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Review Article

Virtual reality and cognitive rehabilitation for older adults with mild cognitive impairment: A systematic review

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A R T I C L E I N F O

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A B S T R A C T

Virtual Reality (VR) has been gaining increasing attention as a potential ecological and effective intervention system for treating Mild Cognitive Impairment (MCI). However, it remains unclear the efficacy and effectiveness of VR-based cognitive rehabilitation therapy (VR-CRT) in comparison with cognitive rehabilitation therapy (CRT). Consequently, a systematic review on Pubmed, Scopus, PsycInfo, and Web Of Science was conducted to assess the state of the art of the literature published between 2003 and April 2023. Only articles that adopted CRT as control group and that included some measure of at least one domain among overall cognitive function, executive function and functional status were included. Participants needed to be older adults aged 65 or over with a diagnosis of MCI. The risk of bias and the quality of evidence were assessed using the Version 2 of the Cochrane risk-of-bias tool for randomized trials. Initially, 6503 records were considered and screened after removing duplicates (n = 1321). Subsequently, 81 full texts were assessed for eligibility. Four articles met the inclusion criteria but 2 of them were merged as they were describing different outcomes of the same research project. Consequently, 3 overall studies with a total of 130 participants were included in the final analysis. Due to the high heterogeneity in the methodology and outcome measures employed, it was not possible to conduct a meta-analysis. Included studies used semi-immersive (k = 2) and full-immersive (k = 1) VR systems in their research. Two articles evaluated overall cognitive function through the MoCA together with specific tests for executive functions (n = 69), while one study adopted a comprehensive neuropsychological battery to evaluate both cognitive function and executive function (n = 61). Finally, one study evaluated functional status through instrumental activities of daily living (n = 34). A However, the limited number of studies, the small sample size, and the potential issues with the quality and methodology of these studies that emerged from the risk of bias assessment may raise doubts about the reliability of their results. Nevertheless, although scarce, results of the present review suggest that VR-CRT may be paramount in treating MCI for its additional ecological and adaptive advantages, as all of the studies highlighted that it was at least as effective as conventional CRT for all the outcome measures. Therefore, more rigorous research that compares VR-CRT and CRT is needed to understand the degree to which VR-CRT is effective with older adults with MCI and the potential role of immersion to influence its efficacy. Indeed, these preliminary findings highlight the need for the development of standardized VR protocols, as the integration of such technology into clinical practice may help improve the quality of life and cognitive outcomes for this growing demographic.

1. Introduction

Mild Cognitive Impairment (MCI), also called Mild Neurocognitive Disorder (American Psychiatric Association, 2013), is a syndrome that refers to a noticeable decline in cognitive abilities that is greater than expected based on a person's age and education level. Individuals with MCI may experience problems with memory, language, attention, reasoning, or other cognitive functions while preserving their ability to carry out everyday activities, which differentiates MCI from dementia (Golomb et al., 2022). Notably, MCI may be due to various factors or

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medical conditions (Ganguli et al., 2019; Sabbagh et al., 2020). Consequently, treating cognitive impairment effectively at an early stage is essential because early detection and intervention may help slow down or even prevent further cognitive decline (Kasper et al., 2020). Furthermore, treating cognitive impairment promptly may improve the overall quality of life by helping individuals cope with cognitive and emotional challenges that they may experience, such as frustration, anxiety, and depression (Anderson, 2019). It has been shown that older adults aged 65 or over are at a higher risk of developing MCI and dementia, probably because they are more likely to experience factors and conditions that negatively affect cognitive well-being (Eshkoor et al., 2015), such as neurodegenerative disorders, (e.g., Alzheimer's Disease; Scheltens et al., 2016), malnutrition (e.g., dietary alterations due to tooth loss; Kossioni, 2018), and chronic diseases (e.g., diabetes; Feinkohl et al., 2018). It is important to note that many different factors play a crucial role in shaping the onset, extent, and severity of cognitive impairment (Subramaniapillai et al., 2021). For example, some studies suggest that women may have a higher prevalence of certain cognitive disorders like Alzheimer's disease compared to men (Mielke et al., 2022; Podcasy and Epperson, 2016; Lin et al., 2015). Similarly, some ethnic groups may be at a higher risk of certain types of cognitive impairment. For instance, some studies suggest that African Americans and Hispanics in the United States may have a higher risk of developing Alzheimer's disease compared to non-Hispanic whites (Khemka et al., 2023; Salazar et al., 2020). However, the reasons for these differences are likely multifactorial and may include genetic, environmental, and socioeconomic factors, as well as racial discrimination, which negatively affects access to healthcare and likelihood of a proper diagnosis (Rosselli et al., 2022; Milani et al., 2020; Quiñones et al., 2020; Salazar et al., 2020). Additionally, lifestyle factors such as exercise, diet, social engagement, and cognitive activities may help reduce dementia risk and enhance cognitive function, as they might mitigate neuropathological damage, while promoting cognitive reserve, a protective mechanism that may delay the onset of the cognitive symptoms despite brain pathology (Meng et al., 2022).

Solutions for managing and treating cognitive impairment include both pharmacological and non-pharmacological interventions. Particularly, pharmacological interventions for MCI typically involve the use of medications to manage cognitive symptoms and tackle specific neurochemical imbalances, which may provide some symptomatic relief, although they often come with potential side effects, and their long-term effectiveness in slowing down the progression of MCI is limited (Kasper et al., 2020). Non-pharmacological interventions, on the other hand, encompass a wide range of strategies such as cognitive training, physical exercise, diet modifications, and social engagement, which focus on enhancing overall brain health, addressing risk factors, and promoting neuroplasticity. For examples, lifestyle modifications such as regular physical activity and a balanced diet can improve blood flow to the brain and reduce the risk of further cognitive decline (Dominguez et al., 2021). Accordingly, cognitive training, which is usually domain-specific and consists in a structured program of exercises and activities designed to enhance and improve specific cognitive skills, can help improve memory and executive function (Butler et al., 2018; Nguyen et al., 2019), while social engagement activities may help individuals adapt to cognitive challenges (Lydon et al., 2022). Furthermore, non-pharmacological interventions may be crucial in empowering individuals to take an active role in managing their condition and may lead to better long-term outcomes. Moreover, they do not carry the potential risks and side effects associated with pharmacological treatments, making them a safer and more sustainable option for individuals with MCI. Currently, however, there is no known cure for older adults with MCI or dementia, as both pharmacological and non-pharmacological interventions may slightly slow down but not reverse cognitive impairment.

However, as the longevity of the population is increasing, the number of people suffering from MCI and dementia is expected to drastically raise, with huge medical and social consequences (Ito et al., 2021; Lissek and Suchan, 2021). Consequently, it is essential to manage symptoms of cognitive impairment as early as possible, as well as develop more efficient, cost-saving, and effective rehabilitation interventions (Chen et al., 2021). Alongside pharmacotherapy, cognitive therapy may be useful in improving both cognitive and non-cognitive outcomes. Particularly, cognitive rehabilitation therapy (CRT) is a form of therapy designed to help individuals with cognitive impairments improve their cognitive skills and regain or compensate for lost cognitive functions. It is commonly used in the rehabilitation of people who have experienced brain injuries (Galetto and Sacco, 2017), strokes (Rogers et al., 2018), or other neurological conditions that affect cognitive abilities, including neurodegenerative disorders (Clare et al., 2018). The therapy techniques used in cognitive rehabilitation can vary depending on the individual's needs. For example, they may include cognitive exercises and training (e.g., puzzles, memory games, and attentional exercises), compensation strategies (e.g., using memory aids like calendars or smartphone apps, organizing daily routines, and using external reminders), and psychoeducation and counseling for the individual and/or their families (Cicerone et al., 2019; Clare et al., 2018; Wood and Fussey, 2018).

Noteworthy, CRT along with other non-pharmacological interventions showed several limitations, including restrained accessibility, financial constraints, geographical limitations, and disparities in healthcare access, which hinders widespread implementation (Lasaponara et al., 2021). To tackle the challenges and issues related to traditional in person CRTs, many different technology-driven devices were developed to administer arrays of cognitive tasks, enabling the provision of real-time feedback mechanisms and the dynamic modulation of task complexity, thus enhancing the precision and adaptability of therapeutic interventions, as well as providing a more structured approach (Lancioni et al., 2023; Marin et al., 2022; Pappadà et al., 2021). For example, a virtual supermarket was developed and proposed for both the assessment and the rehabilitation of cognitive impairment. The tool usually involves tasks that require many different cognitive abilities (e.g., visuospatial orientation, attention, working memory) to be completed such as recalling a shopping list, navigating aisles, finding and picking up items, and paying at the cashier and can be conducted using a wide range of devices (Zygouris et al., 2015). Particularly, interventions tools such as the virtual supermarket might be administered completely or partially through computer programs (Hu et al., 2021), virtual reality systems (Ceccato et al., 2023; Domenicucci et al., 2022) tablets and smartphones (Yousaf et al., 2020), wearable devices (Cote et al., 2021), and gaming consoles and serious games (Ning et al., 2020). Nonetheless, although based on evidence-based cognitive tasks, there is still a lack of consensus on a standardized and structured application of these rehabilitative intervention.

Notably, recently, and particularly after the restrictive measures applied worldwide due to the COVID-19 pandemic, research on the application of computerized cognitive training, and Virtual Reality (VR) in particular, as a therapeutic instrument to tackle cognitive impairment has drastically increased (Hu et al., 2021; Jahn et al., 2021). VR is characterized by a computer-generated, interactive environment with objects, scenes, or other human beings that users can interact with. VR may be distinguished based on the level of immersion (Bamodu and Ye, 2013): non-immersive VR typically involves a computer screen or a projection display where users view a virtual environment that requires input devices like keyboards, mouse, or gamepads for the user to interact with it; semi-immersive VR offers a higher level of immersion compared to non-immersive VR since it involves a larger display screen or multiple screens that surround the user, providing a wider field of view, as well as specialized glasses and some level of haptic feedback or motion tracking; fully immersive VR which aims to create a complete sense of presence within the virtual environment through the use of head-mounted displays that cover the user's eyes and ears, blocking out the real world and replacing it with a virtual world, in addition to motion tracking technology to detect the user's movements and adjust the virtual environment accordingly, allowing users to freely explore and interact with the virtual space. Each type of VR systems offers specific advantages and disadvantages. For example, non-immersive virtual environments may represent the most cost-effective and usable solution and may be more easily incorporated into apps for different devices like smartphones or tablets, but the lower immersive experience may limit their ecological usefulness (Tuena et al., 2020). On the other hand, more immersive VR systems may provide the most immersive and realistic experience, yet they are often more expensive and may face limitations, including the potential for motion sickness or nausea due to sensory conflicts, although strategies can be applied to minimize cybersickness and make immersive VR systems more easily tolerated (Huygelier et al., 2019; Porcino et al., 2021). Additionally, the applicability of semi-immersive and fully immersive VR systems may be constrained by hardware limitations, potentially limiting the reach and accessibility of such interventions among older adults who may not have access to powerful VR-ready devices (Yu et al., 2022). Accordingly, the choice on the level of immersion should be based on individual characteristics and needs, as well as on the specific domains that need to be addressed.

Indeed, from a therapeutic perspective, VR-based healthcare may offer numerous benefits, especially for individuals who experience mobility and economic issues, as they may allow patients to access rehabilitation and training programs regardless of their location and might reduce the need for travel and waiting times. Indeed, VR cognitive rehabilitation may be conducted remotely, allowing individuals to access rehabilitation services from their own homes (Lasaponara et al., 2021). Additionally, they allow adapting task difficulties in real-time based on the individual's actual performance, making cognitive rehabilitation supposedly more engaging, motivating, and beneficial to the patient (Wu et al., 2020). Accordingly, they are supposed to be more ecologically valid than conventional CRT because real-world contexts and situations replicated in VR should allow individuals to more easily transfer skills and strategies acquired in the virtual environment to daily life functioning, especially when they induce high levels of immersion (Son and Park, 2022).

Studies that incorporated VR in post-stroke neurorehabilitation seem to support their usefulness and efficacy for both motor and specific cognitive outcomes (Khan et al., 2023). However, to the best of our knowledge, it remains unclear the extent to which VR-based cognitive rehabilitation therapy (VR-CRT) is effective in comparison with conventional CRT for the older population with MCI. Indeed, it may be easier to develop and evaluate VR-based training in post-stroke neurorehabilitation as a wide variety of standardized treatment approaches have been already established for this kind of population, with promising recovery chances depending on the site and size of the damage (Langhorne et al., 2011). In contrast, MCI lacks clear treatment targets both because its progression is not always linear or predictable, which complicates treatment planning and prognosis and because treating cognitive deficits requires addressing multiple aspects of cognition simultaneously, which can be challenging to achieve effectively (Kasper et al., 2020). Accordingly, most of the literature that focused on investigating the efficacy of VR-based cognitive rehabilitation in older adults with MCI employed inconsistent methodologies and control groups (e.g., passive, placebo, or unspecified care), which lead to mixed results (Domenicucci et al., 2022; Ge et al., 2018; Kim et al., 2019; Yu et al., 2022; Zhong et al., 2021) and did not allow for a direct comparison between VR-CRT and CRT interventions. Nevertheless, considering that CRT interventions have already been proven to be effective in slowing down cognitive decline associated with MCI (Budson and Solomon, 2021), it is crucial to systematically investigate whether and the degree to which VR-based interventions lead to additional beneficial impact in the MCI cognitive rehabilitation. Indeed, if the ecological advantages resulting from the implementation of VR interventions are found to lead to greater and more stable results in time, VR-CRTs could be paramount to face MCI progression. Alternatively, if VR-based cognitive rehabilitation therapy proves to be at least as effective as already available CRT programs, this will allow patients to access rehabilitation services from their own homes, thus hugely enhancing accessibility, feasibility, and monitoring. Given these possible advantages, the present systematic review aimed at evaluating the current state of the art of the efficacy and effectiveness of VR-based cognitive rehabilitation therapy in comparison with its conventional version in older adults with MCI, as well as considering whether differences in outcome measures exist based on the level of immersion elicited by VR-CRT.

2. Methods

2.1. Search strategy

The systematic review was conducted based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Liberati et al., 2009; Page et al., 2021) on papers published between 2003 and April 2023. A protocol was defined prior to commencing the systematic review and adhered to throughout its progression to ensure that the integrity and robustness of the systematic review's findings were preserved, thereby promoting confidence in its conclusions and recommendations for future research and clinical applications. The following electronic databases were searched: PubMed, PsycINFO, Scopus, and Web Of Science. Terms included "virtual reality" (supported by "VR" OR "computer*" OR "digital*"), "Mild Cognitive Impairment" (supported by "MCI" OR "Mild neurocognitive disorder" OR "cognitive decline" OR "cognitive impairment"), and "treatment" (supported by "intervention" OR "rehabilitation" OR "therapy" OR "training"). Each combination of keywords was further combined with the Boolean character "AND". The deliberate exclusion of certain outcomes from the initial keyword selection was driven by our interest in capturing any relevant cognitive measure, such as specific cognitive functions. This approach aimed to avoid unintentionally excluding pertinent articles that might employ different terminology for the desired outcomes, thus cognitive outcomes were subsequently examined manually during the review process.

2.2. Study eligibility

The following inclusion criteria were set accordingly to the PICOS framework:

- Population: individuals aged 65 or over with a diagnosis of MCI following neurological or neuropsychological assessment
- Intervention: VR-based Cognitive Rehabilitation Therapy (VR-CRT)
- Comparator: conventional face-to-face Cognitive Rehabilitation Therapy (CRT)
- Outcome: at least one cognitive measure related to global function, executive functions, and instrumental activities of daily living (IADL)
- Study design: any quantitative study design as long as it respected the other inclusion criteria (e.g., randomized controlled trials, crossovers)

Exclusively studies that employed traditional face-to-face CRT as the active comparator, rather than alternative forms of cognitive training such as remote videoconference sessions, were included. This selection criterion was employed to facilitate a more direct and clinically pertinent assessment of the distinct advantages and challenges associated with virtual reality interventions. Indeed, face-to-face cognitive training currently represents the standard in cognitive rehabilitation for older adults with MCI, reflecting the conventional and widely practiced approach in clinical settings (Kasper et al., 2020). Accordingly, a direct comparison help assess the added value of VR technology within the context of traditional care, while controlling for potentially confounding variables introduced by different modes of delivery, such as internet connectivity, device familiarity, and the inherent differences in the remote communication medium. Since the main outcome of the present systematic review was to investigate the efficacy of VR-CRTs compared to conventional CRTs in older adults with MCI, an age threshold of 65 years was used, which was chosen to ensure a focus on a population generally recognized as entering the senior age group and at higher risk for cognitive decline (Eshkoor et al., 2015). Furthermore, it was decided to include only papers published since 2003 in the present systematic review, which was underpinned by the notable advancements in technology, particularly in the realm of Virtual Reality (VR), that have occurred since that time. Given that VR technology experienced significant developments and widespread adoption from the early 2000 s onwards (Maples-Keller et al., 2017), limiting the review's scope to publications from 2003 onwards helped to conduct an analysis that was reflective of the contemporary landscape of VR applications, leading to a more relevant and comprehensive understanding of its effectiveness in the context of older adults with MCI, as earlier studies might not adequately capture the advancements in the utilization of VR as a therapeutic tool.

Accordingly, exclusion criteria were the following:

- Population: individuals diagnosed with MCI aged under 64 years, individuals aged 65 or over who were not diagnosed with MCI;
- Intervention: any intervention conducted without VR or that did not comprise cognitive rehabilitation (e.g., VR-based motor rehabilitation);
- Comparator: comparator that did not included conventional cognitive treatments
- Study type: background studies and any study that was not quantitative.

Studies written in a language different from English were excluded.

2.3. Screening and review process

The initial phase of this study involved systematic database searches, led by the primary author, who conducted database searches of relevant literature. Subsequently, the retrieved studies were imported into a bibliographical reference manager (Mendeley) to identify duplicate entries, which were double-checked and eliminated manually by the first author. Subsequently, titles and abstracts were thoroughly reviewed by the same author to exclude studies that were evidently irrelevant, including systematic reviews, meta-analyses, and articles that did not align with the predefined inclusion criteria. Following this rigorous screening process, the remaining studies were considered for inclusion in the study, and their full texts were sought whenever feasible. In instances where the categorization of papers required nuanced judgment or uncertainties arose, a consensus was reached through consultation with the second and third authors.

2.4. Risk of bias assessment

The risk of bias was assessed using Version 2 of the Cochrane risk-of-bias tool for randomized trials (RoB 2; Higgins et al., 2019), a widely used tool to assess risks of bias in randomized controlled trials (RCTs) included in systematic reviews. The tool provides a structured approach to evaluate the methodological quality and potential biases in individual studies, through the evaluation of different domains that are categorized as "low risk of bias," "some concerns," or "high risk of bias". Particularly, biases arising from the randomization process, deviations from the intended interventions, missing outcome data, measurement of the outcome, and selection of the reported result were investigated. The first and the second authors judged the risk of bias independently for each study, while the third author was involved to resolve eventual conflicting judgements.

3. Results

3.1. Included studies

A total of 7824 articles were identified by the literature search, which got reduced to 6503 after eliminating duplicates. After screening titles and abstracts, 6421 studies were excluded for being published before 2003 (360), background manuscripts such as systematic reviews, meta-analyses, and book chapters (408), or clearly unrelated (5653). Afterward, the remaining 82 articles were evaluated in their entirety. However, the full text for 1 study was unavailable and therefore it was not possible to screen it. Additionally, 77 articles were excluded for employing wrong study designs (e.g., cross-sectional with a healthy control group), populations (e.g., dementia), outcome (e.g., feasibility only), intervention (no VR), or language. Finally, 4 studies were included in the present review, although 2 of them were merged in their reporting as they described different outcomes (primary and secondary) of the same research. The whole process of data screening and selection is presented in Fig. 1.

3.2. Study characteristics

Study characteristics are shown in Table 1. All the included articles were single-blinded randomized controlled studies as it was not possible to blind participants from the assigned intervention. Participants were living independently in the community (Park et al., 2020) or recruited from communities and daycare centers (Liao et al., 2019, 2020). Rehabilitation sessions were similar among studies in terms of timing and cognitive functions trained. Additionally, no difference in the duration and frequency of training sessions was reported between control groups and experimental groups.

3.3. Narrative synthesis of the results on the outcome measures

An overview of the results of the selected studies are presented in Table 2. Overall, VR-CRTs seemed to produce statistically significant improvements in every outcome measure and were reported to be at least as effective as conventional cognitive interventions. In each study, the same neuropsychological instruments were used for baseline and post-intervention evaluations (no other follow-up was reported). However, each study used different outcome measures, which resulted in heterogeneity in the duration and the modalities of cognitive assessment. Specifically, Liao and colleagues (Liao et al., 2019, 2020) employed the Montreal Cognitive Assessment (MoCA; Nasreddine et al., 2005) to assess global cognition in combination with a 16-channel NIRS device to evaluate changes in brain activation; the Executive Interview 25 (EXIT-25; Royall et al., 1992) to assess executive functions; the Chinese version of the Verbal Learning Test (CVVLT; Chang et al., 2010) to assess immediate and delayed memory; the Lawton Instrumental Activities of Daily Living scale (IADL; Lawton and Brody, 1969) to evaluate functional status; the Trail Making Test A and B (TMT-A/B; Llinàs-Reglà et al., 2017) for visual attention and task switching; and the Stroop Color and Word Test (Golden et al., 1978) for inhibition in executive function. Measures were administered at baseline and after completing the 36 sessions over 12 weeks. Park and colleagues (2020) asked participants to complete the MoCA, the TMT-A/B, and the Digit Span Test forward and backward for evaluating working memory and short-term memory (DST; Tamez et al., 2011) at baseline and after 6 weeks. Additionally, a numeric self-report scale was administered after each training session to evaluate interest and motivation. Finally, Torpil and colleagues (2021) adopted the geriatric version of the Lowenstein Occupational Therapy Cognitive Assessment (LOTCA-G; Katz et al., 1989) as a comprehensive measure of cognitive functioning, which was administered at baseline and after 12 weeks.

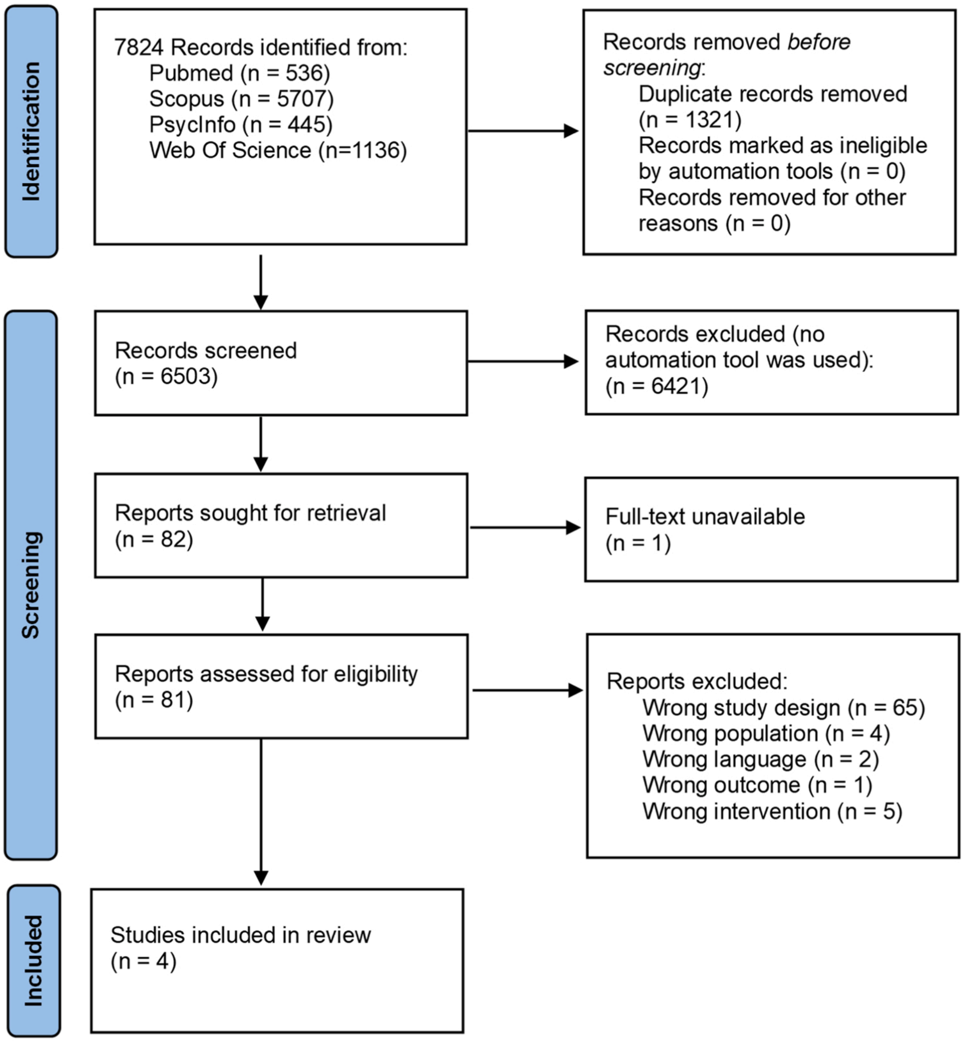

Fig. 1. PRISMA 2020 flow diagram.

Table 1
Study characteristics. RCT: Randomized Controlled Trial; EG: Experimental Group; CG: Control Group.

Author (s)/ Year	Design	Living situation	System/Devices	VR type	Groups	Sessions
Park et al. (2020)	Single-blinded RCT	Community	MOTOCOG (touchscreen monitor + grip air bulb + joysticks or attachments	Semi-Immersive	EG: VR-CRT (daily activities such as driving, bathing, cooking, and shopping) CG: CRT (tabletop activities)	30 min per day, 5 days per week, for 6 weeks
Torpil et al. (2021)	Single-blinded RCT	NA	Microsoft Kinect for PC	Semi-Immersive	EG: VR-CRT + CRT (four commercially available games) CG: CRT	45 min per day, 2 days a week, for 12 weeks
Liao et al. (2019) Liao et al. (2020)	Single-blinded RCT	Communities and daycare centers	VIVE system with Microsoft Kinect for PC + VR glasses and motor controllers	Full-Immersive	EG: physical and cognitive VR-CRT CG: physical and cognitive CRT	60 min per day, 3 days a week, for 12 weeks

3.3.1. *Global cognitive function*

In the study conducted by Park and colleagues (2020) both the VR-CRT group and the CRT group showed significant improvements in global cognitive function measured through the MoCA after the interventions. Interestingly, the improvement was statistically stronger in the VR-CRT group. On the other hand, the research by Liao and colleagues (2019, 2020) found that significant differences between pre-test and post-test in the VR-CRT group but not in the CRT group. However, The inter-group difference (time x group interaction) was not significant, which may suggest that the observed differences in changes between the two groups are not substantial enough to be considered diverging from each other in terms of how they respond to time. Nevertheless, when the LOTCA-G total score was employed as a measure of cognitive function (Torpil et al., 2021) both groups significantly improved, with the group that received VR-CRT in addition to conventional CRT exhibiting significantly greater improvement compared to the control group.

3.3.2. *Executive functions*

Results from the study conducted by Park and colleagues (2020)

Table 2
Study results. EG: Experimental Group; CG: Control Group; MMSE: Mini-Mental State Examination; MoCA: Montreal Cognitive Assessment; TMT: Trail Making Test; LOTCA-G: Loewenstein Occupational Therapy Cognitive Assessment (Geriatric version); EXIT-25: Executive Interview; VLT: Verbal Learning Test; IADL: Lawton Instrumental Activities of Daily Living; NA: information not available; None: Articles reported that no adverse event occurred.

Study	Groups	N	Inclusion criteria	Exclusion criteria	Drop out (with reasons)	Primary outcomes	Primary outcomes' results	Secondary outcomes	Secondary outcomes' results	Adverse events
Park et al. (2020)	EG: 18 CG: 17	35 older adults (age ≥ 65) with MCI (18 women and 17 men)	Diagnosis of MCI, age > 65 years, MMSE score > 16, no limitation in the upper extremity, fair grade on manual muscle testing of upper extremity, ability to grip objects, independence in daily activities, no history of neurological disorders nor of visual perception deficit	unstable medical problems, history of psychiatric disorders, severe communication di fficulties, problem with visual and auditory functions	EG: 2 (refuse to follow-up + poor participation rate) CG: 3 refuse to follow-up	cognitive function (MoCA, TMT-A/B, Digit Span Test forward and backward)	VR-CRT > CRT in MoCA, TMT-A/B, and Digit Span Test forward VR-CRT = CRT in Digit Span Test backward	Interest and motivation	VR-CRT > CRT in interest and motivation	NA
Torpil et al. (2021)	EG: 30 CG: 31	61 older adults (ages between 65 and 75) with MCI (36 women and 25 men)	age between 65 and 75 years, MCI diagnosis, ability to understand and follow verbal instructions	secondary chronic disease that may affect cognitive functioning, auditory and visual problems that may affect rehabilitation implementation and communication, and attending any rehabilitation program during the study period	None	Cognitive function (LOTCA-G)	VR-CRT + CRT > CRT in orientation, visuospatial perception, visuomotor organization, thinking operation, and attention/ concentration VR-CRT + CRT = CRT in the other LOTCA-G domains			NA
Liao et al. (2019) Liao et al. (2020)	EG: 18 CG: 16	34 older adults (age ≥ 65) with MCI (23 women and 11 men)	Age ≥ 65 years old, ability to walk more than 10 m without walking aids, MMSE score ≥ 24, MoCA score < 26, self-reported memory complaints, ability to perform ADLs	Diagnosis of dementia, history of malignant tumors, presence of unstable neurological or orthopedic disease that would have interfered with participation in the study, education level less than six years	3 (health problems unrelated to training) + 5 (2 in EG and 3 in CG) for low motivation	Global cognition (MoCA), executive function (EXIT-25), verbal memory (VLT), functional status (IADL), brain activation (16-channel NIRS during MoCA)	EG > CG only in IADL EG = CG in MoCA, EXIT-25. VLT	TMT-A/B, Stroop Color and Word Test, gait performance (GAIT UP system)	EG= CG in every measure but the TMT-B	None

showed that the VR-CRT group but not the CRT group significantly improved in the TMT-A/B, suggesting that the application of VR-CRT may benefit attention and task switching in older adults with MCI. However, in another study (Liao et al., 2019, 2020) VR-CRT showed significant differences between pre- and post-test only for TMT-B, while TMT-A was not significant for both groups. According to the same research both experimental and control groups showed significant improvements in the Stroop Color and Word Test that did not different between groups according to the group x time interaction. Similarly, a significant improvement was found in the EXIT-25 total score, which was comparable in both groups. Accordingly, analyses of the specific domains (Orientation, Visual-spatial Perception, Visuomotor Organization, Thinking Operation, Attention/Concentration) of the LOTCA-G (Torpil et al., 2021) showed that more improvements were found when VR-CRT was administered in addition to conventional CRT, although both groups significantly improved after the interventions. Finally, when the Digit Span Test (DST) backward and forward was employed (Park et al., 2020), both the experimental and the control groups showed significant differences at the post-test. However, the VR-CRT led to greater improvements compared to CRT in the DST-forward but not in the DST-backward.

3.3.3. *Working memory and short-term memory*

According to the research by Liao and colleagues (2019, 2020), VR-CRT led to significant improvements in both immediate and delayed recall, while the CRT showed significantly higher scores only for the immediate recall. However, in both cases the time x group interaction was not significant. No significant within-group difference was found in the Memory domain of the LOTCA-G (Torpil et al., 2021) in neither group.

3.3.4. Functional Status

Only one study (Liao et al., 2019, 2020) considered functional status, which was investigated through IAD and found that only the VR-CRT group significantly improved after the intervention. This result may represent a crucial finding, as it may suggest that VR-CRT may lead to better real-world functioning and independence in daily life tasks, corroborating the idea that the immersive experience of VR systems may lead to more ecological results compared to conventional CRT.

3.4. Risk of bias

The results of the risk of bias evaluation (Fig. 2), as assessed in accordance with the Cochrane manual for risk of bias, revealed several concerns, especially regarding deviations from the intended interventions, missing outcome data, and in the selection of the reported results. Firstly, to the best of our knowledge none of the included articles made data publicly available, which can hinder the ability to independently verify and replicate the findings, thus undermining transparency and trustworthiness in the research. Furthermore, the absence of pre-registration in 2 of the studies (Park et al., 2020; Torpil et al., 2021) may raise doubts regarding the potential for post hoc analysis and the possibility that the statistical analyses may not have been pre-established, increasing the risk of bias through selective reporting. Additionally, the remaining research (Liao et al., 2019, 2020) registered the study retrospectively, after the beginning of participant enrollment, which introduced the risk of outcome reporting bias, as decisions about which outcomes to report could have been influenced by the study's results, further compromising the overall methodological rigor and validity of the included studies. Finally, despite data could not be provided for participants who dropped out after the beginning of the studies, no analysis to assess the robustness of the results was computed, potentially leading to a biased representation of the study's outcomes).

3.5. Components of VR-CRTs

Each study used a different VR-based training system, which also differ in terms of immersion. Park and colleagues (2020) implemented their study through a touchscreen monitor that the person could interact with using different interactive attachments and controllers. Specifically, the setup was classified as semi-immersive because the attachments employed allowed participants to carry out actions typical of daily life (e.g., a doorknob for opening doors). Furthermore, Torpil and colleagues (2021) used Microsoft Kinect for their VR-based intervention, which consisted in a motion-sensing input device that allowed participants to interact with the virtual environment. Additionally, a 65-inch flat-screen LED screen television was used for the study. Unlike the one conducted by Park and colleagues (2020) however, no attachment was used to resemble the interaction with objects. Consequently, their setup could be considered semi-immersive, although the degree of immersion induced was probably lower. Finally, in the research project by Liao and colleagues (2019, 2020) a VR-based cognitive and physical training using the VIVE system by HTC was applied, which provided a fully immersive experience with VR glasses (head-mounted display) and hand controllers.

3.5.1. Cognitive components

In the included studies, VR-based cognitive rehabilitation was performed using interactive games that were supposed to train cognitive functions and improve functional autonomy, as in the case of games that were based on instrumental activities of daily life. For example, one research (Liao et al., 2019, 2020) employed games that required participants to take the subway, look for a store marked on a map, learn a recipe, and prepare a meal, as well as find and add specific items to a shopping basket in a store. Similarly, another study (Park et al., 2020) asked participants to perform instrumental activities such as batching, cooking, and shopping, using a system that was specifically targeted to VR-based cognitive rehabilitation. On the other hand, Park and colleagues (2020) based their VR intervention on commercially available games that were not specific to daily activities, such as Jet Run, a racing game in which the individual was supposed to control an avatar through jumping and body movements. The rationale behind it was that the selected games required many cognitive abilities such as attention, visuospatial orientation, and cognitive time management.

3.5.2. Physical components

All the studies included physical training to some degree. For example, the commercially available games used in one study (Torpil et al., 2021) intrinsically required motor abilities and visuomotor coordination, as in the case of Jet Run. In the study by Park and colleagues (2020) strengthening of the upper limbs was achieved through the constant use of the grip air bulb and attachments. Finally, Liao and colleagues (2019, 2020) included a simplified 24-form Yang-style Tai Chi, resistance exercise, aerobic exercise, as well as some functional tasks to enhance balance, stability, strength, and physical endurance.

4. Discussion

The present work aimed to evaluate the efficacy and effectiveness of VR-based cognitive treatments (VR-CRT) in comparison with conventional face-to-face and/or paper and pencil cognitive rehabilitation (CRT) for older adults with MCI, as well as investigating eventual differences based on the level of immersion induced by the VR systems. Indeed, comparing VR-based cognitive training with conventional face-to-face training provides valuable insights into the strengths, limitations, and potential applications of VR technology in cognitive training and helps make informed decisions about the most suitable approach for different individuals, settings, and objectives. Noteworthy, a meta-analysis could not be conducted due to the low number of studies included and the heterogeneity of outcome measures employed. Indeed, only 4 studies, conducted with different types of VR, emerged from the systematic review. Notably, 2 of these studies were merged as they reported different outcomes from the same research investigation. Interestingly, although the review took into consideration papers published in the last two decades, all the included studies were published within the last four years. Although the low number of studies that directly compared the two types of cognitive intervention allows us to make only some speculations about the efficacy of VR-CRTs, overall results might suggest that VR-based cognitive training could be at least as effective as conventional cognitive training, conducted face-to-face (Liao et al.,

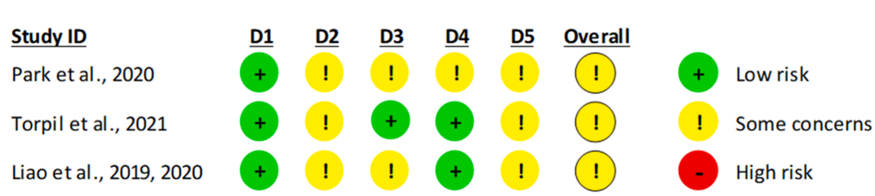

Fig. 2. Risk of bias assessment. D1: Randomization process; D2: Deviations from the intended interventions; D3: Missing outcome data; D4: Measurement of the outcome; D5: Selection of the reported result.

2019, 2020; Park et al., 2020; Torpil et al., 2021). Indeed, the findings encourages further research about the application of VR technology for cognitive rehabilitation and prevention of cognitive impairment, as it might represent a valuable tool in clinical practice, particularly in cases where face-to-face therapy may be limited or unavailable, thus providing a potentially viable alternative or supplement to traditional therapy methods. Indeed, the immersive and interactive nature of VR environments may effectively engage individuals and promote cognitive improvements. Notably, the efficacy of technology-based interventions for people with MCI may depend on a variety of factors that should be carefully addressed, such as the type of technology employed and living situation. Older adults may be less familiar with the use of technology and may be more prone to have negative beliefs and attitudes toward it in comparison with younger individuals (Liu et al., 2020; Yusif et al., 2016). Accordingly, it was suggested that the effectiveness of VR-CRT may depend on the level and quality of support individuals receive from caregivers and professional figures (Domenicucci et al., 2022). Consequently, it may be particularly challenging to develop VR-CRTs that are feasible for older adults with MCI or dementia and to investigate their efficacy and effectiveness in a standardized and unbiased way. Particularly, VR may be beneficial to people with MCI as it offers an immersive and more ecological training setting. However, it should be noted that low-immersive VR settings usually require the use of controllers or keyboards to interact with the environment, which may be harder for older individuals to understand and familiarize themselves with. On the other hand, semi- and full-immersive VR-based systems could be easier to interact with as they typically allow individuals to interact with objects in a way that is more similar to real-life situations, but they are also usually more expensive and hardly implementable in at-home settings (Tuena et al., 2020). In the present review, VR-CRTs resulted to be at least as effective as CRT regardless of the level of immersion. However, studies that employed semi-immersive environments (Park et al., 2020; Torpil et al., 2021) reported that VR-CRTs were superior to CRTs in more cognitive dimensions in comparison with the study conducted using a fully immersive VR-CRT (Liao et al., 2019, 2020). Notably, it remains unclear whether those differences are due to the high heterogeneity in the outcome measures and methodology employed or the technological systems applied. Noteworthy, in the analyzed papers participants' gender was initially recorded solely for descriptive purposes within the sample characterization, yet it was not factored into the subsequent analyses investigating potential gender-based differences in dementia. Moreover, it's remarkable that in one referenced research (Liao et al., 2019, 2020), an imbalance in gender representation was observed, with a greater proportion of women than men, potentially introducing confounding variables. Additionally, the consideration of ethnicity, a crucial determinant in dementia, was regrettably absent from the sample description in all the articles. Similarly, individual differences in many related lifestyle factors such as diet, physical activity, and the socioeconomic status was not considered in any of the considered papers. The oversight of this significant factor may have implications for the comprehensive understanding of dementia-related differences within diverse populations (Khemka et al., 2023; Meng et al., 2022; Mielke et al., 2022; Rosselli et al., 2022; Milani et al., 2020; Quiñones et al., 2020; Salazar et al., 2020; Podcasy and Epperson, 2016; Lin et al., 2015). Additionally, while the included studies showed improvements in many cognitive domains, it should be noted that less promising results were found for working memory and short-term memory (Park et al., 2020; Torpil et al., 2021), for which other forms of digitalized cognitive training such as computerized cognitive training (CCT) may be more useful (Hu et al., 2021; Zhang et al., 2019). Indeed, CCTs usually employ traditional computer programs or apps to deliver cognitive exercises and activities that focus on improving cognitive functions like memory, attention, and problem-solving through screen-based tasks that do not comprise virtual environments. In contrast, VR-based cognitive training leverages virtual reality technology to create immersive and multisensory environments that allow individuals to practice cognitive skills in simulated real-world contexts and facilitate transfer of acquired skills into real life (Son and Park, 2022). However, if not properly designed, VR-based interventions may be less suitable than other forms of cognitive rehabilitation to train specific cognitive processes such as working memory, which may need a more intense and specific training to be adequately enhanced (Morrison, Chein, 2011).

Finally, it may be important to consider that cognitive assessment in older adults can sometimes be challenging and may not always provide completely reliable results for several reasons. For example, fluctuations in cognitive performance due to tiredness, mood, or other situational factors may lead to misleading interpretations of the results (Gamaldo and Allaire, 2015). Additionally, the employment of tools that do not have parallel forms for test-retest evaluation may be subjected to the practice effect, which may lead to an apparent improvement that is nevertheless due to practice rather than actual cognitive changes (Goldberg et al., 2015). For these multiple reasons, a greater number of studies conducted with comparable outcome measures and technology are needed to evaluate the effect of VR in cognitive rehabilitation.

4.1. Limitations

The current systematic review has several limitations. Firstly, given the adopted screening process, some relevant studies may have been excluded due to language restrictions or limited databases accessed. Accordingly, it was not possible to include in the analysis studies that have not been published due to publication bias. Moreover, being VR interventions still not well defined, keywords selected for the literature search might have left out articles that evaluated the effects of specific therapeutic techniques. Noteworthy, the restricted pool of studies that met the inclusion criteria, comprising small sample sizes and divergent methodological approaches, strongly restricts the generalizability of findings and may not fully capture the broader landscape of VR-based cognitive training for older adults with MCI. Accordingly, it is not possible to draw robust conclusion nor to identify optimal practices regarding the implementation of VR-CRTs. Consequently, the findings of the present systematic review should be interpreted carefully.

4.2. Future directions

Future research should focus on evaluating the efficacy and effectiveness of VR-based cognitive interventions using conventional cognitive rehabilitation therapy as an active comparator to ensure that the proposed solutions are at least as effective as their conventional counterparts. Additionally, it should evaluate whether differences exist based on the level of immersion induced by different types of VR technology. Moreover, it should monitor the progression of cognitive decline by implementing longitudinal studies, as they could be crucial for determining the practical utility and real-life impact of VR-based cognitive interventions. Indeed, longitudinal studies comparing VR-based and face-to-face cognitive training can assess the generalizability of acquired skills to real-world functioning and everyday tasks. Furthermore, they would provide an opportunity to identify the most effective training approach for individuals with cognitive decline: by monitoring participants' progress, it could be possible to assess which method yields superior outcomes and facilitate the development of personalized training protocols tailored to the specific needs and progression of individuals with cognitive decline. Accordingly, by analyzing the rate and patterns of cognitive decline in participants, some markers or indicators that predict disease progression might be identified, which may promote early detection, intervention planning, and prognostic assessment for individuals at risk of pathological cognitive decline. Similarly, future research should aim at discerning how baseline characteristics can serve as predictive indicators of the effectiveness of VR-based cognitive rehabilitation, thus allowing for a more tailored and targeted approach that would empower clinicians and researchers to identify which individuals may benefit the most from VR-based cognitive rehabilitation, thereby enhancing its clinical relevance in the broader landscape of cognitive health interventions. Accordingly, future research should delve deeper into exploring how various factors known to impact dementia, including gender, ethnicity, and lifestyle elements may influence the efficacy and effectiveness of rehabilitation interventions. Understanding how these multifaceted determinants interplay with the outcomes of rehabilitation strategies is paramount in optimizing interventions for individuals affected by cognitive impairment as it allows to conduct more targeted and inclusive rehabilitation approaches that are responsive to the diverse and intricate needs of all the individuals who may suffer from cognitive impairment.

Finally, when possible future research should implement instruments with parallel forms in cognitive assessment to avoid misleading results caused by the practice.

5. Conclusion

VR-CRT for older adults with MCI might be an effective and ecological alternative to conventional cognitive interventions, as they provide a simulation of real-life scenarios and daily activities that may allow older adults to practice cognitive skills in contexts similar to their everyday lives, as well as providing them with a real-time adjustment of task difficulty, which could facilitate individuals to receive a personalized rehabilitation based on their actual needs. Indeed, VR-CRTs were found to be at least as effective as conventional face-to-face cognitive rehabilitation therapy in improving global cognitive function and executive functions, with additional benefits in terms of motivation and interest. However, at the current state, not enough well-designed research was published to allow a well-defined understanding of the effects on cognitive functioning induced by VR-CRT in comparison to other forms of cognitive interventions. Nevertheless, although scarce, the results of the studies included in the present systematic review seem promising and future research is encouraged to test the efficacy and effectiveness of VR-CRTs, as well as the eventual role of the degree of immersion and perceived difficulty induced by different VR systems. Indeed, if, the results arising from the present systematic review are replicated, virtual reality technology may have the potential to revolutionize cognitive rehabilitation by improving outcomes for older adults with Mild Cognitive Impairment, for which a cure is not yet available. Notably, clinicians and researchers that are considering VR interventions for older adults should carefully evaluate the accessibility and comfort levels of the VR technology for older adults, taking factors such as user-friendliness, adaptability for varying cognitive abilities, and the need for technical support into account. Furthermore, a decision about the level of immersivity and the device used should be tailored by the specific and individual clinical needs, as different cognitive components may benefit from different types of VR-based CRT. Additionally, the presence and severity of potential side effects such as nausea induced by VR system should be carefully evaluated and monitored. Accordingly, regardless of the VR technology adopted, rigorous outcome assessment and continuous monitoring of progress should be conducted to measure the effectiveness of VR interventions accurately."

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Carla Tortora: Conceptualization, Methodology, Formal analysis, Investigation, Data curation, Visualization, Writing – original draft. **Adolfo Di Crosta**: Data curation, Methodology, Writing – review & editing, Visualization. **Pasquale La Malva**: Data curation, Methodology, Writing – review & editing. **Giulia Prete**: Methodology, Software, Supervision. **Irene Ceccato**: Methodology, Software, Supervision, Validation. **Nicola Mammarella**: Conceptualization, Resources, Supervision, Visualization. **Alberto Di Domenico**: Conceptualization, Resources, Software, Supervision, Visualization. **Rocco Palumbo**: Conceptualization, Project administration, Resources, Supervision, Validation, Visualization, Writing – review & editing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

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