Psychological Profile and Adherence

None of the psychological variables (expectations, motivation, and mood) were associated with the CCT adherence. Regarding the initial expectations, the participants agreed that the CCT with GRADIOR would help to improve their memory, quality of life, free time and relating to others. However, our findings did not point to any of these expectations as predictors of adherence. Probably, GRADIOR could help to satisfy these expectations and consequently 62.8% of the participants were adherents (compliant and persistent).

In fact, the users of the "GRADIOR" CCT program improved their social network throughout the sessions. They found it easier to meet and interact with new people because they shared the same needs and interests *"now, I have friends who understand me, and I can have a coffee with them after working with GRADIOR"*. According to the systematic review of Heins et al. [59], interventions with technology have shown to improve the social support network and therefore alleviate feelings of loneliness. Similarly, CCT probably encourages PwD to become active and participate in the group, improving their mood and motivation [38,60,61]. In our study, mood did not help to predict adherent.

Regarding the level of motivation, it did not help to predict adherent. However, we observed that participants did not need external motivation to participate in the RCT. It can be explained by the consent granted by each participant, since this could be a bias of their participation and voluntary commitment.

The questionnaire used to measure expectations, motivation and mood could have been influenced in part by the cognitive impairment in language comprehension commonly associated with people with dementia [62]. Impairment of this cognitive process is usually more evident and significant as dementia progresses, and based on our initial assessment, most people understood the information. Likewise, and with the aim of reducing this problem, the evaluator explained and repeated each of the questions to the participants as many times as necessary. Due to the above, we consider that we tried to reduce biases regarding the understanding of the questions that made up the questionnaire.

4.5. Previous Use of Technology and Adherence

The previous use of computers was not associated with higher probability of initiating CCT, contrary to what was mentioned by Turunen, Hokkanen, Bäckman, Stigsdotter-Neely, Hänninen, Paajanen, Soininen, Kivipelto and Ngandu [14]. Currently, the use of technology is probably more frequent, and it is supposed to rise in the next years. Consequently, no previous experience can be a challenge for the patient, and the excitement of using technology for the first time can balance prior experience with it.

Authors should discuss the results and how they can be interpreted from the perspective of previous studies and of the working hypotheses. The findings and their implications should be discussed in the broadest context possible. Future research directions may also be highlighted.

4.6. Strengths and Limitations

Regarding the limitations of the study, we are aware that the sample was medium. Nevertheless, this problem is representative of most of the studies carried out with CCT [63]. The main reason was the impact of the onset of a COVID-19 pandemic, which led to the end of the selection process and, in general, the RCT, due to wide mobility restrictions and strict confinement for this vulnerable population. However, this RCT methodologically provides the inclusion of older people with cognitive impairment and their participation for 4 months in a CCT, which is important because most of the published studies on CCT in older people contemplate short periods of CCT [64–66]. It makes this study as a good contribution to the clinic field.

Carrying out this study as part of an RCT presented a series of drawbacks in (1) the process of selecting the sample of older people and (2) its maintenance throughout the 4-month CCT. The above is due to different characteristics, which could negatively influence these two scenarios, such as the following: high mortality rate of the sample, mobility alterations, emotional alterations, the stigma of the disease, the start of a pandemic, little financing, and the high cost of resources [21].

On the other hand, we consider that 83.3% to be a high adherence rate for an RCT with the characteristics described and contributes to a little-explored field "adherence to CCT programs". Even so, the results are more likely to be generalized to people with MCI, as only 37.2% of our sample were people with mild dementia. We consider that adherence to psychosocial approaches will be higher in the early stages of dementia and, consequently,

the timely diagnosis of MCI and dementia is strategic for improving the prognosis, quality of life and social health of these people. Indeed, the progression of cognitive impairment leads to fewer resources and less motivation to attend a complex CCT program, even when improvement is predicted [67].

Our study conducted a comprehensive compilation of possible predictors at the person level. Perhaps a variable at the personal level that was not considered in our study was genetics; for example, we know that the APOE-e4 gene is associated with a higher risk of Alzheimer dementia. These types of variables probably exert some influence on the adherence of these people to various treatments, including CCT. Therefore, it would be interesting to develop this type of study.

Orrell, Yates, Leung, Kang, Hoare, Whitaker, Burns, Knapp, Leroi, Moniz-Cook, Pearson, Simpson, Spector, Roberts, Russell, de Waal, Woods and Orgeta [19] suggested contextual variables and person features modify adherence. However, it was not found in our study, but undoubtedly the contexts in which the interventions were carried out could be different and people supporting the intervention could also have different levels of motivation, experience, and skills. All of them could have influenced in the adherence of the participants to the CCT with "GRADIOR". In any case, it should be noted that all the professionals involved received training and support during the entire RCT to maximize adherence.

Our study did not consider usability and user-experience variables associated with the interface of the "GRADIOR" program in adherence because we had previously performed several usability studies [37] and user-experience. Irazoki, Sánchez-Gómez, Contreras-Somoza, Toribio-Guzmán, Martín-Cilleros, Verdugo-Castro, Jenaro-Río and Franco-Martín [39] and Santos Golino and Flores-Mendoza [68] found that the improvement of instructions helped to rise adherence rates in a CCT program for the elderly. Therefore, it would be interesting for future studies to investigate the association between variables such as usability, user-experience and adherence to CCT programs.

4.7. Recommendations and Implications

Our study has a scientific value because it provides a predictive model of adherence based on evidence, indicating several predictive cognitive processes for being considered in the implementation of CCT programs in people with MCI and mild dementia. Adherence to CCT programs is a subject little studied, and most scientific efforts are focused on effectiveness studies [69–72]. In turn, adherence is a factor that helps determine the effectiveness of a CCT program. Consequently, adherence studies are of great interest, and therefore, scientific efforts should also focus on the development of future research that investigates, corroborates and improves the adherent profiles [73].

The lack of and poor adherence to different psychosocial interventions, including CCT programs such as GRADIOR has clinical implications for people with MCI and mild dementia because it could worsen their cognitive impairment and even social and emotional level. Therefore, this study has clinical value because it helps to propose some strategies to increase adherence to treatment:

1. Make an adequate neuropsychological evaluation, focused on processes such as the following: attention, WM, numerical reasoning, phonological verbal fluency, and cognitive flexibility. To identify those people with the greatest commitment of these processes and, therefore, carry out a more personalized accompaniment and increase the probability of adherence to the CCT.
2. Design personalized CCT plans focused on tasks that involve executive functioning training, specifically in attention, WM, number reasoning, phonological verbal fluency, and cognitive flexibility. Additionally, in turn, modify the level of difficulty of each of the tasks associated with each of the cognitive processes, considering the level and cognitive profile of each of the patients. This will prevent the person from getting bored by the ease of the task or frustrated by its difficulty [74]. In this way, it will be possible to increase the degree of adherence.

It would be interesting for future studies to investigate the influence of involving people with cognitive impairment in decision making on their voluntary participation in the GRADIOR CCT and adherence. Decision making is a process that requires functions such as attention and WM, linked to the adherent rate. We know that decision making could be altered, so the inclusion and support of a reference family member in the process was crucial. However, this point deserves to be studied.

Finally, our study has a practical value because it suggests the importance of developing studies that applying user-centered methodological designs for the development of CCT programs, including end users from the initial stages of their development [74]. It will permit to develop of programs that to meet the physical, cognitive, psychological, and social needs and allow a greater adherence of users.

5. Conclusions

Finally, 62.8% of the participants were adherents to the "GRADIOR" CCT program. Likewise, this group had a high adherence rate of 83.3%. Regarding the predictors, the adherence model consisted of three tests (Digit Symbol of WAIS-III, Arithmetic of WAIS-III and LVF-R). This means that good executive functioning associated with attention, WM, numerical reasoning, phonological verbal fluency, and cognitive flexibility helped predict adherence. Thus, people with MCI and mild dementia with worse scores in these cognitive functions should be considered with higher priority to intervene for preventing the drop out from a CCT program. The adherent group performed better than the non-adherent group in these functions.

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Informed Consent Statement: All subjects gave their informed consent for inclusion before they participated in the study.

Data Availability Statement: The raw data will be provided by the main author to whom it is requested.

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Abbreviations

ADASCog	Alzheimer's Disease Assessment Scale—Cognitive Sub-scale
CAMCOG	Cambridge Cognition Examination.
CCT	Computer-based cognitive training.
EQ-5D-5L	EuroQol.
EF	Executive function.
GDS	Yesavage Geriatric Depression Scale.
GPs	General Practitioners.
iCST	Cognitive Stimulation Therapy.
LVF	Lexical Verbal Fluency.
MCI	Mild Cognitive Impairment.
MMSE	Mini-Mental State Exam.
PwD	People with Dementia.
RBMT	Rivermead Behavior Memory Test.
RCT	Randomized clinical trial.
SVF	Semantic Verbal Fluency.
TMT	Trail Making Test form A–B.
WAIS-III	Wechsler Adult Intelligence Scale.
WM	Working Memory

Appendix A

Table A1. Instrument description.

Determinants	Test	Sub-Scale	Measure	Measurement Scale
Cognition	MMSE		GCS	Score: 0–30
	ADAS-Cog		GCS	Score: 0–70.
				70 = Worse or lower cognitive performance
		Memory of words	Memory: Verbal free recall	10 = maximum number of words not remembered
		Word recognition	Memory: verbal recognition	12 = maximum number of words not remembered
	TMT-A	Time	Processing speed	Time (Percentile): 5–95
		Mistakes	EF: Selective-sustained attention. Cognitive flexibility.	Mistakes = 0–4. 4 = Maximum number of mistakes
	WAIS-III	Total Digits	EF: WM. Auditory immediate memory and attention	Scalar score: 1–19
		Digit Symbol	EF: WM and attention	
		Arithmetic	EF: attention. WM. Numerical reasoning	
	CAMCOG	Visual Reasoning	FE: Visual abstract reasoning	Score: 0–6.
				6 = Maximum number of hits
	RBMT	Drawing recognition	Memory: Visual Recognition	Score: 0–10. 10 = Maximum number of hits
	SVF		EF: Fluency, cognitive flexibility, categorization, and monitoring of performance	Scalar score: 2–18
	LVF-P			
	LVF-M			
	LVF-R			

Table A1. *Cont.*

Determinants	Test	Sub-Scale	Measure	Measurement Scale
Psychological	GDS		Depression level	Score: 0–15 points. 15 = maximum symptoms of depression
	Motivation	Attend	Do you need someone to encourage you to attend GRADIOR?	Score: 1–5. 1 = Nothing. 2 = Something. 3 = I am not sure. 4 = Quite a lot. 5 = A lot
	Expectations	Memory	I think GRADIOR will help my memory?	
		Quality of Life	Do I think my quality of life will improve after GRADIOR?	
		Free time	Do I think that the workshop with GRADIOR will occupy my time in a pleasant way?	
		Relating	I would like to meet new people in the workshop with GRADIOR?	
physical health	EQ-5D-5L	Mobility	Subjective perception of mobility problems	Score: 1–5. 1 = I have no problems. 2 = minor problems. 3 = moderate problems. 4 = serious problems. 5 = I cannot
		Self-Care	Subjective perception of problems bathing and dressing	
		Everyday Activities	Subjective perception of problems to perform DLA	
		Pain/Discomfort	Subjective perception of pain or discomfort	
		Anxiety/Depression	Subjective perception of depression or anxiety	
	Health Condition		Subjective perception of general health status	Score: 0–100. 100 = Excellent health
Technology			Prior Use of Technology	1 = yes. 2 = No

Note: ADAS-Cog, Alzheimer's Disease Assessment Scale—Cognitive Sub-scale; CAMCOG, Cambridge Cognition Examination; DLA, daily life activities; EF, Executive Function; EQ-5D-5L, EuroQol; GCS, Global cognitive state; GDS, Geriatric Depression Scale; LVF, Lexical Verbal Fluency (form P, M R); MMSE, Mini-Mental State Examination; RBMT, The Rivermead Behavioural Memory Test; SVF, Semantic Verbal Fluency; TMT, Trail Making Test; WAIS-III, Wechsler Adult Intelligence Scale; WM, Working memory.

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Capítulo 13

Implementación y utilidad del software de estimulación cognitiva basado en computadora GRADIOR

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GRADIOR es un programa de rehabilitación y estimulación cognitiva para personas con DCL y demencia leve. Este capítulo recopila estudios previos y actuales sobre la implementación del programa de ECC GRADIOR en personas con DCL y demencia leve.. **Resultados y discusión:** se han podido identificar aspectos para mejorar la usabilidad y experiencia de usuario de GRADIOR desde sus primeras versiones. Según los últimos estudios, la versión actual de GRADIOR tiene una buena sostenibilidad y aceptabilidad, una acogida positiva por parte de las personas mayores y se considera una herramienta intuitiva y fácil de usar, pero con algunos aspectos a mejorar en cuanto a los ejercicios. Además, los estudios actuales apuntan a una mejora leve en las funciones cognitivas de las personas con deterioro cognitivo leve y demencia leve que asisten a la intervención con GRADIOR después de 12 meses de entrenamiento. Plantea la necesidad de desarrollar ensayos clínicos a largo plazo. GRADIOR tuvo un impacto positivo y significativo en la atención sostenida y el estado de ánimo de las personas en comparación con el grupo de control. Finalmente, un mayor funcionamiento ejecutivo asociado a funciones como la atención, la memoria de trabajo, la fluidez verbal fonológica, el razonamiento numérico y la flexibilidad cognitiva pueden considerarse predictores de una mayor adherencia a GRADIOR.

Palabras clave: demencia; rehabilitación; entrenamiento cognitivo; Deterioro Cognitivo Leve (DCL).

Capítulo V

Discusión

En esta sección se hace referencia a los resultados y se discute sobre los mismos, asociados al compendio de publicaciones. Así mismo, la presente discusión se agrupa de forma general con base en cada uno de los objetivos e hipótesis planteadas. Específicamente entorno a la descripción de GRADIOR, el diseño metodológico de programas de ECC, la efectividad y adherencia de GRADIOR. Los detalles sobre resultados, el tipo de análisis, las tablas, figuras e interpretación de las mismas, podrá ser revisados en la sección IV sobre el compendio de publicaciones.

Somos conscientes del número y variedad de programas de estimulación cognitiva dirigidos a personas con deterioro cognitivo e incluso a personas sanas con el objetivo de preservar o incluso mejorar dicho funcionamiento, cada uno cuenta con unas particularidades, pero comparten el objetivo de estimular la cognición (Irazoki et al., 2020). Sin embargo, estos no dejan de ser una herramienta más para la rehabilitación cognitiva. El clínico se beneficiará de su uso, pero este deberá ser cauteloso en elegir un programa que se ajuste al paciente, los programas varían desde su forma de acceso hasta el tipo de ejercicios que incluyen y no siempre el paciente se adapta al mismo, esto va a depender no solo de las características del programa, sino también de las características propias del individuo en cuanto a sus aspectos físicos, cognitivos, psicológicos, etc.

GRADIOR

GRADIOR ha sido considerado un programa de rehabilitación cognitiva, porque permite la evaluación y la estimulación. Es un programa que ha venido evolucionando a lo largo del tiempo y, por tanto, generando adaptaciones del mismo a las necesidades de la población y las circunstancias ambientales. Creado por clínicos, lo que garantiza que sus requisitos funcionales y no funcionales sean precisos para las personas objetivo y por informáticos que han instaurado los requisitos estructurales (Diaz-Baquero et al., in press). Se ha implementado para el mantenimiento cognitivo en diferentes patologías de tipo neurológico y psiquiátrico, pero especialmente en personas con DCL y demencia leve.

GRADIOR cuenta con interfaces (Franco-Martin et al., 2020), tales como: a) *la Gestión Clínica*, el terapeuta tiene acceso desde esta función a los usuarios y detalles específicos; b) *Gestión de Historia Clínica*, esta sección presenta los datos sociodemográficos, una observación clínica asociada al diagnóstico, enfermedades, antecedentes, medicación y, resultados de las evaluaciones clínicas y/o cognitivas; c) *Gestión del tratamiento*, en esta sección el terapeuta podrá diseñar el plan de tratamiento acorde con el proceso cognitivo a entrenar, el nivel de dificultad y la duración del mismo; d) *Administración de informes*, en esta sección se podrá obtener informes del rendimiento del paciente por modalidad, sub-modalidad, nivel e incluso por sesiones.

Con el fin de crear una intervención cognitiva con GRADIOR, será necesario: una valoración inicial neuropsicológica con el objetivo de establecer una línea base con el uso de un plan de tratamiento estándar en GRADIOR. De esta forma, se podrá diseñar el plan de entrenamiento cognitivo personalizado con GRADIOR teniendo en cuenta el tipo y nivel cognitivo del paciente, es decir, adaptando el plan de intervención de acuerdo con el rendimiento del paciente (ej.. cada mes).

Son varios los estudios sobre la usabilidad de GRADIOR y experiencia del usuario (Diaz-Baquero et al., in press). Cada uno de estos estudios ha aportado puntos claves para introducir y mejorar las versiones posteriores de GRADIOR. De acuerdo con el estudio de usabilidad de Fumero Vargas et al. (2009), se enlistaron una serie de mejoras a la versión previa de GRADIOR, recomendaciones que fueron subsanadas e incorporadas a la versión 4. Franco-Martín et al. (2011) y Góngora Alonso et al. (2020) mencionaron aspectos claves de la usabilidad de GRADIOR 4: el grado de aceptación, la inclusión de sesiones claras y compresibles y, la satisfacción de expectativas.

Posteriormente, se desarrolló un estudio en el que se combinó GRADIOR con un programa físico (Long Lasting Memories Program) y se evaluó la usabilidad con base en 5 dimensiones, dando como resultado: a) una evaluación afectiva positiva (González-Palau et al., 2013); b) una usabilidad del 87% (Góngora Alonso et al., 2019) con una facilidad de uso para el 60,1% de personas con DCL (González-Palau et al., 2013); c) un buen nivel de

satisfacción de los usuarios por sus beneficios y el cumplimiento de expectativas, d) un marcado interés por continuar el uso con GRADIOR y e) el aumento de una red social (Fumero Vargas et al., 2009).

Más recientemente, Irazoki et al. (2021) desarrollaron un estudio con grupos focales a partir del cual evaluaron la usabilidad de la versión 4.5 de GRADIOR, el cual fue considerado divertido, entretenido, satisfactorio y beneficioso, con una interfaz atractiva aunque con requerimiento de un periodo de familiarización y adaptación con el programa, y como un programa con ejercicios intuitivos y con diferentes niveles de dificultad. Este estudio también señaló puntos de mejora, tales como: evitar las interferencias, proporcionar mensajes de retroalimentación más positivos, crear un acceso fácil y, eliminar la barrera tecnológica y su alcance a contextos rurales. Así mismo, los profesionales consideraron que era una herramienta atractiva y moderna, pero sobre todo beneficiosa para alivianar la labor del mismo. Por tanto, para el desarrollo, implementación y evaluación de estos programas e incluso para los registros electrónicos, se debería tomar en consideración la participación del profesional (Shiells et al., 2020; Shiells et al., in press)

En resumen, GRADIOR cuenta con una gran usabilidad y esto lo convierte en un programa de fácil uso en personas con DCL y demencia leve (Diaz-Baquero et al., in press). Este sea quizás uno de los elementos más importantes cuando hablamos de un programa de ECC. Sin embargo, existen otros elementos para considerar cuando analizamos un programa de este tipo, los cuales serán vistos a continuación.

Diseño Metodológico en el desarrollo de programas de ECC

En los últimos años y desde un enfoque psicosocial se ha venido desarrollando programas de ECC, para el mantenimiento y mejora del funcionamiento cognitivo en personas con distintas patologías neurológicas. Pero cuántos de esos programas están creados o desarrollados con y para personas con DCL y demencia leve, es decir programas diseñados y centrados en el usuario y, por tanto, cuántos de estos programas incluyen estudios sobre

su desarrollo. Por lo anterior, uno de los objetivos (Artículo 2) fue identificar el diseño y método aplicado en el desarrollo de estos programas de ECC (Diaz Baquero et al., 2021).

Tras la búsqueda de bibliografía, 13 estudios fueron identificados, los cuales describieron 11 programas diferentes de ECC (Artículo 2). Los estudios incluidos fueron elegidos si incluían a personas con DCL o demencia leve. Esto plantea un punto importante que merece ser discutido a la luz de un DCU porque si tratamos de comparar entre los programas incluidos en esta revisión sistemática (artículo 2) y los existentes actualmente en el mercado, llegaremos a la conclusión de que algunos de estos programas deberán considerarse con cautela acerca de si son o no eficientes para usarlos con personas con DCL y demencia leve. Con el objetivo de describir el diseño metodológico aplicado en el desarrollo de estos programas, se tuvo en cuenta los criterios propuestos por la ISO9241-210 (2019). Estos, son criterios que proveen un marco de referencia objetivo para el desarrollo de programas usables y eficientes. A continuación, se discutirá brevemente los hallazgos encontrados respecto a cada uno de estos criterios.

Entender y especificar el contexto.

Conocer las características y necesidades de los usuarios finales y el ambiente en el que se aplicaría el programa a partir de una revisión bibliográfica o la observación fue algo que se incluyó desde cada uno de los estudios citados y elegidos en el artículo 2. Una fase importante porque permite más tarde una mayor adopción del programa por parte de personas con DCL y demencia leve.

Especificar los requerimientos de usuario

Para cumplir con este criterio, el uso de una metodología cualitativa (entrevistas, cuestionarios y/o observación) y el diseño de un pre-prototipo ayudó a explicar los requerimientos de usuario. En esta fase se incluyó al usuario final para proponer los requerimientos del usuario desde la relación entre experiencia de usuario y tecnología. Este

criterio fue cumplido por la mitad de los estudios incluidos (54.5%) (Diaz Baquero et al., 2021). Los cuales indicaron en primera instancia algunos de los criterios que sirvieron para plantear dichos requisitos, tales como: el conocimiento y uso previo de tecnología, las dificultades físicas y motoras que influirían en la asistencia presencial a sesiones de entrenamiento (Scase et al., 2018; Scase et al., 2017), y las alteraciones cognitivas (Banovic et al., 2018).

A estos criterios, los programas de ECC incluidos en el artículo 2, propusieron y tomaron en consideración los siguientes requerimientos de usuario, tales como: incluir ejercicios con un nivel de dificultad moderado, que oscile entre lo fácil (Benveniste et al., 2010) y lo difícil (Scase et al., 2017), modificar la intensidad del tratamiento respecto al rendimiento del usuario (Han et al., 2014), la inclusión de un feedback en tiempo real con el objetivo de que el usuario pueda darse cuenta de sus errores y tenga la oportunidad de corregirlos (Haesner et al., 2014), la presencia de validez ecológica en los ejercicios con el fin de que estos se transfieran a la vida diaria y real del usuario (Diaz Baquero, 2019a) y, el diseño de interfaces intuitivas, gráficas, simples, familiares (Benveniste et al., 2010) y atractivas (Haesner et al., 2014).

En este orden de ideas, para proponer los requerimientos de usuario se parte de las necesidades, estas corresponden con las características a nivel psicológico, cognitivo, físico y social (Martin et al., 2018). A pesar de la importancia de este criterio para establecer interfaces que se ajusten a personas con DCL y demencia leve (Toribio-Guzmán et al., 2019; van der Ploeg et al., 2016), el articulo 2 estableció que el 45.5% de los estudios omitieron este criterio (Diaz Baquero et al., 2021). Probablemente omitir este criterio podría suponer costes futuros, quizás porque las personas no se adaptarían al mismo y, por tanto, los cambios serían inevitables.

Desarrollo y Evaluación del programa

Se encontró que la mayoría de los estudios evaluaron aspectos de usabilidad y experiencia de usuario asociados a los programas de ECC (artículo 2). La usabilidad se asoció con la

familiaridad y facilidad de uso. Por lo que, los programas de ECC incluyeron un sistema de navegación con pantalla portátil, lo cual ayudo a subsanar en algunos casos la falta de habilidades con el uso de tecnología. La inclusión de un lenguaje claro y sencillo (Tziraki et al., 2017), el diseño gráfico de la interfaz (Haesner et al., 2015), la facilidad de uso y velocidad del programa (Han et al., 2014).

Con respecto a la experiencia de usuario, los programas DOREMI project (Scase et al., 2018; Scase et al., 2017), WoZ Interface (Dethlefs et al., 2017), y X-top (Ben-Sadoun et al., 2016) resultaron ser muy interesantes y satisfactorios para las personas con DCL y demencia leve. También, los usuarios resaltaron los beneficios obtenidos por el uso de estos programas (Boulay et al., 2011; Dethlefs et al., 2017; Haesner et al., 2015; Han et al., 2014; Otsuka et al., 2015; Peeters et al., 2016; Scase et al., 2018; Scase et al., 2017), aspecto que resultó clave y motivante para continuar con el uso de los mismos.

No obstante, la experiencia del usuario puede están influenciada por otros factores independientes del dispositivo tecnológico, como por ejemplo, el nivel de deterioro cognitivo (Peeters et al., 2016), esto significa que, si una persona presenta un marcado deterioro cognitivo, podría encontrar difícil el uso de estos programas y por tanto, esta experiencia negativa se reflejaría.

Alcance y limitaciones

En resumen, el diseño mayormente empleado por los estudios incluidos en el artículo 2 fue un DCU y aunque, no todos cumplieron con los criterios propuestos por la ISO9241-210 (2019), cada criterio presentó su importancia. Definir el *contexto de uso* ayudará a tener claro hacia qué y dónde se dirige el desarrollo del programa, establecer los *requerimientos de usuario* con su participación provee información cualitativa relevante para su *desarrollo*. Incluir evaluaciones de usabilidad y experiencia de usuario en la *evaluación final* del programa añade un gran valor sobre el nivel de adaptación del usuario, su perspectiva y experiencia.

Aun así, se puede observar un vacío de estudios que detallen el diseño metodológico del desarrollo de los programas de ECC y su aplicabilidad sobre personas con demencia; por tanto, muchos programas de ECC usados en la actualidad no fueron incluidos en esta revisión. En este orden de ideas, esta revisión sistemática tiene un valor científico porque muestra la evidencia y, por tanto, la necesidad de ampliar con estudios que presenten e incluyan el desarrollo de programas de ECC aplicado en personas con DCL y demencia leve, los cuales, brindarían información sobre el uso y aplicabilidad de cada programa de ECC.

Igualmente, presenta un valor práctico para los desarrolladores, proporcionando un análisis desde los diferentes estándares que podrían ser aplicados y tomados en consideración para el desarrollo de programas de ECC desde un DCU y, por tanto, disminuir los costes futuros con respecto a la adaptabilidad en personas con DCL y demencia leve.

Por último, esta revisión sistemática representa un valor para el campo clínico, específicamente para el campo de la neuropsicología, debido a que se podrá disponer de programas más usables y efectivos para mantener y/o retrasar el deterioro cognitivo y, sobre todo, programas dirigidos específicamente para personas con DCL y demencia leve. Así mismo, el clínico deberá preguntarse lo siguiente cuando desee implementar un programa de ECC con personas con MCI y demencia leve:

- ¿Es este programa adecuado para personas con MCI y demencia leve?
- ¿Han incluido a los usuarios finales desde las etapas primarias de desarrollo del programa?
- ¿Existe un diseño metodológico sobre el desarrollo del programa de ECC?
- El programa, ¿toma en consideración las necesidades de las personas con MCI y demencia leve?
- ¿Qué tal es la usabilidad, experiencia de usuario y efectividad del programa?

Tomando en consideración estos interrogantes, el clínico podría tener una base sólida sobre el uso, adaptabilidad y eficiencia del programa de ECC para personas con MCI y demencia leve.

Efectividad de GRADIOR. Un programa de entrenamiento cognitivo en personas con DCL y demencia.

Varios son los estudios de usabilidad y experiencia de usuarios con GRADIOR a lo largo de estos años. También, son bastantes los estudios, cuyo objetivo ha sido evaluar la efectividad de programas de ECC. Sin embrago, son poco los que han incluido periodos largos de entrenamiento con personas con DCL y demencia leve. Por tanto, se desarrolló un ECA (artículo 3) que fuera capaz de ayudar a evidenciar si el programa de entrenamiento cognitivo GRADIOR era efectivo para ayudar a mantener y/o mejorar procesos cognitivos y/o el estado emocional en esta población a lo largo de 12 meses de tratamiento (Diaz Baquero, Franco Martín, et al., 2022). A continuación, se señala y discute los hallazgos más importantes por cada uno de los dominios cognitivos. Para ampliar los hallazgos (ver artículo 3):

Razonamiento visual: fue considerada como una de las funciones con mayor variabilidad con respecto a los grupos y el tiempo. Los hallazgos mostraron que el desempeño al inicio en ambos grupos fue similar, quizás esto se puede atribuir al nivel educativo. Así mismo, esta función puede ser considerada compleja y, por tanto, con la edad se puede deteriorar aun cuando no referenciemos a personas con DCL y demencia leve. No obstante, GRADIOR ayudó a mejorar levemente el rendimiento a los 4 meses en el GE *(d = -0.172)*, siendo evidente el empeoramiento del GC *(d = 0.500)* a los 12 meses. Y, siendo explicito y diferencial como las personas con DCL del GE presentaron más probabilidad de mejorar levemente esta función a lo largo del tiempo en comparación con personas con demencia leve del GE y con personas del GC ($F = 2.753$; $p = 0.08$; $\eta 2 = 0.030$). Las personas que asistieron a GRADIOR entrenaron esta función por medio de

ejercicios de Puzzles mientras que las personas del GC no realizaron ningún tipo de estimulación para esta función.

Por tanto, el tipo de función cognitiva (ej. Razonamiento visual), el tiempo del entrenamiento (12 meses) y el diagnóstico (DCL vs Demencia leve) podrían ser factores que ayuden a determinar la efectividad de un programa de ECC como GRADIOR. Es decir, no solo son las variables asociadas al programa lo que determina su efectividad, sino también lo son las variables individuales y, por tanto, la combinación de estas.

Atención sostenida y velocidad de procesamiento: Se observó una interacción con tamaños del efecto importantes, las personas que asistieron a las sesiones de entrenamiento con GRADIOR presentaron una baja velocidad de procesamiento ($F = 0.908$; $p = 0.41$; $\eta 2 = 0.019$), acompañada de un buen rendimiento a nivel de atención sostenida durante la realización del TMTA a los 4 meses ($F = 1.641$; $p = 0.21$; $\eta 2 = 0.021$) en comparación con el GC, aunque con el tiempo, se observó una muy leve tendencia de mejora en velocidad de procesamiento (Shatil, 2013) y un mantenimiento de la atención en el GE. Es decir, para estas personas fue más importante centrar su atención teniendo especial cuidado en desarrollar la tarea, aunque esto implicará realizarlo lentamente. Por tanto, las personas que realizaron entrenamiento con GRADIOR presentaron una tendencia de mejora en el proceso de atención sostenida (Flak et al., 2019; González-Palau et al., 2014; Hagovská et al., 2017)

Así mismo, la leve mejora de la velocidad de procesamiento hacia los 12 meses podría estar asociado al incremento de la interacción social tras la finalización de cada una de las sesiones (Djabelkhir et al., 2017). No obstante, esto aún merece estudio. Aunque, es un hecho que la asistencia a programas de ECC ayuda a incrementar la interacción social (Góngora Alonso et al., 2019; Pinto-Bruno et al., 2017).

Atención dividida: A diferencia de la atención sostenida, la atención dividida mostró una leve tendencia de mejora tras 12 meses de entrenamiento cognitivo en personas con DCL y demencia leve del GE en comparación con el GC ($F = 1.731$; $p = 0.20$; $\eta 2 =$

0.068). Realizar la tarea de atención dividida a partir del TMTB incluye sub-procesos como la conciencia del error y la capacidad para solucionarlo. Estos procesos probablemente fueron mejorados gracias al feedback, que incluyó GRADIOR durante la realización de cada ejercicio (Adcock et al., 2020; Franco-Martin et al., 2020). Elemento que logró influir en el desarrollo del TMTA (descrito anteriormente).

Fluidez verbal semántica y fonológica: sólo se observó una tendencia de mantenimiento y leve mejora para FVS a los 4 meses (d = –0.273) y FVL-P a los 12 meses en el GE (d = –0.489). Las tareas de FVS representan una menor complejidad en comparación con las tareas de FVL, estas últimas incluyen la evocación de palabras que inician por un sonido y no una categoría como en tareas de FVS. Así, cuando hablamos de entrenamiento cognitivo, este debe ser progresivo desde funciones básicas a complejas y, por tanto, la mejora también será progresiva.
No se observó, diferencias o interacciones entre grupos y tiempo y, tampoco con respecto al diagnóstico. Aun cuando existen estudios que indican como esta función se encuentra mayormente comprometida en personas con demencia (Laisney et al., 2009).

Cálculo y razonamiento numérico: ambos grupos mostraron una preservación de esta función al inicio del ECA. Probablemente, esto se debió a algunas actividades de la vida diaria que contribuyen con su mantenimiento, por ej. Hacer la compra. No obstante, el GE y GC (d = 0.636; d = 0.583, respectivamente) disminuyeron su rendimiento a los 12 meses en comparación con los 4 meses (intragrupo). Probablemente, GRADIOR no ayudo a mantener esta función aun cuando el plan de entrenamiento incluyó ejercicios de cálculo. También, es probable que las personas mayores fallaran en esta tarea por tiempo, teniendo en cuenta que la velocidad de procesamiento fue baja en el TMT.

Memoria de trabajo (MT): Esta función se mostró preservada desde el inicio del ECA. No obstante, las personas que asistieron a GRADIOR mostraron un casi mantenimiento a una muy leve tendencia de mejoría en esta función evaluada por WAIS-III Dígito-símbolo (d= -0.200) después de 12 meses de intervención en comparación con los 4 meses (intra-grupo). Mientras el GC disminuyó su rendimiento a los 12 meses (WAIS-III

dígitos-símbolos: d = 0.200) (intra-grupo) (Hyer et al., 2016; Vermeij et al., 2016; Yang et al., 2019). Un programa de entrenamiento cognitivo deberá abarcar no solo las funciones cognitivas que muestran alguna alteración, sino también aquellas que están preservadas con el objetivo de evitar su declive, resultado que podría verse conforme avanza el deterioro. Lo anterior resulta importante y explica la involución del rendimiento vista en el GC.

Visocontructiva: Al inicio, ambos grupos mostraron un rendimiento similar. Pero lo que más resulto atractivo fue la existencia de una interacción significativa. GRADIOR ayudo a que las personas con DCL y demencia leve del GE mantuvieron su rendimiento a los 12 meses con respecto a los 4 meses y al GC ($F = 3.455$; $p = 0.04$*; $\eta 2 = 0.033$). Este último mostró una disminución en su rendimiento.

La mayoría de los cambios mencionados hasta el momento corresponden con el mantenimiento del rendimiento a lo largo del tiempo en personas que asistieron al entrenamiento con GRADIOR y en algunos casos unas tendencias leves de mejoría.
No podemos esperar cambios a gran escala con el uso de programas de ECC y teniendo en cuenta la naturaleza de progresión del deterioro en personas con demencia, pero sí que esperamos que el rendimiento cognitivo se mantenga en el tiempo y, por tanto, haya un retraso de dicho deterioro cognitivo. Al igual que otras herramientas de tipo psicosocial creadas para tal fin.

Estado de ánimo. Depresión: GRADIOR contribuyó a que las personas del GE mejoraran su sintomatología depresiva tras finalizar el tratamiento en comparación con el GC ($F = 3.414$; $p = 0.04$; $\eta 2 = 0.041$) (García-Casal et al., 2017; González-Palau et al., 2014). Asistir a las sesiones con GRADIOR no solo implicó realizar entrenamiento cognitivo, sino también implicó hacer algo diferente, nuevo y de aprendizaje y, por tanto, conocer personas con las mismas necesidades (Irazoki et al., 2021). Lo que ayudó a mejorar su estado de ánimo que en ocasiones es fruto de la soledad y de un ambiente poco estimulado.

Alcance de un ECA para el estudio de la efectividad de un programa de ECC

Hasta aquí, la efectividad de GRADIOR ha sido descrita y sustentada. A nivel general, se encontró algunos cambios positivos en las funciones cognitivas y el estado de ánimo para el GE en comparación con el GC a los 4 y 12 meses (Hipótesis 3.1.2). También, se encontraron cambios a los 4 meses con respecto a la línea base, pero estos fueron menos representativos y visibles que los cambios hacia los 12 meses de tratamiento para el GE (Hipótesis 3.2.2), también se evidenció para este periodo diferencias entre los dos grupos (GE Y GC), debido a que el GC disminuyó su rendimiento en la mayoría de las escalas en comparación con el GE (Hipótesis 3.2.3), este último se mantuvo y/o presentó una tendencia leve de mejoría (Hipótesis 3.2.2 y 3.3.2) y se encontró diferencias sobre el rendimiento entre personas con DCL-GE, demencia leve-GE, DCL-GC y demencia leve-GC a lo largo del tiempo (Hipótesis 3.4.2).

Hasta ahora, las mayoría de los ECAs sólo incluían periodos de menos de 6 meses (Bahar-Fuchs et al., 2017; Gates et al., 2019; Lee et al., 2018). Estos hallazgos ponen de manifiesto la importancia de implementar programas con largos periodos de ECC para observar los cambios a lo largo del tiempo y a su vez, el mantenimiento de las funciones cognitivas y el estado emocional. Lo anterior no solo aplicado al campo de la investigación, sino también al campo clínico. La demencia es una enfermedad neurodegenerativa y, por tanto, su naturaleza es avanzar hacia un deterioro cada vez mayor, por lo que, incluir un programa de entrenamiento largo será más eficaz que uno corto, con el que quizás sólo se alcancen cambios superficiales y poco duraderos.

Es importante concientizarnos sobre el alcance de estos programas de ECC sobre el funcionamiento cognitivo y emocional de las personas mayores con DCL y demencia leve. Las sesiones con ECC ofrecieron tendencias leves de mejoría y perfiles conservadores con respecto a las funciones cognitivas y el estado emocional. Quizás no podamos hablar de cambios a gran escala, pero sí que podemos defender el objetivo de prever el

mantenimiento de las funciones cognitivas y el estado emocional, lo que se opone al declive rápido y progresivo en esta población.

No obstante, diversos factores (Diaz Baquero, Franco Martín, et al., 2022) podrán influir de manera negativa para conseguir un objetivo tan ambicioso como este, pero necesario para definir la efectividad de estos programas de ECC de forma más fiable. En este orden de ideas, uno de los factores fue de tipo ambiental, el inicio del COVID19 resultó ser una situación que influyó negativamente sobre el mantenimiento de la muestra total, debido a que muchos centros sociosanitarios debieron cerrar para reducir el contagio y aunque, se logró implementar el uso del programa a través de Tablet en algunos casos, en otros tantos y casi en la gran mayoría, no se pudo implementar debido a problemas de conexión y accesibilidad. Por lo que se recomienda que futuras investigaciones y centros dedicados a la atención y cuidado de personas mayores implementen el uso de Tablet o dispositivos portátiles para crear un acceso fácil al programa de ECC y busquen soluciones a los problemas de conexión o de acceso a internet con el objetivo de llegar a la población objetivo y en estado de vulnerabilidad, es decir a personas con pocos recursos y/o con ubicación en el área rural.

Este ECA involucro la colaboración de diferentes centros, clínicas de memoria, residencias, etc. Contó con la ayuda de profesional cualificado para llevar a cabo evaluaciones e intervenciones. Y con una coordinación y sincronización de tareas y actividades para la consecución de objetivos, siendo esta visible, estricta y mantenida. Futuros estudios podrán tomar en consideración estos puntos para recolectar una mayor muestra y de esta forma, la perdida de participantes no influiría sobre el tamaño final de la muestra. No obstante, estos puntos involucran un coste elevado que no se puede hacer frente si no se tiene fuentes de financiación y recursos humanos suficientes.

Esta tesis doctoral partió de un proyecto Europeo Marie Curie (INDUCT) y desde este se propuso no sólo un periodo de entrenamiento de 12 meses, sino también un periodo de seguimiento. Para esta tesis doctoral, no se incluyó los resultados de este periodo de seguimiento, debido a que estos serán analizados y publicados próximamente. Pero es

relevante mencionar este aspecto, porque esta ECA no sólo mencionaría los cambios dentro de esos 12 meses, sino también aquellos durante el periodo de seguimiento y que son interesantes para saber si las personas que asistieron a este ECC mantuvieron su rendimiento o, por el contrario, declinó, y si declina de qué forma lo hacen con respecto al GC.

También, crear planes de entrenamiento personalizado a las características cognitivas (tipo y nivel de deterioro) del paciente (Diaz Baquero et al., 2021) promueve la satisfacción y un mayor grado de implicación, motivación (Toribio Guzmán et al., 2017) y una mejora sobre el funcionamiento cognitivo. El entrenamiento cognitivo tanto desde una metodología de lápiz y papel y, una desde programas de EEC promueve el mantenimiento y/o la mejora de las funciones cognitivas en personas con DCL y demencia leve. No obstante, los programas de ECC exigen cierto tipo de manejo con respecto a la tecnología, por lo que talleres sobre alfabetización tecnológica para personas mayores serán muy interesantes (Martins Van Jaarsveld, 2020).

Por último, consideramos que el ECC es beneficioso, pero existen otro tipo de intervenciones como la reminiscencia o programas de entrenamiento físico o social que podría complementar muy bien al ECC y generar resultados positivos y prometedores a nivel multidominio. Por lo que se espera que futuros estudios indaguen sobre la eficacia de la combinación de diferentes intervenciones sobre el funcionamiento cognitivo y emocional de las personas mayores.

Adherencia a GRADIOR

Los estudios sobre efectividad no son suficientes cuando tratamos de evaluar programas de ECC. Por lo que estudios sobre adherencia representan un complemento para ayudar a mostrar la tasa de adherencia y los factores (sociodemográficos, cognitivos, psicológicos y físicos) que contribuyen a que las personas con DCL y demencia leve sean adherente o no a un programa de ECC. Quizás una persona inicia el entrenamiento, pero no lo termina, o lo

intenta terminar de forma discontinua y/o usando parámetros diferentes a los propuestos inicialmente. Identificar estos factores que contribuyen a que una persona sea o no adherente permitirá tomar medidas preventivas para lograr una mayor adherencia y en efecto, una mayor efectividad en futuros estudios.

El artículo 4 mostró que el 62.8% de las personas con DCL y demencia leve fueron adherente. Este mismo grupo mostró una tasa representativa de adherencia del 83.3% (Hipótesis 4.1.2.) (Diaz Baquero, Perea Bartolomé, et al., 2022). La adherencia es mayor en las primeras etapas de la demencia, debido a que la progresión del deterioro cognitivo conduce a menos recursos y motivación para ser parte de un entrenamiento cognitivo (Choi & Twamley, 2013). Probablemente sea esta una de las razones por la cual tuvimos un buen porcentaje de personas que fueron adherentes. Futuros estudios deberían estudiar esto mismo con personas con demencia moderada a grave.

Con respecto a las variables sociodemográficas, algunos estudios han encontrado la edad como un predictor de la adherencia (Maseda et al., 2013). Aunque no fue el caso en nuestro estudio. Al igual que la edad, los años de educación no predijeron la adherencia (Turunen et al., 2019) contrario a algunos estudios (Bagwell & West, 2008; Shatil, 2013). El sexo y diagnóstico tampoco correspondieron con factores de adherencia, quizás esto se deba a que la mayoría de la muestra estuvo compuesta por mujeres y personas con DCL, lo que no nos permitió tener unos grupos más homogéneos con respecto a estas variables.

No se halló factores físicos que ayudaran a determinar la adherencia o no a un programa de ECC. Nuestros participantes no mostraron ningún problema físico que les impidiera ir al entrenamiento, probablemente se deba a que el deterioro cognitivo era leve para estas personas. Tolea et al. (2016) mencionó que el deterioro físico está relacionado con el deterioro cognitivo. Aunque nuestra población no mostró graves problemas físicos, no olvidemos que podría ser un factor importante que impidiera asistir presencialmente a sesiones, por lo que, la accesibilidad a estos programas de ECC deberá ser posible desde casa (Blackwood et al., 2016; Gigler et al., 2013).

El modelo de adherencia (Artículo 4) no estuvo conformador por ninguna variable psicológica (expectativas, motivación y/o estado de ánimo). Aunque algunos estudios mencionan una mejoría en el estado de ánimo y motivación en personas que han participado del ECC (Franco Martín et al., 2002; Góngora Alonso et al., 2019; Pinto-Bruno et al., 2017). El uso previo de ordenador tampoco resultó ser un factor que ayudara a determinar la adherencia o no a un programa de ECC. Este hallazgo fue contrario a lo propuesto por Turunen et al. (2019).

Las funciones ejecutivas tales como la atención, MT, el razonamiento numérico y la fluidez verbal evaluadas por las escalas de Aritmética, Dígito-Símbolo del WAIS-III y Fluidez verbal lexical-R conformaron el modelo de adherencia que ayudó a predecir que una persona fuera o no adherente a un programa de ECC como GRADIOR (Diaz Baquero, Perea Bartolomé, et al., 2022). Las funciones ejecutivas (Anderson-Hanley et al., 2014) y la MT (Hyer et al., 2016; Vermeij et al., 2016) han sido señaladas como factores de adherencia. La atención como función necesaria durante tareas de MT para seleccionar la información relevante que será retenida en dicha memoria mientras se usa o manipula para un objetivo concreto, por ejemplo, para solucionar un problema matemático (escala de Aritmética del WAIS-III).

En el artículo 4, se comparó el rendimiento cognitivo asociado a las escalas mencionadas entre grupo adherente y no adherente, encontrando: a) El grupo adherente tuvo un mejor rendimiento respecto al grupo no adherente al inicio del ECA en cada una de las escalas mencionadas (Hipótesis 4.2.2), b) se comprobó la Hipótesis 4.3.2., debido a que hubo evidencia para afirmar que las personas con DCL adherentes obtuvieron un mejor rendimiento que las personas con demencia leve adherentes y c) el grupo con DCL y demencia leve adherente tuvo un mejor desempeño en estas funciones con respecto al grupo no adherente (Hipótesis 4.4.2 y 4.4.4).

Alcance y limitaciones

La falta o poca adherencia de las personas con DCL y demencia leve a intervenciones psicosociales, tales como el ECC conlleva una serie de implicaciones clínicas para estas personas debido a que podrían empeorar su estado cognitivo influyendo en otras áreas, y a su vez, la incidencia aumentaría. Por lo tanto, el desarrollo de estrategias y la creación de planes de entrenamiento cognitivo personalizado que se focalicen especialmente pero no de forma única en estas funciones (propuestas en el modelo de adherencia) ayudará a ejercer una mayor influencia para vincular y mantener a personas con DCL y demencia leve. Lo que constituirá un valor práctico en el campo clínico.

Como lo hemos mencionado, son pocos los estudios de adherencia a programas de ECC y son más representativos aquellos asociados al campo de la farmacología. También la deserción de personas a estos programas de ECC es común, por lo que el desarrollo de estudios desde esta perspectiva producirá gran valor y aporte científico. Consideramos que este estudio aporta un definición, operacionalización y aplicabilidad solida sobre el concepto de adherencia, aun así, valdría la pena continuar redefiniendo y clarificando el concepto de adherencia desde un enfoque psicosocial.

Con respecto al alcance, el artículo 4 incluyó diferentes tipos de variables de estudio a nivel personal. Sin embargo, variables genéticas e incluso variables contextuales (Orrell et al., 2017), tales como: el contexto de intervención y la cualificación de los profesionales para realizar evaluaciones e intervenciones, podrían ser variables asociadas con la adherencia. Y aunque contamos con estudios de usabilidad (Franco-Martín et al., 2011) y experiencia de usuario sobre GRADIOR (Santos Golino & Flores-Mendoza, 2016), resultaría interesante que futuros estudios asocien factores de usabilidad y experiencia de usuario con la adherencia a GRADIOR y otros programas.

Así mismo, es un estudio en el que quizás la muestra fue pequeña, por lo que futuros estudios podrían ampliarla con el objetivo de obtener resultados que puedan ser generalizables a la población.

Capítulo VI

Conclusiones

Respecto al objetivo 1, describir el desarrollo de la última versión del programa de rehabilitación cognitiva basado en computadora GRADIOR en personas con DCL y demencia leve ha llevado a las siguientes conclusiones:

1. GRADIOR es un programa de rehabilitación cognitiva y ha sido desarrollado por profesionales clínicos, quienes propusieron una serie de requisitos no funcionales con el fin de que GRADIOR resultará más amigable para las personas con deterioro y facilitará al trabajo a los profesionales. También ha sido diseñado por informáticos, quienes se han encargado de plantear requisitos tecnológicos y de implementación (Objetivo 1.1).
2. GRADIOR incluye diversas interfaces y cada una presenta una funcionalidad: la Gestión Clínica, Gestión de Historia Clínica, Gestión del tratamiento, Administración de informes (Objetivo 1.2).
3. Se han realizado diferentes estudios de usabilidad acerca de GRADIOR, realizándose los respectivos cambios o modificaciones señaladas por versiones posteriores. El estudio más reciente indicó algunos puntos clave a mejorar, tales como: interferencias, retroalimentación positiva, acceso fácil y aplicación en contextos rurales (Objetivo 1.3).

Con relación al objetivo 2 sobre identificar el diseño metodológico aplicado en el desarrollo de programas de entrenamiento cognitivo computarizado para la rehabilitación del funcionamiento cognitivo en personas con DCL y demencia leve. Y teniendo en cuenta los objetivos específicos, se llegó a las siguientes conclusiones:

1. Tomando como referencia la variedad de programas de ECC que se emplean con personas con DCL y demencia leve en la actualidad. Son pocos los estudios sobre desarrollo (11 programas) en lo que se incluyeron a estas personas. En otros casos, se incluyeron otras etiologías (15.4%). Lo cual permite considerar su uso para ese tipo de población. No obstante, el 53.9% de los estudios incluyeron a personas con DCL y el 30.8% trabajaron con personas con demencia leve. Por otra parte, el 30.8% de los estudios informaron abandonos, con tasas que oscilaron entre el 26% y el 40%.

La edad estuvo comprendida entre 50-88 años para personas con DCL y demencia leve y, 60-85 años para personas sanas. Para el reclutamiento de la población, este se llevó a cabo en hospitales, residencias y centros de día (Objetivo 2.1).

2. Tan sólo se identificó 13 estudios correspondientes a 11 programas de ECC que emplearon un diseño metodológico centrado en el usuario para el diseño y desarrollo de estos en personas con DCL y demencia leve. Los estudios incluidos en esta revisión sistemática especificaron el contexto de uso, fase previa a la especificación de los requerimientos de usuario. En cuya fase, el 54.5% de los estudios usaron un pre-prototipo con el objetivo de identificar estos requerimientos. Una vez desarrollado el prototipo, este fue evaluado a partir de criterios de usabilidad en siete estudios y de experiencia de usuario en diez de los estudios incluidos (Objetivo 2.2).

Con respecto al objetivo 3 de evaluar la efectividad del programa ECC GRADIOR sobre la cognición y la situación afectivo-emocional en personas con DCL y demencia leve a los 4 y 12 meses de tratamiento. Se llegó a las siguientes conclusiones por cada una de las hipótesis planteadas:

1. Se identificaron diferencias entre GE y GC durante T1 y también durante T2 (Objetivo 3.1 / Hipótesis 3.1.2.). Con respecto al GE, este tuvo un mejor desempeño en comparación con el GC en razonamiento visual a los 4 meses y en memoria por reconocimiento visual a los 12 meses. Contrario a lo que ocurrió con TMTB-tiempo, Aritmética del WAIS-III a los 4 meses y Dígitos-Símbolos a los 12 meses. Es probable que el GC hubiese tenido un mejor rendimiento con respecto al GE para alguna condición, pero esto no quiere decir que GRADIOR no sea efectivo. La efectividad se observó tras el tiempo de intervención y/o cuando comparamos el rendimiento entre los 4 y 12 meses.
2. En cuanto a los cambios observados entre línea base y los 4 meses para GE, destacamos una leve tendencia de mejoría de GE a los 4 meses, para: razonamiento visual, FVS, y atención sostenida (Objetivo 3.2 / Hipótesis 3.2.2). No obstante, también se identificaron algunas mejoras en el GC.
3. También, hubo una leve tendencia de mejoría para el GE a los 12 meses con respecto

a los 4 meses en razonamiento visual, MT, atención dividida, reconocimiento visual, FVL-P, velocidad de procesamiento y síntomas depresivos (Objetivo 3.2 / Hipótesis 3.2.2). Se evidenció un decremento mucho más marcado por parte del GC en la mayoría de las escalas (Objetivo 3.2 / Hipótesis 3.2.3). Por tanto, resultó interesante ver una tendencia marcada de mejoría en el GE en comparación con el GC a los 12 meses en contraste con los 4 meses.

4. Hubo una leve mejoría para el GE en su atención sostenida y sintomatología depresiva a los 12 meses en comparación con los 4 meses y el GC (Objetivo 3.3 / Hipótesis 3.3.2).
5. También hubo un mantenimiento significativo en la habilidad viso constructivo ($F = 3.455$; $p = 0.04$*; $\eta 2 = 0.033$) y una leve tendencia de mejoría en atención dividida ($F = 1.731$; $p = 0.20$; $\eta 2 = 0.068$) en personas con DCL y demencia leve del GE a los 12 meses en comparación con personas con DCL y demencia leve del GC, respectivamente. Estos últimos presentaron un decremento de estas funciones. Por otra parte, personas con DCL del GE mejoraron levemente en razonamiento visual a los 12 meses en comparación con personas con demencia leve del GE y del GC ($F = 2.753$; $p = 0.08$; $\eta 2 = 0.030$) (Objetivo 3.4 / Hipótesis 3.4.2).

Respecto al modelo sobre los determinantes a nivel sociodemográfico, cognitivo, psicológico y físico que ayudan a predecir o no la adherencia a un programa de ECC GRADIOR en personas con DCL y demencia leve (Objetivo 4) y tomando en cuenta las hipótesis planteadas para este objetivo. Concluimos que:

1. El 62.8% de los participantes del ECA fueron adherentes a GRADIOR y estos presentaron una tasa de adherencia del 83.3%. La literatura señala como punto de corte el 66% para considerar una persona adherente o no (Coley et al., 2019; Heesch et al., 2003; Sjösten et al., 2007). Por lo tanto, la tasa de adherencia a GRADIOR fue alta y representativa (Hipótesis 4.1.2).
2. El modelo de adherencia estuvo constituido por Dígitos-Símbolos y Aritmética del WAIS-III y, FVL-R y tuvo una sensibilidad del 90%, una especificidad del 50% y una precisión del 75% para identificar correctamente al grupo adherente. Las

personas adherentes presentaron un mejor rendimiento con respecto al grupo no-adherente en estas escalas, presentando tamaños del efecto moderados-altos con significancia en Dígitos y símbolos del WAIS-III ($p = 0.016$; $rb = 0.444$), Aritmética del WAIS-III ($p = 0.022$; $rb = 0.419$) y FVL-R ($p = 0.014$; d-cohen = 0.812) (Hipótesis 4.2.2). Probablemente el buen rendimiento estuvo asociado con que la persona deseará participar y ser adherente a un programa de ECC.

3. Las personas con DCL-adherente obtuvieron un mejor rendimiento en las escalas (Dígitos Símbolos del WAIS-III: $p = 0.010$; $rb = -0.591$; Aritmética del WAIS-III: $p = 0.005$; $rb = -0.642$; y FVL-R: $p = 0.030$; $rb = -0.500$) que conformaron el modelo de adherencia en comparación con las personas con demencia leve adherentes. (Hipótesis 4.3.2). Esto significo que las personas con DCL-adherentes tuvieron mejor rendimiento en atención, MT, razonamiento numérico y fluidez verbal.
4. El grupo adherente diagnosticado con DCL obtuvo una tendencia de mejoría en su desempeño en Dígitos-símbolos y Aritmética WAIS ($rb = -0.358$, respectivamente) en comparación con el grupo no adherente. Así mismo, el grupo adherente con diagnóstico de demencia leve presentó una tendencia de mejoría en su desempeño en las escalas Aritmética y FVL-R ($rb = -0,417$, respectivamente) en comparación con el grupo no adherente (Hipótesis 4.4.2 / 4.4.4).

Por último, con respecto al objetivo de recopilar estudios previos y actuales sobre la implementación de GRADIOR en personas con DCL y demencia leve (Capítulo 13), concluimos que:

- Los estudios señalan que GRADIOR tiene una adecuada usabilidad y experiencia de usuario. Este fue considerado intuitivo y fácil de usar para personas con DCL. Los usuarios y profesionales presentaron una experiencia positiva. Sin embargo, el acceso al programa debe mejorarse mediante la participación de usuario en el programa. En términos de eficacia y efectividad, GRADIOR mostró mejores resultados a los 12 meses. Por lo tanto, se recomienda proporcionar este tipo de tratamientos durante mucho tiempo. Los determinantes de la adherencia a GRADIOR fueron el buen funcionamiento ejecutivo asociado a funciones como

atención, memoria de trabajo, fluidez verbal fonológica, razonamiento numérico y flexibilidad cognitiva (Objetivo 5).

Conclusions

Regarding objective 1, describing the development of the latest version of the GRADIOR computer-based cognitive rehabilitation program in people with MCI and mild dementia has led to the following conclusions:

1. GRADIOR is a cognitive rehabilitation program and has been developed by clinical professionals, who proposed a series of non-functional requirements in order to make GRADIOR more friendly for people with impairments and will make work easier for professionals. It has also been designed by computer scientists, who have been in charge of proposing technological and implementation requirements (Objective 1.1).
2. GRADIOR includes various interfaces and each one has a functionality: Clinical Management, Clinical History Management, Treatment Management, Report Management (Objective 1.2).
3. Different usability studies have been carried out on GRADIOR, making the respective changes or modifications indicated by later versions. The most recent study indicated some key points to improve, such as: interference, positive feedback, easy access, and application in rural contexts (Objective 1.3).

In relation to the objective 2 about identifying the methodological design applied in the development of CCT programs for the rehabilitation of cognitive functioning in people with MCI and mild dementia. And considering the specific objectives, the following conclusions were reached:

1. Taking as reference the variety of CCT programs currently being used with people with MCI and mild dementia. There are few studies on development (11 programs) in which only these people were included. In other cases, in which other etiologies were included (15.4%). This allows us to consider its use for this type of population. However, 53.9% of the studies included people with MCI and 30.8% worked with people with mild dementia. Furthermore, 30.8% of studies reported dropouts, with

rates ranging from 26% to 40%. The age was between 50-88 years for people with MCI and mild dementia and 60-85 years for healthy people. For the recruitment of the population, this was carried out in hospitals, residences, and day centers (Objective 2.1).

2. Only 13 studies were identified corresponding to 11 CCT programs that used a user-centered methodological design for the design and development of these, in people with MCI and mild dementia. The studies included in this systematic review specified the context of use, phase prior to the specification of user requirements. In which phase, 54.5% of the studies used a pre-prototype to identify these requirements. Once the prototype was developed, it was evaluated based on usability criteria in seven studies and user experience in ten of the included studies (Objective 2.2).

Regarding the objective 3 of evaluating the effectiveness of the GRADIOR CCT program on cognition and the affective-emotional situation in people with MCI and mild dementia at 4 and 12 months of treatment. The following conclusions were reached for each of the hypotheses:

1. Differences between EG and control group (CG) were identified during T1 and during T2 (Objective 3.1 / Hypothesis 3.1.2.). Regarding the EG, it performed better than the CG in visual reasoning at 4 months and in visual recognition at 12 months. Contrary to what happened with TMTB-time, WAIS-III Arithmetic at 4 months and Digits and Symbols at 12 months. It is probable that the CG would have performed better than the EG for some conditions, but this does not mean that GRADIOR is not effective. The effectiveness was observed after the intervention time and/or when we compared the performance between 4 and 12 months.
2. Regarding the changes observed between baseline-4 months for EG, we highlight a slight trend of improvement in EG at 4 months, for: visual reasoning, semantic verbal fluency (SVF), and sustained attention (Objective 3.2 / Hypothesis 3.2.2). However, some improvements were also identified in the CG.
3. Also, there was a slight trend of improvement for the EG at 12 months compared to 4 months in visual reasoning, WM, divided attention, visual recognition, lexical

verbal fluency (LVF), processing speed, and depressive symptoms (Objective 3.2 / Hypothesis 3.2.2). We evidence a much more marked decrease on the part of the CG in most of the scales (Objective 3.2 / Hypothesis 3.2.3). So, it is interesting to see a marked trend of improvement in the EG compared to the CG at 12 months in contrast to 4 months.

4. There was a slight improvement for the EG in their sustained attention and depressive symptomatology at 12 months compared to 4 months and the CG (Objective 3.3 / Hypothesis 3.3.2).
5. There was also significant maintenance of visuo-constructive ability ($F = 3.455$; $p = 0.04$*; $\eta 2 = 0.033$) and a slight trend of improvement in divided attention ($F = 1.731$; $p = 0.20$; $\eta 2 = 0.068$) in people with MCI and mild dementia of EG at 12 months compared with people with MCI and mild dementia of CG, respectively. The latter presented a decrease in their functions. On the other hand, people with MCI from the EG slight improved in visual reasoning at 12 months compared to people with mild dementia from the EG and the CG ($F = 2.753$; $p = 0.08$; $\eta 2 = 0.030$) (Objective 3.4 / Hypothesis 3.4.2).

Lastly, and regarding the model on sociodemographic, cognitive, psychological, and physical determinants that help predict or not adherence to a GRADIOR CCT program in people with MCI and mild dementia (Objective 4) and taking into account the hypotheses raised for this purpose. We conclude that:

1. A total of 62.8% of the RCT participants were adherent to GRADIOR and these presented an adherence rate of 83.3%. The literature indicates 66% as a cut-off point to consider a person adherent or not (Coley et al., 2019; Heesch et al., 2003; Sjösten et al., 2007). Therefore, the rate of adherence to GRADIOR was high and representative (hypothesis 4.1.2).
2. The adherence model consisted of Digits-Symbols and Arithmetic of WAIS-III and LVF-R and had a sensitivity of 90%, a specificity of 50% and an accuracy of 75% to correctly identify the adherent group. The adherent people presented a better performance with respect to the non-adherent group in these scales, presenting

moderate-high effect sizes with significance in WAIS-III Digits and Symbols (p = 0.016*; rb = 0.444), WAIS-III Arithmetic (p = 0.022*; rb = 0.419) and FVL-R (p = 0.014*; d-cohen = 0.812) (Hypothesis 4.2.2). Good performance was probably associated with the person wanting to participate and adhere to an CCT program.

3. People with MCI-adherent had better performance on the scales (WAIS-III Digit Symbols: p = 0.010; rb = −0.591; WAIS-III Arithmetic: p = 0.005; rb = −0.642; and FVL-R: p = 0.030; rb = −0.500) that conformed the adherence model compared to people with mild dementia-adherent. (Hypothesis 4.3.2). This meant that people with MCI-adherent had better performance in attention, WM, numerical reasoning, and verbal fluency.
4. The adherent group diagnosed with MCI obtained a trend of improvement in their performance in Digits-symbols and WAIS Arithmetic (rb = −0.358, respectively) compared to the non-adherent group. Likewise, the adherent group with a diagnosis of mild dementia showed a trend of improvement in their performance on the Arithmetic and FVL-R scales (rb = −0.417, respectively) compared to the non-adherent group (Hypothesis 4.4.2 / 4.4.4).

Finally, regarding the objective of collecting previous and future studies on the implementation of GRADIOR in people with MCI and mild dementia (Chapter 13), we conclude that:

- The studies pointed out that GRADIOR have adequate usability and user experience. This was considered intuitive and easy to use for people with MCI. Users and professionals presented a positive experience. However, access to the program should be improved through user participation in the program. In terms of efficacy and effectiveness, GRADIOR showed better results at 12 months. Therefore, it is recommended to provide this type of treatment for a long time. The determinants of adherence to GRADIOR were good executive functioning associated with functions such as attention, WM, phonological verbal fluency, numerical reasoning, and cognitive flexibility (Objective 5)

Abreviaturas

CAMCOG, Cambridge Cognition Examination;

CCT, Computerized cognitive training;

CG, Control Group;

DCL, Deterioro Cognitivo Leve;

DCU, Diseño centrado en el usuario;

DOREMI, Decrease of cOgnitive decline, malnutRition, and sedEntariness by elderly empowerment in lifestyle Management and social Inclusion;

ECA, Ensayo clínico aleatorizado;

ECC, Entrenamiento cognitivo computarizado;

EG, Experimental Group;

EQ-5D-5L, EuroQol;

FVL, Fluidez Verbal Lexical;

FVS, Fluidez verbal semántica;

GC, Grupo control;

GDS, Yesavage Geriatric Depression Scale;

GE, Grupo experimental;

LVF, Lexical verbal Fluency;

MCI, Mild cognitive impairment;

MMSE, Mini mental state examination;

MT, Memoria de trabajo;

SVF, Semantic verbal Fluency;

RBMT, Rivermead Behavior Memory Test;

USMART, The Ubiquitous Spaced Retrieval-based Memory Advancement and Rehabilitation Training;

TMT, Trail Making Test form A–B;

WAIS-III, Wechsler Adult Intelligence Scale;

WM, Working memory;

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ANEXOS

Todos los anexos asociados a esta tesis doctoral han sido publicados en páginas web. Por lo tanto, para la versión impresa y digital de esta tesis doctoral, serán visibles de forma parcial. No obstante, estos podrán ser visualizados de forma completa a través de los links.

ANEXO 1

Disponible en:

Staff perspectives on the usability of electronic patient records for planning and delivering dementia care in nursing homes: a multiple case study. https://doi.org/10.1186/s12911-020-01160-8

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BMC Medical Informatics and Decision Making

RESEARCH ARTICLE Open Access

Staff perspectives on the usability of electronic patient records for planning and delivering dementia care in nursing homes: a multiple case study

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Abstract

Background: The electronic patient record (EPR) has been introduced into nursing homes in order to facilitate documentation practices such as assessment and care planning, which play an integral role in the provision of dementia care. However, little is known about how the EPR facilitates or hinders these practices from the end-user's perspective. Therefore, the objective of this qualitative study was to explore the usability issues associated with the EPR for assessment and care planning for people with dementia in nursing homes from a staff perspective.

Methods: An exploratory, qualitative research design with a multiple case study approach was used. Contextual Inquiry was carried out with a variety of staff members ($n = 21$) who used the EPR in three nursing homes situated in Belgium, Czech Republic and Spain. Thematic analysis was used to code interview data, with codes then sorted into a priori components of the Health Information Technology Evaluation Framework: device, software functionality, organisational support. Two additional themes, structure and content, were also added.

Results: Staff provided numerous examples of the ways in which EPR systems are facilitating and hindering assessment and care planning under each component, particularly for people with dementia, who may have more complex needs in comparison to other residents. The way in which EPR systems were not customisable was a common theme across all three homes. A comparison of organisational policies and practices revealed the importance of training, system support, and access, which may be linked with the successful adoption of the EPR system in nursing homes.

Conclusions: EPR systems introduced into the nursing home environment should be customisable and reflect best practice guidelines for dementia care, which may lead to improved outcomes and quality of life for people with dementia living in nursing homes. All levels of nursing home staff should be consulted during the development, implementation and evaluation of EPR systems as part of an iterative, user-centred design process.

Keywords: Assessment, Dementia, Care plan, Electronic health records, Electronic patient records, Nursing home

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Background

Nursing homes currently face a multitude of pressures, such as difficulties in recruiting staff, high employee turnover and low staff morale [1]. Added to these pressures is a growing demand for documentation, which has come about from 'increasing regulatory scrutiny' [2]. Two of the principal nursing processes which are required to be documented and regularly updated are assessment and care planning. Assessment involves 'the gathering of data relating to a person's physical, psychological, and social status' [3] and may take place in a direct or proxy manner, where information is gathered from family members or by observing individuals. Assessment is often a time-consuming process for staff and can be a stressful activity for the individual, particularly those with dementia [3]. However, it is an important first step in the nursing process, establishing a 'baseline against which changes can be measured for clinical purposes' [4]. Furthermore, assessment provides a core set of information from which to identify personalised interventions that maximise an individual's functionality, so that quality of life can be maintained [4]. These interventions form part of an individual's care plan [5].

Care plans have been described as 'prescriptions for nursing care' [6] and act as a reference for nurses to facilitate continuity of care [7]. Furthermore, care plans are often used to provide evidence of the quality of care which has been delivered [8], in this way, protecting staff in case of complaints [7]. An essential element of the care plan is that it should be personalised to reflect the individual [9]. In addition to containing information about a person's physical care needs, care plans should also be developed with an individual's life history in mind, ensuring that care provided is in line with previous lifestyles and routines, which helps to maintain identity and personhood [10]. Care planning plays an important role in the provision of care for people with dementia [11], specifically in nursing homes where, for example, in the United Kingdom, approximately 70% of residents will have a diagnosis of dementia [12].

Defined as an application incorporating 'the clinical data repository, clinical decision support, controlled medical vocabulary, order entry, computerized provider order entry, pharmacy, and clinical documentation applications' [13], the electronic patient record (EPR), was introduced to assist with documentation processes such as assessment and care planning. For nursing homes, the EPR has the potential to reduce administrative burdens [14], improve the quality of documentation [15], as well as allow for the identification of care needs [15] and management of long-term conditions more effectively [16]. If EPR systems are interoperable, data can also be shared across healthcare providers [17]. With demands for documentation alleviated, staff potentially have more time to spend with residents providing direct care [18]. The EPR may be particularly valuable for providing care for people with dementia, as it may allow access to detailed background information at the point of care when, for instance, staff may require more information about the cause of an individual's behaviour [19].

Despite the potential benefits associated with this technology, the EPR has been described as a burden by nursing home staff, which has been linked with issues associated with its usability [20, 21]. In this study, the ISO definition of usability as 'the extent to which a product can be used by specified users to achieve specified goals with effectiveness, efficiency and satisfaction in a specified context of use' [22] is adopted. General usability issues associated with the EPR in nursing homes commonly identified in the literature include: separate software programmes for various nursing documentation, which is inefficient [23]; use of incorrect nursing terminology in drop-down menus or templates [8, 24]; lack of space for free data entry [23, 25]; missing forms, meaning paper forms continue to be used [25, 26]; slow log-in processes [27]; and lack of interoperability [23].

The persistent usability issues associated with the EPR in nursing homes highlight the need for a participatory design and evaluation process, where end users' feedback is gathered as part of an iterative cycle and systems are tailored to their needs [28, 29]. However, previous studies investigating the EPR specifically for care planning in nursing homes have used audit methods to examine the quality and completeness of electronic care plans [8, 30–32], with no input from end users. Problems of usability have also been linked with a lack of consideration of the context in which the EPR is implemented, which has resulted in 'clashes between the model of health care work inscribed in these tools with the actual nature of work' [33]. Therefore, through a qualitative lens, this study aims to address the following question: what are the usability issues associated with the EPR for assessment and care planning for people with dementia in nursing homes?

Methods

Study design

The study is underpinned by the socio-technical systems theory, which has been suggested as an appropriate framework with which to evaluate Health Information Technology (HIT) such as the EPR [33–35]. This paradigm states that 'organisational and human (socio) factors and information technology system factors (technical) are inter-related parts of one system, each shaping the other' [36]. In order to explore these factors, a case study design was selected, which enables the researcher to examine a phenomenon within its natural setting [37, 38]. Furthermore, a multiple case study

ANEXO 2

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Contents

Chapter 1 INTRODUCTION

Technology and dementia

Though the evidence is still limited, policy-makers, care professionals and researchers often see technology applications as promising solutions to promote independence and autonomy in people with dementia.

Technologies are increasingly vital in today's activities in homes and communities. Nevertheless, little attention has been given to the consequences of the increasing complexity and reliance on them, for example at home, in shops, traffic situations, meaningful activities and health care services. The users' ability to manage products and services has been largely neglected or taken for granted. People with dementia often do not use the available technology because it does not match their needs and capacities.

The rapid growth of the technological landscape and related new services have the potential to improve the overall effectiveness and cost-effectiveness of health and social services and facilitate social participation and engagement in activities. But which technology is effective and how is this evaluated best?

Successful implementation of technology in dementia care depends not merely on its effectiveness but also on other facilitating or impeding factors on a micro, meso and macro level, related to e.g. the personal living environment (privacy, autonomy and obtrusiveness); the outside world (stigma and human contact); design (personalisability, affordability and safety), and ethics on these subjects.

Best Practice Guidance Human interaction with technology in dementia

This Best Practice Guidance results from the literature and field research conducted within the INDUCT project (2016-2020), a Marie Sklodowska Curie funded Innovative Training Network, which focused on technology for people with dementia in three areas (everyday life, meaningful activities and healthcare). The main aim was to develop a multi-disciplinary, intersectorial educational research framework for Europe to improve technology and care for people with dementia, and to provide the evidence to show how technology can improve the lives of people with dementia.

In the update of the Best Practice Guidance of December 2021 the first recommendations of a second Marie Sklodowska Curie funded Innovative Training Network on Technology and dementia, called DISTINCT (2019-2023) are included. The main aim of this second ITN is to provide the evidence to show how technology can improve the social health of people living with dementia by enabling them to 1) fulfil their potential on a societal level, 2) manage their own life and 3) participate in social and meaningful activities,

Regarding the research, both the INDUCT and the DISTINCT network had (have) three main objectives:

- Identifying practical, cognitive & social factors that improve the usability of technology for people with dementia;

- Evaluating the effectiveness of specific contemporary technology; and

- Tracing facilitators & barriers for implementation of technology in dementia care.

The recommendations for improving the usability, effectiveness and implementation of technology in dementia which are presented in this Best Practice Guidance are meant to be helpful for different target groups: people with dementia, their formal and informal carers, policymakers, designers and researchers. For this reason representatives of these target groups were consulted and involved throughout the INDUCT and DISTINCT project.

Patient and Public Involvement in INDUCT [by Kate Shiells]

The importance of Patient and Public Involvement (PPI) in dementia research has been highlighted at a European level by Alzheimer's Europe as a way in which to enhance the 'transparency, validity and legitimacy' of research (Gove et al., 2017). PPI has been embedded throughout the INDUCT project. For instance, INDUCT was initially conceived following consultations with people with dementia and carers, who highlighted the need for the development of effective, user-friendly technologies that meet their needs in a range of environments. In addition, via Alzheimer's Europe the European Working Group of People with Dementia (EWGPWD) was consulted and provided feedback with strong support for the proposal. Since taking up their posts across Europe, Early Stage Researchers (ESRs) have then continued to involve people with dementia, their formal or informal carers and other relevant stakeholders throughout the research cycle. In particular, the European Working Group of People with Dementia (EWGPWD) has been crucial in the design, dissemination and implementation of projects. Members were present at INDUCT schools in the first and second year, where they advised ESRs on how to engage and recruit people with dementia in research, for example, by using dementia-friendly language in information sheets and consent forms. A subsequent meeting was arranged with the EWGPWD in the third year of the project to share preliminary results and gather their ideas on how best to implement and disseminate findings to appropriate stakeholders.

There are also numerous specific examples of stakeholder engagement activities within each individual project, which have assisted ESRs to develop their recommendations according to each of the three INDUCT objectives. For instance, ESR 1 conducted PPI groups with people with dementia and their carers to elicit their views on empowerment in relation to surveillance technologies, using results to form recommendations on the effectiveness of this technology (Objective 4). ESRs 3 and 4 shared data from their research on the characteristics of Everyday Technologies and the interplay with participation in public space with a PPI group of people with dementia who provided alternative interpretations of the data, leading to recommendations on the usability and implementation of these technologies (resp.Objective 3 and 5). ESR 6 carried out consultations with a PPI group, exploring their opinions of four art applications. This resulted in the selection of two art applications to be used in the proof-of-principle study, examining the barriers and facilitators of implementing digital art in touchscreen devices in nursing homes (Objective 5). Finally, second-level partners in industry have also provided valuable PPI input. For example, ESR 7 collaborated with SilverFit in the Netherlands, a company producing innovative technology to improve elderly care, who provided insight into the implementation of exergaming systems, leading to a publication on the 'do's and don'ts of exergaming for people living with dementia' (Objective 5).

Reference

Dianne Gove, Ana Diaz-Ponce, Jean Georges, Esme Moniz-Cook, Gail Mountain, Rabih Chattat, Laila Øksnebjerg & The European Working Group of People with Dementia (2017): Alzheimer Europe's position on involving people with dementia in research through PPI (patient and public involvement), Aging & Mental Health, DOI: 10.1080/13607863.2017.1317334

Promoting Social health by means of enabling technology: an Occupational therapy perspective [by Pascale Heins and Wei Qi Koh, WFOT representatives Ritchard Ledgerd and Claudia von Zweck, and Louise Nygård, Karolinska Institute]

Occupational therapy promotes engagement in activities that people need or want to do in all domains of daily life. With this role, assistive technology is a key contributor in occupational therapy for facilitating management of such activities. In today's digitalized society, technologies are interwoven into all activity domains. Optimising the potential for social engagement of people living with dementia therefore requires a clear understanding of how and when technology can be used to promote social health, i.e. to enable people with dementia to (1) fulfil their potential and obligations, (2) manage life with some degree of independence, and (3) participate in social activities. Therefore, this guidance provides recommendations to improve the usability, effectiveness, and implementation of technology in dementia care and research, incorporating amongst others the occupational therapy perspective.

From an occupational therapy perspective, activities are both a *means* and an *end* to facilitate people with dementia's social health. This means that occupational therapists work on mediating both the *process* of activity performance, and the *outcomes* of their participation in social activities that are meaningful to an individual. Activities are always performed within, and in interaction with, a *context*. This entails carefully deliberated attention to the transactions that unfold when people engage in activities in their daily life context. These key features of an occupational therapy perspective are also of importance when we strive to develop knowledge about how to support people with dementia through the use of technologies. It is not enough to evaluate only outcomes of a technology intervention. The 'means' (process) is equally important, where considerations regarding individuals' abilities, preferences, values, and disease trajectory, should be taken into account. Considering this, it is for current and future research in the field of technology and dementia care valuable to include people with dementia as both research participants and co-researchers, based on their expertise by experience.

Overall, taking the occupational therapy perspective into account, researchers, healthcare professionals and technology designers should aim to optimise the fit between: (1) a person with dementia's individual abilities and desire to engage in social activities, (2) the characteristics of the activity, (3) the studied or applied technology, and (4) the context. Moreover, as all of these elements interact with each other and may change throughout the course of dementia and the individual's life span, we need to be continuously prepared to revise and adapt this fit.

Chapter 2 Best Practice Guidance at a glance

<table>
<tr><td>3.1.</td><td colspan="2">Practical, cognitive & social factors to improve usability of technology for people with dementia

Technologies are increasingly vital in today’s activities in homes and communities. Nevertheless, little attention has been given to the consequences of the increasing complexity and reliance on them, for example, at home, in shops, traffic situations, meaningful activities and health care services. The users’ ability to manage products and services has been largely neglected or taken for granted. People with dementia often do not use the available technology because it does not match their needs and capacities.
This section provides recommendations to improve the usability of technology used in daily life, for meaningful activities, in healthcare and in the context of promoting the Social Health of people with dementia.</td></tr>
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<tr><td>3.2.</td><td colspan="2">Evaluating the effectiveness of specific contemporary technology

The rapid growth of the technological landscape and related new services have the potential to improve the effectiveness and cost-effectiveness of health and social services and facilitate social participation and engagement in activities. But which technology is effective and how is this evaluated best? This section provides recommendations to evaluate the effectiveness of technology in daily life, meaningful activities and healthcare services as well as of technologies aimed to promote the Social Health of people with dementia. Examples of useful technologies in some of these areas are provided.</td></tr>
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<tr><td>3.3.</td><td colspan="2">Implementation of technology in dementia care: facilitators & barriers

Successful implementation of technology in dementia care depends not merely on its effectiveness but also on other facilitating or impeding factors related to e.g. the personal living environment (privacy, autonomy and obtrusiveness); the outside world (stigma and human contact); design (personalisability, affordability and safety), and ethics on these subjects. This section provides recommendations on the implementation of technology in everyday life, for meaningful activities, healthcare technology and technology promoting Social Health.</td></tr>
<tr><td></td><td>3.3.1</td><td>Technology in everyday life</td></tr>
<tr><td></td><td>3.3.2.</td><td>Technology for meaningful activities</td></tr>
</table>

	3.3.3.	Healthcare technology
	3.3.4.	Social Health Domain 1: Fulfill ones potential and obligations
	3.3.5.	Social Health Domain 2: Manage ones own life and promote independence
	3.3.6.	Social Health Domain 3: Technology to promote social participation
3.4	Glossary	The glossary provides an explanation of words that are not commonly used in daily life
	INDEX 1 Thematic	This index will help you to find the recommendations of your interest based on keywords
	INDEX 2 Target group	This index will help people from different backgrounds (people with dementia, caregivers, policy makers, researchers) to find relevant recommendations for their own purpose

Vermeer, Y. Analysing advertisements of older adults: controlling the senile back then and wanderers now? (submitted)

Vermeer, Y., van Santen, J., Charlesworth, G., & Higgs, P. (2020). People with dementia and carers online discussing surveillance. Journal of Enabling Technologies, *14*(1), 55-70. https://doi.org/10.1108/JET-07-2019-0032

Vermeer, Y., Higgs, P., Charlesworth, G. (2019). Surveillance Technology in dementia care: implicit assumptions and unresolved tensions. In: N. Hendriks, K. Slegers, A. Wilkinson (eds.) DementiaLab 2019, Making design work: engaging with dementia in context. Springer International Publishing, p101-113.

Vermeer, Y., Higgs, P., & Charlesworth, G. (2019). What do we require from surveillance technology? A review of the needs of people with dementia and informal caregivers. Journal of Rehabilitation and Assistive Technologies Engineering, *6*. doi: 10.1177/2055668319869517

- ***Consider different needs*** [3.1.1.2]

Guidance: During the development or use of technological devices, the individual needs of the person with cognitive impairments (e.g. dementia or MCI) and carer should be considered. This includes not only everyday technology, but also surveillance technology (ST) and technology used during cognitive training sessions. Increased awareness and offered assistance is recommended.

Explanation and Examples: People with dementia tend to face more and other difficulties than people with MCI when using relevant everyday technologies such as cash machines, calling or texting with a cell phone or using a DVD player, and thus need more assistance in technology use. This may also be the case with ST and technology used for cognitive training.

For example, ST are often presented as a neutral technology, which enables carers to minimise risk. However, the views of users have not been sought by ST developers, which limits the usefulness of ST and suggests the need for the empowerment of user groups. Therefore, a study of audience reception was undertaken through focus groups, online discussions (Netherlands) and PPI (UK). Hereby people with dementia could speak for themselves, which has allowed their needs to be compared with carers. There was no clear recognition that such needs differed between people with dementia and carers, and it has not previously been recognized that this leads to a mismatch between a user's situation and the product design and how this plays out in the acceptance and use of ST. Although, carers and people with dementia have not yet reached an agreement on the privacy debate and on how the media should portray dementia, it is clear that carers often tamper with ST to make up for a lack in current designs. The results suggest that ST are being resold or rebranded by providers to use for dementia, whilst users may experience physical and cognitive barriers to using such technologies for safety reasons.

Regarding technology for cognitive training: As older people have little experience with technological devices, and so may experience problems, professionals involved in cognitive training should monitor training sessions from the outset. The professional must observe and ensure the ability of the older person to understand the instructions given through the technological device, so that the person can really benefit from the cognitive training by computer. For example, in sessions with GRADIOR, a cognitive rehabilitation program, there is always a professional in charge who helps older people to understand the exercises they may experience difficulty with.

Keywords: People with dementia, MCI, carers, needs, everyday technology, surveillance technologies, product design, assistance, usability

Target group: People with dementia; family carers; professional carers, policymakers, technology developers, researchers, clinicians, who promote the use of technology to people with cognitive impairments.

Type of evidence
Yvette Vermeer (INDUCT ESR1), Sara Bartels (INDUCT ESR9), Angie Alejandra Diaz (ESR 15)
Literature review, RCT, cross-sectional and focus group studies, online discussions, PPI

References
Vermeer Y, Higgs P, Charlesworth G. What do we require from surveillance technology? A review of the needs of people with dementia and informal caregivers. J Rehabil Assist Technol Eng. 2019 Dec 2;6. doi: 10.1177/2055668319869517.

Vermeer, Y., van Santen, J., Charlesworth, G., & Higgs, P. (2020). People with dementia and carers online discussing surveillance. Journal of Enabling Technologies, *14*(1), 55-70. https://doi.org/10.1108/JET-07-2019-0032

S. L. Bartels, S. Assander, A.-H. Patomella, J. Jamnadas-Khoda & C. Malinowsky (2019): Do you observe what I perceive? The relationship between two perspectives on the ability of people with cognitive impairments to use everyday technology, Aging & Mental Health, ePub 6May2019 https://doi.org/10.1080/13607863.2019.1609902

- ***Consider undesired side effects of dementia prevention technologies and discourses*** [3.1.1.3]

Guidance: Public health policy should more fully consider the undesired side effects of dementia prevention technologies and discourses which may reinforce the fear of dementia and imply a moral responsibility on people who cannot maintain cognition in later life due to the progression of the condition.

Explanation and Examples: A review of the literature shows there is little evidence for the effectiveness of brain training to prevent dementia. Furthermore, ethnographic research has generated evidence that engagement with it can act as a form of social exclusion by separating older people into those who have 'successfully cognitively aged' and those who have not. Indeed, the promotion of this technology implies an individual responsibility to stay cognitively healthy, implicitly reinforcing anxiety and blame around the condition and people who live with it. These side effects can reinforce the exclusion of people with the condition.

Keywords: Brain training, social exclusion, successful ageing, dementia

Target group: Researchers; policymakers

Type of evidence

Sébastien Libert (INDUCT ESR2)

Literature review, Ethnography

References

Libert, S., Charlesworth, G., & Higgs, P. (2020). Cognitive decline and distinction: A new line of fracture in later life? Ageing and Society, 40(12), 2574-2592. doi:10.1017/S0144686X19000734

- ***Adaptations to enable more accessible public transport*** [3.1.1.4]

Guidance:

Public transport providers and policy-makers should be more aware of barriers to access and consider adaptations to enable better accessibility for people with cognitive issues or disabilities living with dementia.

Shiells, K., Pivodic, L., Holmerova, I., Van den Block, L. (2020). Self-reported needs and experiences of people with dementia in nursing homes: a scoping review. Aging & Mental Health, 24:10,1553-1568, DOI: 10.1080/13607863.2019.1625303

- ***Technology design focused on the characteristics of the population provides usability*** [3.1.3.6]

Guidance: To improve usability design of the technology should be developed specifically on the characteristics of the person with dementia, with respect to vision, auditory and cognitive capacities.

Explanation and Examples: Dementia is mainly suffered by elderly people. It´s well known the visual and auditorily perception changes. Shapes, colours, glares, temporal frequency of stimuli, visual acuity, and relevant visual stimuli can be bad perceived. Therefore, the design of any technology should be focused and fitted to these perceptual changes. Consequently, it is important to increase the lighting of the context of the task, the level of contrast and font size.

Equally elderly people might suffer impaired hearing, especially in sensitivity to high frequencies, discrimination of tones and differentiation of the speech of the background noise. Therefore, it is necessary for any technology to increase the intensity of the stimuli, control the background noise, avoid stimuli with high frequencies and adapt the speed of the words.

The design of the technology should take into account the cognitive impairment of a person with dementia (type, level, and deficits associated with impairment). Technology for rehabilitation must comprise different difficulty levels, take slow processing speed into account by extending response intervals of exercises, and an increase the variety in types of exercises.

The degree of usability of a technology will influence the user´s experience, generating a degree of satisfaction in the person with dementia that will affect their level of motivation to continue using a rehabilitation program such as Gradior.

Keywords: Visual-auditory abilities, cognitive impairment, user´s experience, degree of satisfaction, motivation, usability.

Target group: Researchers, developers, people with dementia

Type of evidence
Angie Alejandra Diaz Baquero (INDUCT ESR15)
RCT
RCT Gradior Validation
Other sources of support:

References
Toribio Guzmán, J. M., Franco Martin, M.A., Perea Bartolomé, M.V. (2015). Long Lasting Memories, an integrated ICT platform against age-related cognitive decline: usability study. (Doctoral), Department of basic psychology, psychobiology and methodology of behavioral sciences - Faculty of psychology. University of Salamanca, Spain.

- ***Consider user-centred design in the development of computer-based cognitive rehabilitation programs for people with dementia*** [3.1.3.7]

Guidance: User-centered design should be considered in the development of any technology or computer-based program for cognitive rehabilitation in people with dementia.

Explanation and examples: User-centered design is a methodology applied in the development of programs or new technologies for cognitive rehabilitation in people with dementia. This design takes into account the target population from the beginning to the end of the development process, with the

aim of investigating their needs and expectations, developing a prototype that meets these needs and evaluating the final prototype based on usability and user experience criteria.

Keywords: Dementia, computer-based program, development design, cognitive.

Target group: Researchers, developers, people with dementia, policy makers

Type of evidence
Angie Alejandra Diaz Baquero (INDUCT ESR15)
Systematic literature review.

References

Diaz Baquero, A. A., Dröes, R. M., Perea Bartolomé, M. V., Irazoki, E., Toribio-Guzmán, J. M., Franco-Martín, M. A., & van der Roest, H. (2021). Methodological Designs Applied in the Development of Computer-Based Training Programs for the Cognitive Rehabilitation in People with Mild Cognitive Impairment (MCI) and Mild Dementia. Systematic Review. Journal of clinical medicine, *10*(6), 1222. https://doi.org/10.3390/jcm10061222.

3.1.4. Social Health Domain 1: Fulfill ones potential and obligations

[no recommendations yet]

3.1.5. Social Health Domain 2: Manage ones own life and promote independence

[no recommendations yet]

3.1.6. Social Health Domain 3: Technology to promote social participation

- ***Include social interaction elements in technological interventions that aim to promote social participation*** [3.1.6.1]

Guidance: Technological interventions aiming to promote social participation among older adults (with and without dementia) should incorporate a social interaction element.

Explanation/ examples: The number of people with dementia who live in the community and are socially isolated is growing. Social isolation can negatively affect health and well-being. Therefore, psychosocial interventions are needed to promote the social participation of people with dementia living in the community. A systematic literature review was conducted to explore the effects of technological interventions on the social participation of older adults with and without dementia. Findings from 36 studies suggest that technological interventions that include a social interaction element (e.g. face-to-face contact, phone calls, text messages) are successful in promoting social participation among older adults. Examples are group interventions that provide regular interactions within a group, or interventions that enable to connect and communicate with other people (e.g. family, friends, or other older adults).

Keywords: Social participation, designing technological interventions, social interaction, older adults, dementia

Target group:

Technology developers designing technology to promote social participation

Researchers evaluating the effect of technology on social participation

Type of evidence:

Pascale Heins (DISTINCT ESR11)

Systematic literature review

References:

Heins, P., Boots, L.M.M., Koh, W.Q., Neven, A., Verhey, F.J., and de Vugt, M.E. (2021). The Effects of Technological Interventions on Social Participation of Community-Dwelling Older Adults with and without Dementia: A Systematic Review. *Journal of Clinical Medicine*, *10*, 2308. doi: 10.3390/jcm10112308

3.2 Evaluating the effectiveness of specific contemporary technology

3.2.1 Technology for everyday life

- ***Ecological validity contributes to the effectiveness of a technology*** [3.2.1.1]

Guidance: The ecological validity and cultural context in which the technology will be implemented should be taken into account, to ensure it is applicable to the 'real life situation' of the person with dementia

Explanation & Example*:* When cognitive rehabilitation is applied to people with dementia, it is necessary to consider the ecological validity of each tool or instrument used to perform cognitive rehabilitation, training or stimulation. Ecological validity is determined by the ability of those tools, instruments or techniques used for cognitive training to be transferred to the patient's daily life. Therefore, the patient may feel that using these techniques or tools in their daily lives can bring them benefits and influence their daily life, "beyond the rehabilitation session". For example: Gradior includes images of real objects which are well-known to the users. These objects are close to those of real life, among others: calculation exercises associated with real adult life (shopping at a supermarket), presents quizzes of daily activities (prepare a specific recipe). New technologies for rehabilitation or cognitive training should consider ecological validity as their main objective otherwise it may not be appropriate for the person with dementia who uses it.

The context is a factor that must be considered in the design of new technologies, that is, it is not enough to delimit the population and its characteristics. For example: a technology may be applied in an urban context but not necessarily in a rural one, due to the difficulties that this context may have in terms of the existence and scope of communication systems (internet connection, presence of devices, etc.).

Consequently, Gradior was developed free of contents. This means that it is easy to change the contents of the software and objects interacting with the person with dementia. In this way, it can be fitted to different environments in an easy way. It is necessary that the exercises and objects have significance to the users.

Keywords**:** Ecological validity, cultural context, effectiveness, GRADIOR

Target group*:* Researchers, developers, dementia people, Policy makers

Type of evidence

Angie Alejandra Diaz Baquero (INDUCT ESR15)

RCT GRADIOR

References

None

Explanation and example: Several studies have been done to find moderators of effects of online training programs for carers of people with dementia. Some studies have demonstrated that some programs were more effective for certain subgroups of carers. However, in our analyses we could not replicate these findings. Our analyses on the effect of age, gender, level of education, relationship with the person with dementia, functional status of the person with dementia and frequency of appearance of challenging behaviour suggests that the program is equally effective for all the subgroups analysed. More research is needed before we have definitive answers. A better understanding of moderators of carers' training programs could lead to better tailoring of programs based on the specific characteristic of the carer.

Keywords: carer training programmes, mental health, mediators and moderators

Target group: Researchers

Type of evidence

Ángel C. Pinto Bruno (INDUCT ESR14)

Preliminary results of moderation analyses 'Mastery over dementia'

References

Pinto-Bruno, A. C., Blom, M., Kleiboer, A., Dröes, R-M., van Straten, A., & Pot, A. M. (unpublished). Moderation analyses of an online support program for carers of people with dementia.

- ***Consider the factors that potentially determine adherence to a computer-based cognitive rehabilitation program to generate corresponding adaptations*** [3.2.3.5]

Guidance: When evaluating adherence of people with dementia to a computer-based cognitive rehabilitation program, sociodemographic, cognitive, and psychological factors should be taken into account.

Explanation and examples: When we consider evaluating the adherence of people with dementia to a computer-based program for cognitive rehabilitation, it is important to consider sociodemographic (age, sex, educational level), cognitive (memory, attention, executive function) and psychological factors (level of motivation, expectations, previous computer use). For this purpose, a periodic evaluation will help to evaluate these factors and their relation to the amount and the time that a person spends in using a computer program for cognitive rehabilitation. In this way, significant modifications could be made to the program, so that the program meets the needs of people with dementia.

Keywords: dementia, rehabilitation, software, computer-based program, cognition, psychology.

Target group: Researchers, people with dementia, policy makers

Type of evidence

Angie Alejandra Diaz Baquero (INDUCT ESR 15)
Study into adherence profile in people with mild cognitive impairment and mild dementia in the computer-based cognitive training program "GRADIOR"

References

Diaz Baquero, A.A., Franco-Martín, M. A., Parra Vidales, E., Toribio-Guzmán, J. M., Martínez Abad, F., Perea Bartolomé, M. V., Asl, A.M., & van der Roest, H. G. (2021). The effectiveness of GRADIOR. A neuropsychological rehabilitation program for people with mild cognitive impairment (MCI) and mild dementia. Results of a Randomized Controlled Trial (RCT) after 4 and 12 months of treatment. Journal of Alzheimer's Disease (accepted).

3.2.4. Social Health Domain 1: Fulfill ones potential and obligations

References

Gilissen, J., Pivodic, L., Wendrich-van Dael, A., Gastmans, C., Vander Stichele, R., Van Humbeeck, L., Deliens, L., & Van den Block, L. (2019). Implementing advance care planning in routine nursing home care: The development of the theory-based ACP+ program.*PloS one*, *14*(10), e0223586. https://doi.org/10.1371/journal.pone.0223586

Wendrich-van Dael, A., Gilissen, J., Van Humbeeck, L., Deliens, L., Vander Stichele, R., Gastmans, C., Pivodic, L., & Van den Block, L. (2021). Advance care planning in nursing homes: new conversation and documentation tools. *BMJ supportive & palliative care*, *11*(3), 312–317. https://doi.org/10.1136/bmjspcare-2021-003008

- ***Accessibility to technology should be ensured for all people with dementia*** [3.3.3.6]

Guidance: Cognitive rehabilitation technology should be accessible physically and in terms of cost, taking into account the mobility problems and the low income of many older people with dementia. To increase the accessibility of technology it is necessary to deliver it at low cost or promote the financing of licenses for people with dementia.

Explanation: Programs for cognitive rehabilitation for people with dementia may be inaccessible due to high costs or difficulty getting access to the location that provides the program because of mobility issues. Technology associated with cognitive rehabilitation or stimulation should be accessible to all those who could benefit from it. Technologies for cognitive rehabilitation should be accessible at home, especially in people living in rural areas or with mobility problems who are not able to travel to a center to perform cognitive rehabilitation.

Keywords: Accessibility, economic constraints, physical impairment.

Target group: Researchers, policy-makers, health technology assessment, people with dementia

Type of evidence

Angie Alejandra Diaz (INDUCT ESR15)

RCT Gradior Validation

References

Fumero Vargas, G., Franco Martin, M.A., Perea Bartolomé, M.V. (2009). Start-up and study of usability of a computer cognitive rehabilitation program "Gradior" in the treatment of neurocognitive deficits (Doctoral), Department of basic psychology, psychobiology and methodology of behavioural sciences- Faculty of psychology.

- ***Take into account the level of cognitive impairment when implementing technologies*** [3.3.3.7]

Guidance: The level of cognitive impairment must be taken into account in the design of technology because people with severe dementia have different needs vs. mild dementia.

Explanation & Example: People with severe cognitive impairment will have more problems learning to use different and new devices. They need more explanation and a longer learning time, due to limited cognitive capacities. For example, the clinical experience with Gradior shows that people with moderate and severe dementia should have the therapist as a permanent guide. According to this, Gradior possibly would have to adopt new systems and tools to become effective in people with moderate and severe dementia, and in turn, allow a level of autonomy of the person with dementia who uses this technology. Indeed, the help of a therapist in the first steps of applying a technological-based therapy is strategic for implementing and accepting the approach.

Keywords: Grade of cognitive impairment, implementation, usability.

Target group: Researchers, developers, dementia people, policy-makers

Type of evidence

Angie Alejandra Diaz (INDUCT ESR15)

RCT Gradior Validation

References

Fumero Vargas, G., Franco Martin, M.A., Perea Bartolomé, M.V. (2009). Start-up and study of usability of a computer cognitive rehabilitation program "Gradior" in the treatment of neurocognitive deficits (Doctoral thesis), Department of basic psychology, psychobiology and methodology of behavioural sciences- Faculty of psychology.

Toribio Guzmán, J. M., Franco Martin, M.A., Perea Bartolomé, M.V. (2015). Long Lasting Memories, an integrated ICT platform against age-related cognitive decline: usability study. (Doctoral thesis), Department of basic psychology, psychobiology and methodology of behavioural sciences - Faculty of psychology.

- ***Nursing home managers should ensure the appropriate conditions for implementation of EPR systems*** [3.3.3.8]

Guidance: Issues such as access to the EPR system, appropriate training and system development and support should all be considered by nursing homes before and during the implementation of EPR systems.

Explanation & Examples: Access or non-access to various parts of the EPR system should be discussed and put in place. For instance, management should consider whether auxiliary staff should be allowed to access medical information, such as dementia diagnosis, and whether this would consequently entail training in the field of dementia. Appropriate training in the EPR system according to individual staff needs is also required, as some staff may be more experienced in the use of technology than others. Training 'on the job' was found to be preferred by many over classroom-based teaching. Finally, software developers should consider working alongside nursing homes during the design of EPR systems in order to ensure software is appropriate for their needs. Developers should continue to be involved in improving the EPR following implementation, as part of an iterative cycle.

Keywords: electronic patient record; implementation; nursing home; software development; training

Target group: Developers of EPR, Nursing home management

Type of evidence

Kate Shiells (INDUCT ESR13)

Qualitative study

References

Shiells, K., Diaz Baquero, A. A., Stepankova, O., & Holmerova, I. (2020). Staff perspectives on the usability of electronic patient records for planning and delivering dementia care in nursing homes: a multiple case study. BMC Medical Informatics and Decision Making, 20, 159. https://doi.org/10.1186/s12911-020-01160-8

ANEXO 3

Disponible en:

Our Induct Experiences. Interdisciplinary Network for Dementia Using Current Technology. https://www.dementiainduct.eu/wp- content/uploads/2019/06/INDUCT-newsletter-Spring-2019.pdf

INDUCT consortium members greatly contributed to the 29th Alzheimer Europe conference in The Hague. https://www.dementiainduct.eu/news/induct-consortium-members-greatly- contributed-to-the-29th-alzheimer-europe-conference-in-the-hague/

Meeting Centers in the Netherlands and Spain. MeetingDem Newsletter. https://www.meetingdem.eu/wp- content/uploads/2019/12/MeetingDem-Newsletter-December- 2019_v1.0DEF.pdf

Interdisciplinary Network for Dementia Using Current Technology

www.dementiainduct.eu

INDUCT NEWSLETTER Spring 2019 @INDUCT_MSC

WELCOME!

Welcome to the seventh INDUCT newsletter. This bi-annual document is to inform project collaborators, stakeholders and interested members of the community about the content and development of INDUCT. There have been a number of changes in the INDUCT team over the last few months. In January, we sadly said goodbye to our project manager, Dr Déborah de Oliveira, who has returned to Brazil to take up an exciting research opportunity. However, we are very pleased to welcome Dr Orii McDermott as the new project manager. We also said goodbye to Floriana Mangiaracina (ESR 8). On page 7, you can read more about the new ESR 8, Kim Beentjes, who has recently taken up this post. Many ESRs will be leaving the INDUCT project as their three year contracts draw to an end in August. Therefore, the majority of this issue is dedicated to ESRs sharing their INDUCT experiences. However, please do keep an eye on the INDUCT website and Twitter for ongoing updates, which will be produced throughout the remainder of 2019 and into 2020 as ESRs publish their important results. Finally, the INDUCT recommendations, a culmination of the work of all fifteen ESRs, will be released in the autumn and can be accessed on the INDUCT website from that time.

Kate Shiells (ESR 13)

THE FIFTH INDUCT SCHOOL, LONDON, UK

From 13-17 May, the fifth and final INDUCT school took place in London, organised by the University of Hertfordshire. The school began with ESRs delivering an update on their recommendations, which will form the basis of the INDUCT transversal objectives on the usability, effectiveness and implementation of technology for people with dementia.

During the school, ESRs also had the chance to visit the multisensory environment laboratory (PAMELA) at UCL and, listen to several experts, including Professor Nick Tyler, discuss the latest in accessibility and public transport research.

INTERDEM Academy members joined for the remainder of the week with a thought-provoking debate on advance care planning, as well as sessions on PPI, entrepreneurship, project management, realist methods and career development.

Professor Nick Tyler from the PAMELA lab

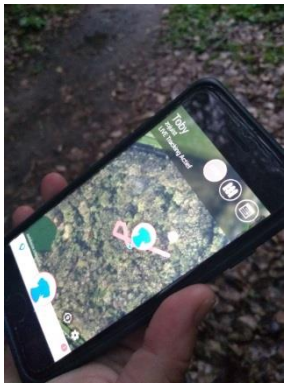
INDUCT has received funding from the European Union's Horizon 2020
research and innovation programme under the Marie Skłodowska-Curie grant agreement number 676265

OUR INDUCT EXPERIENCES

Yvette Vermeer (ESR 1). University College London, UK

y.vermeer@ucl.ac.uk

Seconded to: KI, Sweden and Alzheimer Nederland/Alzheimer Europe, the Netherlands



My research: *The needs for surveillance technology and caring media products*: Helping to empower people living with dementia and support carers.

How I hope my research will benefit people with dementia and their carers:

Advertisers considerably portray stereotypes of dementia to sell surveillance technologies (e.g. GPS, tracking devices) to increase the safety and independence of people with dementia. This study recognised that people with dementia have different needs from their carers when it comes to such technologies and advertisements, which will give insights to designers, developers and researchers. The results are hoped to ensure that products are meeting individual needs, are not stigmatising and will empower (rather than disempower) people with dementia. As a result, carers will be supported by having the person with dementia accepting the product to the benefit of all.

Skills gained during INDUCT: This has been a great learning experience and journey all in one. The question is, what skills did I not gain from this whole experience?

Highlights from the last three years: Running around London and discovering new places every day; the privilege and ability to live in Stockholm and learn basic Swedish; flying and driving around Europe for secondments and symposiums; attending a masterclass and presenting at a conference in Florida, the United States.

Phrase which sums up my INDUCT experience in [English]:

It's okay if it does and it's okay if it doesn't

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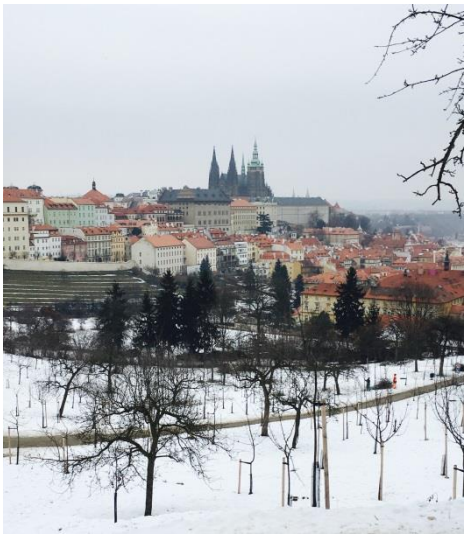
research and innovation programme under the Marie Skłodowska-Curie grant agreement number 676265

Skills gained during INDUCT: Patience and resilience are two of the most important skills I have acquired during the last three years (in relation to finding somewhere to live in Prague, trying to speak Czech, and of course, the publishing process). Secondly, having previously studied languages at university, joining this project I initially felt thrown in at the deep end. But, thanks to the wealth of training opportunities and expertise of supervisors, I am now beginning to feel like a researcher!



Prague Castle from Petřín hill

Highlights from the last three years: To have had the fantastic opportunity to live and feel like a local in one of the most beautiful cities in the world; spending summer evenings on Slovanský Ostrov-my favourite island in Prague; coming together with other ESRs for secondments, schools and conferences at various locations around Europe and the world.

Poster presentation at Alzheimer Europe conference 2017

Phrase which sums up my INDUCT experience in [Czech]:

Trpělivost růže přináší

(Good things come to those who wait)

Angie Alejandra Diaz Baquero (ESR 15). INTRAS, Zamora, Spain

npasalejandradiaz93@gmail.com

Seconded to: Nottingham University, UK

My research: Effectiveness of the GRADIOR rehabilitation program in people with MCI and mild dementia

How I expect my research to benefit people with dementia and their caregivers: Gradior is a computer program designed for the cognitive rehabilitation of people with MCI and mild dementia. I hope that GRADIOR will help improve the cognitive functioning (memory, attention, language, cognitive functioning) of people with MCI and mild dementia who participate in the research and that, in turn, this will contribute to improvements in their mood and their relationships with their caregivers.

INDUCT has received funding from the European Union's Horizon 2020
research and innovation programme under the Marie Skłodowska-Curie grant agreement number 676265

Skills acquired during INDUCT: Discipline and flexibility are two of the skills that every researcher must have, since research requires an organized mind, as well as the ability to develop solutions to the situations that are presented to us. Perseverance in difficult situations and resilience in the face of obstacles are key to the path that guides our actions towards what we want to achieve-*nobody said that the road would be easy, it comes loaded with adversities*.

Highlights of the last three years: Training opportunities in different places have allowed for continuous learning and interaction with other cultures. It has been a pleasure to get to know each person (supervisors, teachers, ESRs) that makes up INDUCT and the collaborative work has assisted in the development of my own project, as well as the clinical experience with people with MCI and mild dementia. And, of course, I have had the opportunity to live in Zamora, that small but cozy town.

Phrase that summarizes my INDUCT experience in [English]:

Cognitive flexibility is vital as it will allow us to adapt our behavior and thought to multiple contexts.

MORE INFORMATION

For more information, please access our website: www.dementiainduct.eu

Follow us on Twitter: @INDUCT_MSC

INDUCT has received funding from the European Union's Horizon 2020
research and innovation programme under the Marie Skłodowska-Curie grant agreement number 676265

INDUCT consortium members greatly contributed to the 29th Alzheimer Europe conference in The Hague

The 29th conference of Alzheimer Europe took place at the World Forum in The Hague the Netherlands from 23 to 25 October. Many INDUCT consortium members contributed by means of oral presentations and posters. During the

and carers with her presentation on the needs associated with young people with dementia. Later, Marjolein de Vugt presented the significant effects of the Program Partner in Balance and the development of the "RHAPSODI" project for caregivers of young people with dementia.

On Thursday morning there was also a parallel session of INDUCT on Best Practices in Human Interaction with Technology in Dementia. During this session, 11 ESRs pitched some of the recommendations resulting from their projects and which are included in a web-based Best Practice Guidance for technology in Dementia which was officially launched and explained by Rose-Marie Dröes at the end of the session. The recommendations focused on how technology can improve the lives of people with dementia and included three technological areas: daily life, meaningful activities and health care.

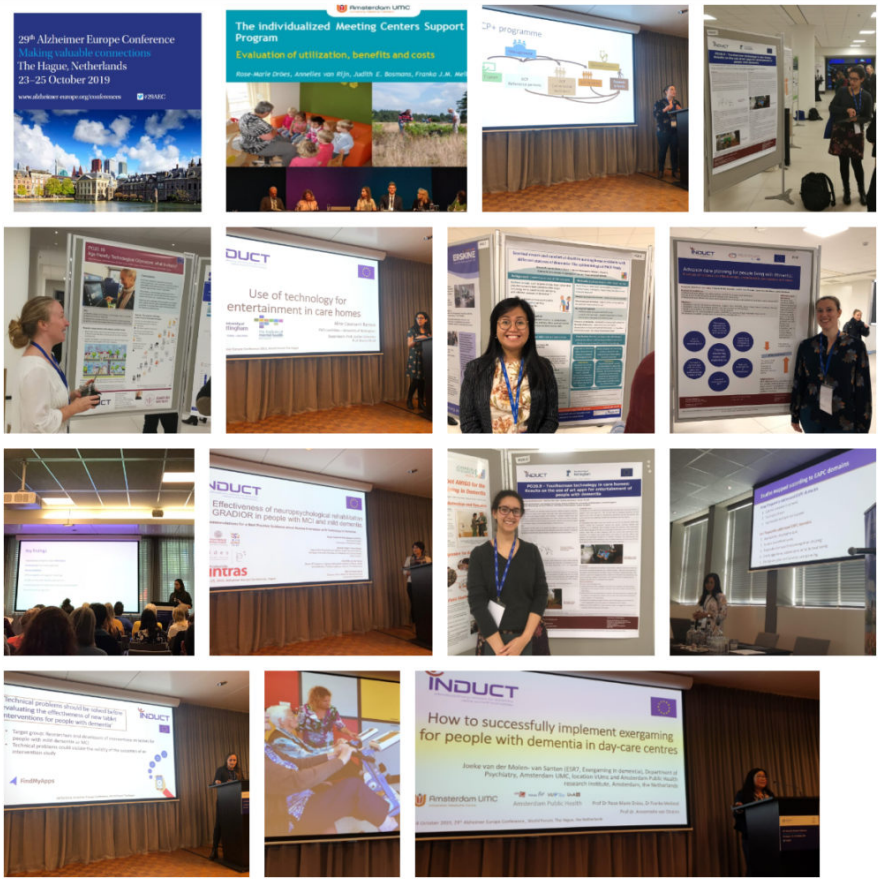
Several ESRs also presented posters and oral presentations in the afternoon parallel sessions. Sarah Walcook presented a poster on her project and pointed out the importance of designing accessible technologies to outside the home for people with dementia

Yvette Vermeer presented on an online discussion of people with dementia and carers. Joeke van Santen showed the results of a randomized clinical trial into the evaluation and cost-effectiveness of exergaming compared to regular activities in day-care centers for people with dementia. The study showed how the use of exergaming helps reduce the emotional burden in informal caregivers. Aline Cavalcanti talked the effect of the use of touchscreen technology and visual art app in people with dementia. Sara Bartels talked about how personalized feedback is an important aspect of the Experience Sampling Method (ESM) that facilitates a change in daily behavior of caregivers of people with dementia, following an RCT with 72 caregivers.

Rose-Marie Dröes demonstrated the impact of Dement-Talent volunteer work compared to the regular Meeting Centers support program in people with dementia. Dement Talent benefits the mental and social health of people with dementia by stimulating the use of their talents, which enables them to contribute to society and to participate in meaningful activities. This helps them to increase their sense of being useful and promotes emotional balance resulting in less behaviour and mood disruptions and less emotion burden in their carers.

On Friday, Lieve Van den Block talked about a palliative care program for people with and without dementia in nursing homes and showed that this program was effective in improving some aspects of the quality of care. Rose Miranda had a poster and reported on a systematic review, which she conducted to examine the evidence on palliative care of people with dementia in nursing homes. And, Annelien Van Dael presented a poster on her systematic review on the effectiveness, experiences, perceptions and views of advanced care planning for people with dementia. Finally, Rose-Marie Dröes reported on the new individualized MeetingCenters Support Programme providing DemenTalent to people with dementia and Dementelcoach (telephone coaching) and STAR eLearning to carers, which has been shown to be effective in an RCT which was carried out in 29 Meeting Centres across the Netherlands.

Angie Alejandra Diaz Baquero, Institute of Biomedical Research of Salamanca (IBSAL), University of Salamanca, Salamanca, Spain



‹ INDUCT launched Best Practice Guidance for Technology in Dementia at Alzheimer Europe conference in The Hague, the Netherlands

New INDUCT Lay Report Published ›

Leave a Reply

December 2019

MeetingDem Newsletter

The MeetingDem Newsletter is an edition of the MeetingDem Network (www.meetingdem.eu). This newsletter is disseminated among the network of interested stakeholders and Meeting Centres for people with dementia and carers worldwide. Sign up for this newsletter at www.meetingdem.eu or by sending an email to meetingdem.eu@gmail.com.

One year after the last MEETINGDEM Network Newsletter, it is incredible to see how much has happened around Meeting Centres initiatives in Europe and worldwide!

In this newsletter we will update you on the actions undertaken in the different countries and the impressive results and experiences this has led to. Some highlights: several new centres in different, also rural, regions in Italy, new centres and many new initiatives in the UK, several centres in preparation in the Poznań region in Poland and new Meeting Centres in preparation in Chili, Ohio, Japan and Singapore! And last but not least a further increase to 166 centres in the Netherlands. New individualized, outreaching, interventions were introduced and evaluated in Dutch Meeting Centres under the name individualized Meeting Centres Support Programme (iMCSP).

Much respect and our congratulations to Mrs Joke Bos, who in June this year was made Officer in the Order of Orange-Nassau by the vice-mayor of Amsterdam on behalf of the King of the Netherlands, for her 35 years of development work in dementia care, 25 of which as coordinator of Meeting Centre De Pijp.

Congratulations also to the Association for Dementia Studies of the University of Worcester. In November they received the prestigious Times Higher Education Award for their work on Meeting Centres, which were praised as a "genuine partnership between a truly dedicated research centre team and local help points" (#THEAwards)

We would like to thank everybody who supported the dissemination and implementation of the Meeting Centres in the past year and very much look forward to further developments in 2020! We wish you all a Merry Christmas and a sparkling New Year!

iMCSP presented at IPA in Santiago and Alzheimer Europe conference in The Hague

At the congress of the International Psychogeriatric Association in Santiago de la Compostella (Spain), 31 August-1 September, and the Alzheimer Europe conference in The Hague The Netherlands, 23-25 October 2019, prof Rose-Marie Dröes introduced a new individualized programme offered by several Meeting Centres in the Netherlands. This individualized MCSP (iMCSP) consists of volunteer work for people with dementia in the community (called DemenTalent), and telephone coaching (Dementelcoach) and an online course on the Internet (www.STARtraining.eu) for carers of people with dementia. Since 2016 several Dutch Meeting Centres are offering this programme in addition to the group-oriented programme in the centres. iMCSP aims to reach and support people with dementia and carers who are not willing or able to join the groups at the centres or who prefer (additional) individualized support or guidance. Thus the programme aims to better meet the varied needs of people living with dementia and carers.

iMCSP has been scientifically evaluated in 16 Meeting Centres in the past three years. Compared to the regular MCSP (13 control centres) the broadened offer indeed appeared to attract a broader target group. Overall, the individualized programme proved an effective, and also cost-effective, alternative for the regular MCSP. Participants in DemenTalent showed a decrease in severity of behaviour and mood symptoms and an increase in positive affect. Their carers felt less emotionally burdened as a result. Carers who used the individualized carer interventions tended to become happier than carers who did not receive support, as demonstrated by a comparison with a reference group from a national database (TOPICS-MDS).

For more information on the study results download the free online publication: Dröes et al. (2019) https://www.dovepress.com/utilization-effect-and-benefit-of-the-individualized-meeting-centers-s-peer-reviewed-fulltext-article-CIA

Royal decoration

During a symposium on iMCSP 7 June in Amsterdam, Joke Bos, programme coordinator of Amsterdam Meeting Centre De Pijp, was made Knight in the order of Orange-Nassau, in recognition of her exceptional service to socie-

ty. In her speech deputy-mayor Simone Kukenheim highlighted Joke's boundless dedication to improving care for people with dementia and their carers and to putting the Meeting Centres on the map worldwide. A much deserved recognition of 35 years of innovative work with a great impact on society!

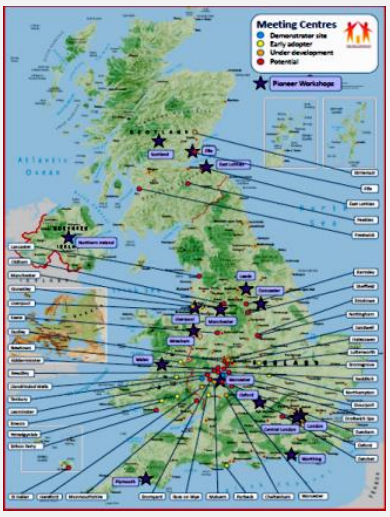
Developments in the UK Meeting Centres

The University of Worcester has won the prestigious Times Higher Education Award 2019 for Outstanding Contribution to the Local Community for our work with Meeting Centres. The award was presented at a glittering event at the Grosvenor in Park Lane, London on the 28th November 2019.

Left to right: Julian Clary – Awards Dinner host, Professor Dawn Brooker, Dr Shirley Evans and Sir Deian Hopkin - former vice-chancellor, London South Bank University who presented the awards

In the last newsletter we reported on activity around our UK Meeting Centre Support Programme project, funded by the National Lottery Community Fund which had just started. This time we update you on how this project is contributing to our vision for a Meeting Centre in every town across the UK.

Our original demonstrator sites, Droitwich Spa and Leominster, have gone from strength to strength.



Meeting Centres developments in the UK

Both have been awarded National Lottery Community Fund grants for almost half of their running costs for up to four years. These and the other six original Centres are joined by Kirriemuir as the first MC in Scotland, by Purbeck in Dorset, Oldbury in the West Midlands and Newtown as Powys' 4th Meeting Centre in Wales. Powys also received lottery funding and Kirriemuir has funding from the Life Changes Trust. Our map shows the current spread of Meeting Centres and gives a flavour of interest and activity. The purple stars indicate where we have held Pioneer Workshops, fourteen in all, which have been attended by up to 60 people in each (!). These workshops are springboards for Meeting Centres and we estimate there will be at least another 20 new Centres over the next two years supporting around 2000 affected by dementia.

Find out more about Meeting Centres UK, please contact meetingcentres@worc.ac.uk or visit our website http://bit.ly/2rwXCYS Twitter: @MeetingCentres

Professor Dawn Brooker and Dr Shirley Evans, Association for Dementia Studies, University of Worcester, UK

Italy: dissemination in four regions

The number of meeting centres (MC) In Italy has grown in 2019 and new ones are planned in the coming months. At present 15 MCs are operating in 4 different regions: Lombardia, Emilia-Romagna, Campania (see photo) and Puglia. New centres opened in Fidenza (near Parma), in Gambettola (near Cesena), in Cattolica (near Rimini) and in Bari. In rural areas near Rimini, a new Meeting Centre is also running, and two training courses for staff have been offered.

In the coming year other MCs are planned. In Milan the Association of Patients With Dementia (A.M.A. Onlus), member of the initiative group of the Milan Meeting Centre chaired by Dr. Elisabetta Farina (2013-2017), will open another Meeting Centre around April 2020. A pioneer training course is planned in Milan in April, in order to meet the needs of those interested in setting up a MC and for the national dissemination of the model. Other MCs ready to open in 2020 will be in Formigine (near Modena) and in Bologna.

The combined interest of public bodies (municipality or health agency) and family associations, as well as the positive experiences already achieved, are important facilitating factors in the dissemination of MCs in Italy. People with dementia and their family are involved in setting up the MC and the rural MCs meet the needs of people in these areas, where there is a lack of services that are generally available in larger centres or cities.

Prof. Rabih Chattat, University of Bologna, Italy

Poland: Wroclaw and Poznań Meeting Centre

In the Wrocław's Meeting Centre the first quarter of the year has been rich in carnival-themed events such as a ball and performances. Also health promotion, for example how to manage posture and mobility living with Parkinson's disease. In January, seniors took part in a Creativity Olympiad 'Destination Imagination'.

Strengthening bonds and empathy, and integration with people with disabilities or children, was promoted through collaborative Easter preparation. Spring and summer season's focus was all on journeys - both literal by local trips or field games, but also sentimental. Participants went back to tastes of childhood, engaged in an art project 'Half a century between us', where high school students portrayed seniors, creating a very interesting cross-generational dynamic.

There was also room for singing with the seniors' group 'Charm of memories' and listening to a folk band. Autumn, in turn, brought the 'Wroclaw Senior Days' celebration and a wide range of rehabilitation activities and concerts. At the end of October, the agenda of the Meeting Centre was introduced to Australian researchers who visited the centre in order to present country-specific trends in care organizations. Additionally, support groups for carers and informative meetings, were held all through the year.

Poznań, the second Polish city that adopted the Meeting Centre model, has extended its offer to healthy people at-risk aged above 50 years old. Furthermore, the competences of new teams and leaders are being developed so that three additional Meeting Centre-inspired initiatives can be implemented in 2020.

Marta Ciułkowicz

The Meeting Centres of 3Bridges Australia

Two years on, the first Australian MCSP is offered at two locations, one at Carss Park and the other at Summer Hill, Sydney. Both Meeting Centres are well established and run at full capacity, accommodating a maximum of fourteen participants per day. Currently there are over 40 active participants across the two sites with 12 participants diagnosed with Younger Onset Dementia (YOD). Feedback from members and carers has been overwhelmingly positive, especially from people diagnosed with YOD and their carers, as the practical engagement with activities, meal preparation and assisting older members with tasks seems to be supporting their need for purpose and meaning.

As we are celebrating our second birthday this November, we are reflecting not only on the importance of the MCSP for our families but for 3Bridges as well. It has provided us with opportunities to grow and has helped us to identify dementia as an important and emerging issue that now has become one of the main areas of focus within the organisation. 3Bridges is aiming on becoming a Dementia Friendly Organisation after successfully leading a few dementia friendly community initiatives in the area. We are currently engaging with culturally and linguistically diverse communities in South East Sydney to raise awareness and provide community education on dementia as well as provide professional development to multicultural and ethno-specific community care staff.

Engaging with our local communities and providing opportunities to have open conversations about dementia is the only way we can help destigmatise and address issues related to dementia and care of people living with dementia and their families.

Amal Madani, Meeting Centre Three Bridges, Sydney, Australia

Meeting Centres in the Netherlands and Spain

My name is Angie Alejandra Diaz Baquero. As an early stage researcher within the INDUCT (Interdisciplinary Network for Dementia Using Current Technology) project I did my internship at the VU University Medi-

cal Center in Amsterdam. The network is funded by the EU (H2020-Marie Skłodowska Curie Actions). One of my objectives during the internship was to visit some Meeting Centres in the Netherlands to experience the activities in the centres, and to compare them with Meeting Centres in Spain, such as Orillas del Duero MC of the INTRAS foundation in Zamora. I visited three Dutch Meeting Centres: De Pijp and Buitenveldert in Amsterdam, and Zandstroom in Zandvoort.

Dance class in Dutch MC Zandstroom

Both the Dutch and the Spanish Meeting Centres adopt a person-centred psychosocial approach, eliminating the "patient" etiquette because of its stigmatizing connotation. The centres promote active aging in older people with cognitive impairment through activities that provide cognitive, emotional, physical and social stimulation. However, there are also differences between these centres. In the Dutch Meeting Centers for example, artists, dancers and musicians contribute to the activity programme in addition to the centre staff. In the Spanish centre, the staff consists of psychologists and neuropsychologists.

Reminiscence Workshop in Ethnographic Museum-Intras Foundation

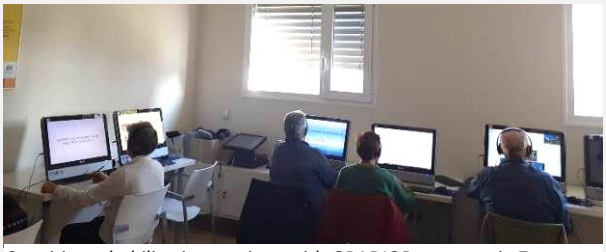
The Dutch as well as the Spanish centres offer stimulating activities. Reminiscence therapy aims to generate autobiographical memories by the use of stimuli from the past (e.g, old CDs, magazines). In the Spanish meeting centre, the Ethnographic Museum of Zamora offers these materials.

The centres also provide space for social interaction in social and cultural centres with the aim of including people in society and promoting interaction with the caregivers. For cognitive stimulation, board games are used and simple 'question and answer' games (e.g. PIM-PAM-PET in the Netherlands).

Arts class (Painting) in MC De Pijp

In addition, the Dutch Meeting Centers also offer group classes of singing, dance, music and painting. These classes provide a combination of cognitive, emotional and physical stimulation, but in a sociable atmosphere in which the participants have the opportunity to interact.

By contrast, the MC of the INTRAS Foundation uses mainly individual cognitive training sessions through "pencil and paper" activities and by means of a computerized cognitive rehabilitation program-GRADIOR. In this way the activities can be adapted and personalized to the individual person, according to their cognitive level.



Cognitive rehabilitation sessions with GRADIOR program in Zamora

In conclusion, the Meeting Centres contribute to the care of older people by providing various activities aimed at promoting multifunctional stimulation. The centres promote space for social interaction through dialogue, empathy, feeling and physical-visual contact *"It is a place to find new opportunities and create new things."* (Person attending Meeting Centre De Pijp).

Angie Alejandra Diaz Baquero and Rose-Marie Dröes

Meeting Centres in development

Chili

Arthur Berkhoff of the Fundación Kok-Berkhoff in Chili reports that in the past year they have been busy with preparations for a Meeting Centre in Chile. Obtaining the proper registration for their foundation is a slow process due to bureaucracy.

In recent months the foundation has given some presentations to explain the goals they want to realize by creating a Meeting Centre. These presentations were attended by an average of 100 persons (patients, carers). They have also been promoting the Meeting Centre on Facebook in the region where they did the presentations. In addition, they did several

ANEXO 4

Disponible en:

https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42020159027

ESTRATEGÍA DE BÚSQUEDA PUBMED
28-10-2019

Mild dementia and MCI
"Dementia"[Mesh:NoExp] OR "Alzheimer Disease"[Mesh] OR "Dementia, Vascular"[Mesh] OR "Frontotemporal Lobar Degeneration"[Mesh] OR "Cognitive Dysfunction"[Mesh] OR dementi* [tiab] OR CADASIL [tiab] OR Alzheimer* [tiab] OR frontotemporal degeneration* [tiab] OR mild cognitive impairment* [tiab] OR (MCI [tiab] AND mild [tiab]) OR (MCI [tiab] AND cognitive [tiab])

Design/Development

"Software Design"[Mesh] OR Computing Methodolog* [tiab] OR development technolog* [tiab] OR computer program develop* [tiab] OR Training Design* [tiab] OR Design approach* [tiab] OR User-centered design* [tiab] OR development process* [tiab] OR Conceptual design* [tiab] OR design proces*[tiab] OR user-participatory design* [tiab] OR iterative process* [tiab] OR iterative design* [tiab] OR development* [ti] OR design* [ti] OR development* [ot] OR design* [ot]

Computer-based program

"Telerehabilitation"[Mesh] OR "Therapy, Computer-Assisted" [Mesh] OR "Virtual Reality"[Mesh] OR "Mobile applications"[Mesh] OR "Virtual Reality Exposure Therapy"[Mesh] OR "Telemedicine" [Mesh] OR serious game* [tiab] OR gamified [tiab] OR computer-based* [tiab] OR computerized training* [tiab] OR computerised training* [tiab] OR computer-assisted* [tiab] OR virtual realit* [tiab] OR smart health technolog* [tiab] OR mobile application* [tiab] OR Web-based [tiab] OR E-health [tiab] OR mobile health [tiab] OR wearable* [tiab] OR mobile phone* [tiab] OR smartphone* [tiab] OR smart phone* [tiab] OR smartwatch* [tiab] OR mobile device* [tiab] OR Tablet [tiab] OR mobile app [tiab] OR mobile application [tiab] OR m-health [tiab] OR ehealth [tiab] OR mhealth [tiab] OR iPad* [tiab] OR iPhone* [tiab] OR blended [tiab] OR VR [tiab] OR telemedicine* [tiab] OR telerehabilitation* [tiab] OR online-based* [tiab] OR internet-based* [tiab] OR exergam* [tiab]

Cognition

"Cognitive Dysfunction"[Mesh] OR "Cognition"[Mesh] OR cognitive [tiab] OR cognition* [tiab]

Search	Query	Items found
#5	Search (((#1) AND #2) AND #3) AND #4	63
#4	Search "Cognitive Dysfunction"[Mesh] OR "Cognition"[Mesh] OR cognitive [tiab] OR cognition* [tiab]	450398
#3	Search "Telerehabilitation"[Mesh] OR "Therapy, Computer-Assisted" [Mesh] OR "Virtual Reality"[Mesh] OR "Mobile applications"[Mesh] OR "Virtual Reality Exposure	234620

Search	Query	Items found
	Therapy"[Mesh] OR "Telemedicine" [Mesh] OR serious game* [tiab] OR gamified [tiab] OR computer-based* [tiab] OR computerized training* [tiab] OR computerised training* [tiab] OR computer-assisted* [tiab] OR virtual realit* [tiab] OR smart health technolog* [tiab] OR mobile application* [tiab] OR Web-based [tiab] OR E-health [tiab] OR mobile health [tiab] OR wearable* [tiab] OR mobile phone* [tiab] OR smartphone* [tiab] OR smart phone* [tiab] OR smartwatch* [tiab] OR mobile device* [tiab] OR Tablet [tiab] OR mobile app [tiab] OR mobile application [tiab] OR m-health [tiab] OR ehealth [tiab] OR mhealth [tiab] OR iPad* [tiab] OR iPhone* [tiab] OR blended [tiab] OR VR [tiab] OR telemedicine* [tiab] OR telerehabilitation* [tiab] OR online-based* [tiab] OR internet-based* [tiab] OR exergam* [tiab]	
#2	Search "Software Design"[Mesh] OR Computing Methodolog* [tiab] OR development technolog* [tiab] OR computer program develop* [tiab] OR Training Design* [tiab] OR Design approach* [tiab] OR User-centered design* [tiab] OR development process* [tiab] OR Conceptual design* [tiab] OR design proces*[tiab] OR user-participatory design* [tiab] OR iterative process* [tiab] OR iterative design* [tiab] OR development* [ti] OR design* [ti] OR development* [ot] OR design* [ot]	680225
#1	Search "Dementia"[Mesh:NoExp] OR "Alzheimer Disease"[Mesh] OR "Dementia, Vascular"[Mesh] OR "Frontotemporal Lobar Degeneration"[Mesh] OR "Cognitive Dysfunction"[Mesh] OR dementi* [tiab] OR CADASIL [tiab] OR Alzheimer* [tiab] OR frontotemporal degeneration* [tiab] OR mild cognitive impairment* [tiab] OR (MCI [tiab] AND mild [tiab]) OR (MCI [tiab] AND cognitive [tiab])	234186

ESTRATEGÍA DE BÚSQUEDA EN PsycINFO (EBSCO)
5-11-2019

Mild dementia and MCI
DE "Vascular Dementia" OR DE "Cognitive Impairment" OR DE "Alzheimer's Disease" OR DE "Semantic Dementia" OR DE "Dementia" OR TI(dementi* OR CADASIL OR Alzheimer* OR “frontotemporal degeneration*” OR “mild cognitive impairment*” OR (MCI AND mild) OR (MCI AND cognitive)) OR AB(dementi* OR CADASIL OR Alzheimer* OR “frontotemporal degeneration*” OR “mild cognitive impairment*” OR (MCI AND mild) OR (MCI AND cognitive)) OR KW(dementi* OR CADASIL OR Alzheimer* OR “frontotemporal degeneration*” OR “mild cognitive impairment*” OR (MCI AND mild) OR (MCI AND cognitive))

Design/Development
DE "Computer Assisted Design" OR DE "Computer Software" OR DE "Computers" OR DE "Systems Design" OR DE "Human Machine Systems Design" OR DE "Product Design" OR DE "Development" OR TI(“Computing Methodolog*” OR “development technolog*” OR “computer program develop*” OR “Training Design*” OR “Design approach*” OR “User-centered design*” OR “development process*” OR “Conceptual design*” OR “design proces*” OR “user-participatory design*” OR “iterative process*” OR “iterative design*” OR development* OR design*) OR AB(“Computing Methodolog*” OR “development technolog*” OR “computer program develop*” OR

“Training Design*” OR “Design approach*” OR “User-centered design*” OR “development process*” OR “Conceptual design*” OR “design proces*” OR “user-participatory design*” OR “iterative process*” OR “iterative design*”) OR KW(“Computing Methodolog*” OR “development technolog*” OR “computer program develop*” OR “Training Design*” OR “Design approach*” OR “User-centered design*” OR “development process*” OR “Conceptual design*” OR “design proces*” OR “user-participatory design*” OR “iterative process*” OR “iterative design*” OR development* OR design*)

Computer-based program

DE "Telerehabilitation" OR DE "Computer Assisted Therapy" OR DE "Virtual Reality" OR DE "Virtual Reality Exposure Therapy" OR DE "Computer Applications" OR DE "Computer Assisted Therapy" OR DE "Computer Games" OR DE "Human Computer Interaction" OR DE "Mobile Applications" OR DE "Mobile Devices" OR DE "Mobile Health" OR DE "Mobile Learning" OR DE "Mobile Technology" OR DE "Telemedicine" OR DE "Computer Training" OR DE "Computers" OR DE "Smartphone Use" OR DE "Smartphones" OR DE "Tablet Computers" OR DE "Internet" OR TI(“serious game*” OR gamified OR “computer-based*” OR “computerized training*” OR “computerised training*” OR “computer-assisted*” OR “virtual realit*” OR “smart health technolog*” OR “mobile application*” OR “Web-based” OR “E-health” OR “mobile health” OR wearable* OR “mobile phone*” OR smartphone* OR “smart phone*” OR smartwatch* OR “mobile device*” OR Tablet OR “mobile app” OR “mobile application” OR “m-health” OR ehealth OR mhealth OR iPad* OR iPhone* OR blended OR VR OR telemedicine* OR telerehabilitation* OR “online-based*” OR “internet-based*” OR exergam*) OR AB(“serious game*” OR gamified OR “computer-based*” OR “computerized training*” OR “computerised training*” OR “computer-assisted*” OR “virtual realit*” OR “smart health technolog*” OR “mobile application*” OR “Web-based” OR “E-health” OR “mobile health” OR wearable* OR “mobile phone*” OR smartphone* OR “smart phone*” OR smartwatch* OR “mobile device*” OR Tablet OR “mobile app” OR “mobile application” OR “m-health” OR ehealth OR mhealth OR iPad* OR iPhone* OR blended OR VR OR telemedicine* OR telerehabilitation* OR “online-based*” OR “internet-based*” OR exergam*) OR KW(“serious game*” OR gamified OR “computer-based*” OR “computerized training*” OR “computerised training*” OR “computer-assisted*” OR “virtual realit*” OR “smart health technolog*” OR “mobile application*” OR “Web-based” OR “E-health” OR “mobile health” OR wearable* OR “mobile phone*” OR smartphone* OR “smart phone*” OR smartwatch* OR “mobile device*” OR Tablet OR “mobile app” OR “mobile application” OR “m-health” OR ehealth OR mhealth OR iPad* OR iPhone* OR blended OR VR OR telemedicine* OR telerehabilitation* OR “online-based*” OR “internet-based*” OR exergam*)

Cognition

DE "Cognitive Impairment" OR DE "Cognition" OR DE "Cognitive Rehabilitation" OR DE "Brain Training" OR TI(cognitive OR cognition*) OR AB(cognitive OR cognition*) OR KW(cognitive OR cognition*)

#	Query	Limiters/Expanders	Results
S5	S1 AND S2 AND S3 AND S4	Search modes - Boolean/Phrase	127
S4	DE "Cognitive Impairment" OR DE "Cognition" OR DE "Cognitive Rehabilitation" OR DE "Brain Training" OR TI(cognitive OR cognition*) OR AB(cognitive OR cognition*) OR KW(cognitive OR cognition*)	Search modes - Boolean/Phrase	476,109
S3	DE "Telerehabilitation" OR DE "Computer Assisted Therapy" OR DE "Virtual Reality" OR DE "Virtual Reality Exposure Therapy" OR DE "Computer Applications" OR DE "Computer Assisted Therapy" OR DE "Computer Games" OR DE "Human Computer Interaction" OR DE "Mobile Applications" OR DE "Mobile Devices" OR DE "Mobile Health" OR DE "Mobile Learning" OR DE "Mobile Technology" OR DE "Telemedicine" OR DE "Computer Training" OR DE "Computers" OR DE "Smartphone Use" OR DE "Smartphones" OR DE "Tablet Computers" OR DE "Internet" OR TI(“serious game*” OR gamified OR “computer-based*” OR “computerized training*” OR “computerised training*” OR “computer-assisted*” OR “virtual realit*” OR “smart health technolog*” OR “mobile application*” OR “Web-based” OR “E-health” OR “mobile health” OR wearable* OR “mobile phone*” OR smartphone* OR “smart phone*” OR smartwatch* OR “mobile device*” OR Tablet OR “mobile app” OR “mobile application” OR “m-health” OR ehealth OR mhealth OR iPad* OR iPhone* OR blended OR VR OR telemedicine* OR telerehabilitation* OR “online-based*” OR “internet-based*” OR exergam*) OR AB(“serious game*” OR gamified OR “computer-based*” OR “computerized training*” OR “computerised training*” OR “computer-assisted*” OR “virtual realit*” OR “smart health technolog*” OR “mobile application*” OR “Web-based” OR “E-health” OR “mobile health” OR wearable* OR “mobile phone*” OR smartphone* OR “smart phone*” OR smartwatch* OR “mobile device*” OR Tablet OR “mobile app” OR “mobile application” OR “m-health” OR ehealth OR mhealth OR iPad* OR iPhone* OR blended OR VR OR telemedicine* OR telerehabilitation* OR “online-based*” OR “internet-based*” OR exergam*) OR KW(“serious game*” OR gamified OR “computer-based*” OR “computerized training*” OR “computerised training*” OR “computer-assisted*” OR “virtual realit*” OR “smart health technolog*” OR “mobile application*” OR “Web-based” OR “E-health” OR “mobile health” OR wearable* OR “mobile phone*” OR smartphone* OR “smart phone*” OR smartwatch* OR “mobile device*” OR Tablet OR “mobile app” OR “mobile application” OR “m-health” OR ehealth OR mhealth OR iPad* OR iPhone* OR blended OR VR OR telemedicine* OR telerehabilitation* OR “online-based*” OR “internet-based*” OR exergam*)	Search modes - Boolean/Phrase	120,124
S2	DE "Computer Assisted Design" OR DE "Computer Software" OR DE "Computers" OR DE "Systems Design" OR DE "Human Machine Systems Design" OR DE "Product Design" OR DE "Development" OR TI(“Computing Methodolog*” OR “development technolog*” OR	Search modes - Boolean/Phrase	379,291

	“computer program develop*” OR “Training Design*” OR “Design approach*” OR “User-centered design*” OR “development process*” OR “Conceptual design*” OR “design proces*” OR “user-participatory design*” OR “iterative process*” OR “iterative design*” OR development* OR design*) OR AB(“Computing Methodolog*” OR “development technolog*” OR “computer program develop*” OR “Training Design*” OR “Design approach*” OR “User-centered design*” OR “development process*” OR “Conceptual design*” OR “design proces*” OR “user-participatory design*” OR “iterative process*” OR “iterative design*”) OR KW(“Computing Methodolog*” OR “development technolog*” OR “computer program develop*” OR “Training Design*” OR “Design approach*” OR “User-centered design*” OR “development process*” OR “Conceptual design*” OR “design proces*” OR “user-participatory design*” OR “iterative process*” OR “iterative design*” OR development* OR design*)		
S1	DE "Vascular Dementia" OR DE "Cognitive Impairment" OR DE "Alzheimer's Disease" OR DE "Semantic Dementia" OR DE "Dementia" OR TI(dementi* OR CADASIL OR Alzheimer* OR “frontotemporal degeneration*” OR “mild cognitive impairment*” OR (MCI AND mild) OR (MCI AND cognitive)) OR AB(dementi* OR CADASIL OR Alzheimer* OR “frontotemporal degeneration*” OR “mild cognitive impairment*” OR (MCI AND mild) OR (MCI AND cognitive)) OR KW(dementi* OR CADASIL OR Alzheimer* OR “frontotemporal degeneration*” OR “mild cognitive impairment*” OR (MCI AND mild) OR (MCI AND cognitive))	Search modes - Boolean/Phrase	120,824