Effects of VR Training on Cognitive Function and Neural Mechanisms in Older Adults with Mild Cognitive Impairment

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Abstract

Elderly individuals with mild cognitive impairment (MCI) constitute a high-risk population for dementia; however, their brains retain plasticity. Training interventions based on virtual reality (VR) technology can help delay the progression from MCI to dementia. VR training can improve overall cognitive function in elderly individuals with MCI, particularly memory, attention, and executive function, with intervention efficacy influenced by factors such as immersion level, training format, and task content. VR training enhances neural activity efficiency in the brains of elderly individuals with MCI, manifested as changes in activation levels of relevant brain regions and improved inter-regional connectivity. VR training is expected to become a complementary approach for cognitive improvement in elderly individuals with MCI; future research should clarify the dose-response relationship of VR interventions, investigate its long-term effects, and deeply explore the underlying mechanisms through which VR training improves cognitive function in elderly individuals with MCI.

Full Text

Effects of VR Training on Cognitive Function in Older Adults with Mild Cognitive Impairment and Its Neural Mechanisms

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Abstract: Older adults with mild cognitive impairment (MCI) represent a high-risk population for dementia; however, their brains retain considerable plasticity. Virtual reality (VR)-based training interventions can help delay the progression from MCI to dementia. VR training improves overall cognitive function in elderly individuals with MCI, particularly in memory, attention, and executive function, with intervention effects influenced by factors such as immersion level, training modality, and task content. VR training enhances neural activity efficiency in MCI patients, manifested through altered activation levels in relevant brain regions and increased inter-regional connectivity. VR training shows promise as a supplementary approach for cognitive improvement in MCI patients. Future research should clarify the dose-response relationship of VR interventions, examine long-term effects, and further explore the underlying mechanisms through which VR training improves cognitive function in elderly MCI patients.

Keywords: virtual reality, mild cognitive impairment, elderly, cognitive function, brain function

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Mild cognitive impairment (MCI) refers to a condition in which the degree of impairment in multiple cognitive domains—including memory, attention, and executive function—exceeds what would be expected from normal aging alone, yet does not meet diagnostic criteria for dementia or Alzheimer's disease (Petersen, 2003; Winblad et al., 2004). Older adults with MCI constitute a high-risk group for dementia, with incidence rates reaching 14.9% among MCI patients over 65 years of age (Petersen et al., 2018), substantially higher than the 1–2% incidence observed in the general population (Roberts et al., 2014). Nevertheless, research indicates that the brains of elderly MCI patients retain plasticity and that the MCI state is partially reversible, providing a critical window for dementia prevention (Belleville et al., 2011; Walsh et al., 2020).

Current interventions for cognitive function in MCI patients fall into three main categories. The first addresses transient cognitive decline resulting from other medical conditions or medication side effects by modifying external factors. The second involves pharmacological interventions; however, existing drug therapy research yields numerous contradictory results and adverse events (董宣如, 2020). The third category comprises non-pharmacological interventions, which currently receive the most attention and focus primarily on cognitive training and physical exercise. For older adults, limitations in physical mobility, restricted activity ranges, and facility constraints can hinder participation in certain exercises, while most cognitive tasks are monotonous and lack appeal, resulting in low sustained engagement and consequently diminished intervention efficacy.

Virtual reality (VR) technology, as an emerging approach, provides users with multisensory, dynamic, and interactive virtual environments (Doniger et al., 2018). Different VR devices can alter the sense of immersion in virtual worlds and the perception of the real world. Non-immersive virtual reality (NIVR) utilizes computers or gaming systems controlled via mouse, keyboard, or gamepad, offering the lowest level of virtual environment immersion (Salatino et al., 2023). Semi-immersive virtual reality (SIVR) typically comprises screens, haptic feedback devices, and infrared cameras, allowing users to perceive the real world while interacting with the virtual environment (Bamodu & Ye, 2013). Immersive virtual reality (IVR) generally includes head-mounted displays and hand controllers, achieving complete visual occlusion (Salatino et al., 2023). VR systems can record user task data and provide feedback as needed while integrating with health monitoring, motion capture, and eye-tracking devices, making them ideal platforms for cognitive and motor training programs (Kwan et al., 2021). VR-based training interventions have been applied to enhance cognitive function in elderly MCI patients.

VR training refers to interventions that involve completing a series of tasks in virtual environments to improve individual cognitive function levels, encompassing various content types such as daily living tasks, skill-learning tasks, function-oriented tasks, and serious games. Based on whether large muscle group movements are performed, these can be categorized as physical training, cognitive training, or combined training integrating both elements. Diverse forms and content can enhance rehabilitation motivation and promote active patient participation (Jong-Hwan Park et al., 2020). VR training imposes minimal space requirements, typically feasible in ordinary living spaces, thereby overcoming barriers related to geographic distance, mobility limitations due to physical decline, and economic burden. Since the user's actual environment is controllable, safety is higher compared to traditional interventions conducted in real-world settings. Additionally, environments tailored to training content increase MCI patients' task engagement, thereby improving intervention completion rates and sustainability.

Research on VR applications as a cognitive impairment treatment tool has grown rapidly following the COVID-19 pandemic and associated mobility restrictions worldwide (Hu et al., 2021; Jahn et al., 2021). Studies demonstrate that elderly MCI patients show significant improvements in overall cognitive function, memory, attention, and executive function following VR training, accompanied by corresponding positive changes in brain function during both task and resting states. However, the magnitude of benefit, long-term effects, and underlying mechanisms of VR training for improving various cognitive functions in elderly MCI patients remain unclear. As VR training shows promise as an adjunctive treatment for MCI, summarizing research findings on VR technology's role in improving cognitive function in elderly MCI patients, clarifying relevant influencing factors, and examining associated brain function changes can facilitate further research and real-world application, ultimately enhancing health outcomes for older adults.

2.1 Overall Cognitive Function

Assessment of overall cognitive function in elderly MCI patients typically employs the Montreal Cognitive Assessment (MoCA) and the Mini-Mental State Examination (MMSE). A systematic analysis of three studies by Tortora et al. (2024) found VR training and traditional cognitive therapy to be equally effective in improving overall cognitive function in elderly MCI patients. Other studies suggest VR training may produce more pronounced effects than conventional cognitive or physical training.

In Liao et al. (2020), MCI patients in the experimental group received 12 weeks of immersive VR combined training. Physical training included aerobic and resistance exercises along with function-oriented tasks such as window cleaning, goldfish scooping, and obstacle navigation, while cognitive training utilized four different types of VR games. The control group underwent equivalent physical and cognitive training in real-world settings. Post-intervention, only the experimental group demonstrated significant improvement in MoCA scores. Another randomized controlled study assigned MCI patients in the experimental group to non-immersive VR kayaking training, while the control group performed home exercises including Williams flexion exercises, side leg raises, and prone leg lifts. After six weeks, the experimental group showed significant improvement in both MoCA and General Practitioner Assessment of Cognition (GPCOG) scores, with significant between-group differences (Choi & Lee, 2019). Similar results were observed in a study targeting patients with both physical frailty and MCI: following eight weeks of immersive VR combined training, the experimental group showed significant MoCA score improvement, whereas the control group participating in real-world exercise and tablet-based cognitive training showed no significant changes (Kwan et al., 2021).

However, some studies indicate that VR training does not significantly affect overall cognitive function in elderly MCI patients. In these studies, experimental groups undergoing four to eight weeks of immersive VR combined training or immersive VR cognitive training with game elements showed only non-significant slight improvements or no changes in MMSE scores (Mrakic-Sposta et al., 2018; Thapa et al., 2020; Kang et al., 2021). These discrepancies may result from differences in scale sensitivity. Research indicates that MoCA outperforms MMSE in MCI screening, demonstrating higher sensitivity (Ciesielska et al., 2016; Zhao et al., 2023) and more accurately reflecting cognitive changes. In MCI research, the two measures typically serve different purposes; for example, in Goumopoulos et al. (2023), MMSE was used only to exclude dementia patients during screening, while MoCA assessed cognitive changes pre- and post-intervention. Some studies report different findings, with significant MMSE score improvements following immersive or semi-immersive VR training (Amjad et al., 2019; Yang et al., 2022). However, substantial heterogeneity exists across these studies in VR training content design, intervention duration and frequency, and device type, necessitating further investigation into whether assessment sensitivity differences account for these divergent results.

2.2 Memory

Memory impairment represents a hallmark feature of dementia (Ban et al., 2020). As a prodromal state of dementia, MCI is characterized by compromised episodic memory, which shows sharp decline in pathological aging such as Alzheimer's disease (Christman et al., 2020). Verbal learning tests are commonly used to assess episodic memory changes following VR intervention. In Jin-Hyuck Park (2022), MCI patients in the experimental group underwent non-immersive VR training, completing tasks such as acquiring gems and locating positions in virtual environments. Results showed significant improvement in recall test scores after eight weeks of intervention, while recognition performance showed no significant changes. Goumopoulos et al. (2023) obtained similar results, administering personalized ten-item cognitive tasks based on patients' cognitive profiles during a 12-week semi-immersive VR training program. Rey Auditory Verbal Learning Test (RAVLT) results indicated that compared to the control group receiving normal daily activities and care, the experimental group showed significant improvement in delayed recall and slight enhancement in recognition testing.

Although some studies demonstrate positive effects of VR training on memory function in elderly MCI patients, its superiority over other interventions remains unconfirmed. In a randomized controlled study, both RAVLT and Rey-Osterrieth Complex Figure Test (RCFT) results indicated that after ten weeks of intervention, MCI patients undergoing semi-immersive VR motor training did not show significantly greater improvement than the control group using computers for cognitive training (Ji-Hyuk Park & Jin-Hyuck Park, 2018). In another study of stroke patients with MCI, researchers used the Digit Span Test (DST) to assess immediate memory, short-term memory, and working memory. After six weeks of intervention, both the experimental group receiving immersive VR cognitive training and the control group undergoing traditional cognitive training showed significant memory function improvement, with no between-group differences (Liu et al., 2022).

Currently, the efficacy of VR training for improving memory function in elderly MCI patients remains controversial. A systematic review by Yan et al. (2022) showed that VR combined training integrating cognitive and physical interventions did not produce positive effects on memory function in elderly MCI patients. However, a subsequent meta-analysis indicated that VR training significantly improved short-term memory in elderly MCI patients (Yu et al., 2023). Methodological limitations prevent some studies from yielding robust evidence. For instance, in Maeng et al. (2021), MCI patients showed significant verbal memory improvement after four weeks of immersive VR supermarket shopping training, but the absence of a control group precludes ruling out confounding factors. In another study of elderly individuals with subjective cognitive decline or diagnosed MCI, verbal memory delayed recall scores improved significantly after four weeks of immersive VR cognitive training compared to baseline; however, since both experimental and control groups took dementia-preventive medication during the intervention period and between-group differences were non-significant, the improvement cannot be definitively attributed to VR training (Kang et al., 2021).

2.3 Attention

Attention deficits represent an important manifestation of Alzheimer's disease, appearing early in the disease course (Perry et al., 2000). A meta-analysis by Zhu et al. (2021) of 14 randomized controlled studies using VR training to intervene in cognitive function among elderly MCI or dementia patients demonstrated that VR training significantly improved attention in experimental groups. Subsequent research further confirmed this conclusion: Torpil et al. (2021) randomly assigned 64 MCI patients to two groups, with the experimental group receiving four different types of non-immersive VR cognitive training alongside conventional cognitive rehabilitation, while the control group received only conventional training. After 12 weeks, both groups showed significant improvement in attention as measured by the LOTCA-G cognitive assessment system, with the experimental group demonstrating significantly greater improvement.

Research findings vary considerably regarding whether VR interventions produce superior effects compared to other modalities. In a randomized controlled study by Ji-Hyuk Park and Jin-Hyuck Park (2018), the experimental group of elderly MCI patients underwent semi-immersive VR motor training while the control group used computers for cognitive training encompassing attention, memory, and visuospatial abilities. After ten weeks, both groups showed significant attention improvement, with the experimental group demonstrating significantly greater enhancement, indicating superior effects of VR training. Conversely, in a study of elderly patients with post-stroke MCI, no significant differences in attention improvement were observed between the experimental group receiving immersive VR cognitive training and the control group undergoing traditional cognitive training (Liu et al., 2022).

Current evidence regarding attention function remains relatively limited, with some studies exhibiting methodological deficiencies. In Zhu et al. (2022), 18 elderly MCI patients and 13 dementia patients underwent five weeks of immersive VR virtual supermarket tasks, with results showing significant attention improvement across all participants; however, the absence of a control group precludes excluding confounding factors. In studies by Thapa (2020) and Yang (2022), researchers observed positive changes in brain activity related to attention in elderly MCI patients following immersive VR training using EEG technology, but lacked corresponding behavioral evidence of change.

2.4 Executive Function

Executive functions involve high-level cognitive abilities related to planning, initiating, monitoring, and inhibiting goal-directed behavior, with core components including inhibitory control, working memory, and cognitive flexibility (Diamond, 2013). The Trail Making Test (TMT) is commonly used to detect executive dysfunction, comprising two subscales: TMT-A primarily assesses visuospatial ability and psychomotor speed, while TMT-B evaluates processing speed and cognitive flexibility (田金洲 et al., 2016). In Amjad et al. (2019), 22 elderly MCI patients in the experimental group underwent semi-immersive VR training encompassing five domains: logic, memory, reaction, mathematical calculation, and physical activity. The intervention lasted 25–30 minutes per session, five times weekly for six weeks. The control group performed normal joint activities and upper/lower limb stretching exercises during the same period, with participants ensured to avoid any electronic gaming activities. Results showed significant reductions in both TMT subscale scores in the experimental group, indicating improved executive function. Two additional randomized controlled trials implementing six weeks of non-immersive VR cognitive training and 12 weeks of immersive VR cognitive training obtained similar results (J. S. Park et al., 2020; Goumopoulos et al., 2023). Some studies observed significant improvement only in subscale A (Maeng et al., 2021; Yang et al., 2022), while others noted improvement only in subscale B (Liao et al., 2019; Thapa et al., 2020).

Some studies employed the backward digit span task from DST to assess working memory changes pre- and post-intervention. In Liu et al. (2022), both the experimental group receiving immersive VR cognitive training and the control group undergoing traditional cognitive training showed significant DST improvement after six weeks, without between-group differences. In Ji-Su Park et al. (2020), the experimental group of elderly MCI patients received six weeks of VR cognitive-motor rehabilitation while the control group performed conventional cognitive rehabilitation activities; both groups showed significant within-group differences in forward and backward DST, with the experimental group demonstrating superior improvement in forward testing. Another study using immersive VR cognitive training based on Korean traditional culture for 12 weeks in elderly MCI patients found no significant within- or between-group DST changes compared to a control group maintaining normal daily activities (Jong-Hwan Park et al., 2020). Research indicates that TMT-B can also reflect working memory levels (Llinas-Regla et al., 2017). Thapa et al. (2020) found that elderly MCI patients in the experimental group showed significantly reduced TMT-B completion time after immersive VR cognitive training, indicating working memory improvement, while the control group receiving health education showed increased completion time.

Regarding inhibitory control, a meta-analysis of three randomized controlled studies using the Stroop color-word test concluded that VR training did not improve this executive function in elderly MCI patients (Yu et al., 2023). A subsequent randomized controlled trial found no significant improvement in Stroop performance after ten weeks of semi-immersive VR cognitive training or computer-based cognitive training (Ji-Hyuk Park & Jin-Hyuck Park, 2018), consistent with previous findings. Another meta-analysis indicated that VR combined interventions did not show significant positive effects on executive function in elderly MCI patients (Yan et al., 2022). However, executive function encompasses planning, decision-making, and volitional processes (Potmesilova et al., 2023), representing comprehensive abilities required for task completion. Whether VR training can improve other executive functions and daily task performance in elderly MCI patients requires further investigation.

3.1 Immersion Level

The degree of immersion in virtual environments influences VR training efficacy in elderly MCI patients. High-immersion virtual environments produce the strongest "sense of presence." Immersive virtual environments may facilitate specific functions in cognitively impaired patients, affecting communication, interaction, motivation, engagement, and positive attitudes toward others (Garcia et al., 2012). Compared to non-immersive VR, immersive VR creates stronger presence and provides more accurate spatial cognitive cues, enabling better task performance (Tseng & Giau, 2022). Immersive VR devices offer richer sensory experiences, but this increases the likelihood of cybersickness—the most common discomfort symptom associated with VR use, typically including nausea, disorientation, and oculomotor symptoms (Kennedy et al., 1993). Discomfort symptoms can reduce engagement, compromise safety, cause task interruption, adverse events, and poor sustainability, thereby diminishing VR training efficacy. Research indicates that elderly MCI patients experience higher proportions of disorientation and nausea symptoms compared to healthy older adults (Maeng et al., 2021). When using semi-immersive or non-immersive VR devices, the ability to simultaneously perceive the real world significantly reduces cybersickness symptoms, though lower immersion may limit ecological validity (Tuena et al., 2020).

Increasing immersion in VR training can enhance user-environment interaction frequency, provide more information for processing, and improve task engagement. Moreover, VR training simulating real environments, being closer to real-life scenarios, can reproduce everyday experiences as realistically as possible, thereby improving ecological validity and enhancing VR training's effectiveness in improving cognitive function in elderly MCI patients. Conversely, reducing immersion can effectively decrease cybersickness symptoms, improve training safety and sustainability, and enhance training completion rates, thereby improving efficacy. Additionally, non-immersive virtual environments provided by computers, tablets, TV projections, or smartphones are more cost-effective, increasing the likelihood of spontaneous, long-term use by elderly MCI patients in daily life.

3.2 Training Modality

Cognitive training or physical training represent common forms of VR training for elderly MCI patients. VR combined training integrates both modalities, including cognitive tasks and physical exercise, with serial training referring to separate execution of the two task types and parallel training involving simultaneous execution (Herold et al., 2018). A systematic review by Lauenroth et al. (2016) demonstrated that in non-virtual environment training interventions, combined training more effectively promoted cognitive function in older adults or neurodegenerative disease patients compared to single-modality physical or cognitive training. In virtual environments, combined training also effectively improves cognitive function in elderly MCI patients. Yan et al. (2022) conducted a meta-analysis of eight randomized controlled studies using VR combined training for elderly MCI patients, finding that VR combined training significantly improved overall cognitive function, with parallel training demonstrating superior effects compared to serial training.

Compared to healthy controls, MCI patients exhibit deficits in complex daily activity abilities, with instrumental activities of daily living (IADL) related to memory and frontal executive functions particularly severely affected (Ahn et al., 2009). Significant improvements in executive function and immediate memory following cognitive training do not transfer to IADL (Bruderer-hofstetter et al., 2018), while both cognitive ability and physical function are crucial for IADL (Burton et al., 2018; Lai et al., 2022). Combined interventions integrating cognitive and physical training may further promote cognitive function improvement by better enhancing IADL in elderly MCI patients. Parallel VR combined training typically requires participants to allocate attention, formulate plans, make decisions, coordinate physical activities with instructions or cues, and maintain volition—a coherent and logical process more closely resembling daily activities. This training modality can improve complex daily activity abilities in elderly MCI patients and thus demonstrates more significant cognitive improvement effects compared to single-modality training. However, due to varying degrees of physical decline in older adults, some elderly MCI patients are not suitable for VR physical training for safety reasons. When implementing single-modality VR cognitive training, efficacy can be enhanced through targeted training of relatively weak cognitive functions or by designing comprehensive tasks approximating daily activities.

3.3 Task Content

VR training content in existing studies exhibits considerable diversity. Virtual supermarkets represent a common VR intervention scenario, with researchers typically designing different tasks according to study objectives. Mrakic-Sposta et al. (2018) implemented route selection and correct product identification tasks to train attention and visuospatial abilities, while Zhu (2022) and Maeng (2021) incorporated list-recall tasks into the shopping process to train memory function. Given the diverse etiologies of MCI and substantial individual differences in symptom presentation, personalized content is more beneficial for improving individual cognitive function than uniformly prescribed training content. Goumopoulos et al. (2023) combined and sequentially allocated independent training tasks targeting memory, attention, perception, and executive function, providing targeted training based on individual cognitive weaknesses. Results showed significant improvement across all cognitive domains in elderly MCI patients, with increased self-efficacy scores; 70% of participants expressed willingness to continue training after the experiment due to perceived effectiveness and improved quality of life. Some MCI patients experience subjective cognitive complaints—awareness and judgment of their own cognitive decline—and completing desired task content may enhance self-efficacy, facilitating cognitive improvement.

In VR training based on real-world activities, the authenticity, timeliness, and cultural appropriateness of task scenario details directly affect task completion. According to the neural mismatch model, unpleasant symptoms emerge when sensory information is inconsistent with individuals' past experiences (Reason, 1978). For example, in supermarket task scenarios, mismatches between product packaging and participants' prior purchasing experiences can cause difficulties in task completion (Mrakic-Sposta et al., 2018). In Faria et al. (2016), stroke patients with cognitive impairment completed cognitive tasks in scenarios including supermarkets, post offices, banks, pharmacies, and connecting city streets, which displayed billboards, real-world products, and locally familiar trademarks. This helped participants connect the VR world with their real-world experiences, preventing task failure due to information inconsistency. Additionally, due to individual differences, VR training content designed based on real-world activities that does not align with participants' daily habits may generate boredom and reduce intervention efficacy. In Zhu et al. (2022), the VR group underwent five weeks of intervention with three training days per week, each requiring three 20–30 minute virtual supermarket tasks; one elderly MCI patient who disliked real-life shopping found the intervention overly frequent.

Some VR training is designed based on game training. Research indicates that VR interventions incorporating game elements produce more significant cognitive impairment improvements than cognitive training programs alone (Moulaei et al., 2024), and virtual rewards for task completion enhance user motivation (Ferreira-Brito et al., 2019). Game elements increase fun, enhancing motivation intensity and task engagement, thereby improving training completion and sustainability. However, compared to traditional game training, VR training requires operation of multiple novel devices, necessitating consideration of characteristics of elderly MCI patients and their technology acceptance. Mondellini et al. (2022) found significant differences in VR technology acceptance between Estonian and Italian elderly MCI patients, with less accepting Estonian participants showing significantly reduced willingness to continue VR training after experiencing the tasks. Research indicates that elderly MCI patients experience anxiety when facing unfamiliar new technologies (Goumopoulos et al., 2023), require more assistance learning to use VR devices (Hassandra et al., 2021), and still need professional support during formal training even after instruction (Maeng et al., 2021). Some elderly MCI patients also reported incomplete comprehension of training instructions (Liu et al., 2022). When game-element VR training content exhibits high novelty, the negative impacts of increased device operation difficulty and more numerous or complex instructions may offset the motivational advantages of game-based training, potentially reducing training efficacy.

4 Neural Mechanisms of VR Training Effects on Cognitive Function in Elderly MCI Patients

The potential mechanisms through which VR training improves cognitive function in elderly MCI patients remain unclear. Current explanations suggest that virtual environment stimulation activates brain metabolism, increases cerebral blood flow and neurotransmitter release (You et al., 2005; Carrieri et al., 2016), and reactivates and improves various cortical functions (García-Betances et al., 2015; Carrieri et al., 2016). Current research primarily uses electroencephalography (EEG), functional near-infrared spectroscopy (fNIRS), and functional magnetic resonance imaging (fMRI) to observe brain function changes in elderly MCI patients during VR training. VR training affects brain region activity related to cognitive function in elderly MCI patients during both resting and task states, showing phenomenological and magnitude differences from traditional motor and cognitive training. Furthermore, different VR content produces different effects on brain function in older adults. Analyzing brain function changes in elderly MCI patients during resting and task states can facilitate preliminary exploration of the neural mechanisms through which VR training improves cognitive function.

4.1 Effects of VR Training on Resting-State Brain Function Resting state refers to a condition in which participants perform no tasks (Xie et al., 2023). During this state, the brain expends substantial energy on spontaneous activity, with changes in regional blood flow and blood oxygen levels (Lv et al., 2018; Raimondo et al., 2021). Resting-state brain function imaging is commonly used to distinguish MCI patients from healthy older adults and identify potential markers predicting MCI conversion to Alzheimer's disease (Iliadou et al., 2021).

One study found positive changes in attention-related brain activity following VR training in elderly MCI patients (Thapa et al., 2020). Sixty-eight elderly MCI patients were randomly assigned to an experimental group receiving immersive VR training and health education or a control group receiving only health education. The experimental group completed 24 VR cognitive training sessions including four game series: juice making, crow shooting, fireworks sorting, and object memory. Researchers conducted resting-state EEG measurements before and after the eight-week intervention. Band power analysis revealed significantly reduced theta waves in parietal and temporal regions compared to baseline. Power ratio analysis showed decreased TBR (theta/beta ratio) in temporal and parietal brain regions. Research indicates that increased theta waves are associated with cognitive impairment risk (Prichep et al., 2006; Sánchez-Moguel et al., 2017), while higher TBR typically indicates mind-wandering and reduced attention (Van et al., 2019). Resting-state TBR negatively correlates with attentional control, attention restoration, and cognitive processing capacity (Angelidis et al., 2016; Putman et al., 2014; Clarke et al., 2019). Reduced theta waves following VR training indicate positive cognitive effects, while decreased TBR suggests improved attention levels.

Yang et al. (2022) further compared differences in brain band power, power ratios, and functional connectivity between immersive VR training and traditional exercise training in elderly MCI patients. Building upon Thapa et al. (2020), the researchers added an experimental group performing aerobic and resistance exercise in real-world settings and conducted resting-state EEG measurements post-intervention. Band power analysis revealed significantly reduced parietal theta power in the VR group compared to the exercise group, consistent with neuropsychological test results: Symbol Digit Substitution Test (SDST) results showed significantly greater improvement in the VR group, and while both groups demonstrated significant within-group differences in MMSE scores post-intervention, only the VR group showed significant between-group differences compared to the health education control group; TMT-A testing showed significant within-group differences only in the VR group. However, power ratio analysis favored the exercise group: both groups showed numerically lower parietal TBR than the control group, but only the exercise group demonstrated significant between-group differences; the exercise group also showed significantly lower DAR (delta/alpha ratio) in frontal and temporal regions post-intervention compared to the VR group. Research indicates that elevated DAR is associated with cognitive impairment (Finnigan et al., 2016). Furthermore, researchers found higher resting-state alpha connectivity in prefrontal cortex, anterior cingulate cortex, temporal, and parietal regions in the exercise group compared to the VR group post-intervention. A review showed reduced alpha connectivity in MCI patients compared to healthy populations (Lejko et al., 2020), potentially related to cholinergic dysfunction (Haense et al., 2012). Alpha waves are modulated by neurotransmitters such as acetylcholine (Suffczynski et al., 2001), and exercise increases acetylcholine levels (Li et al., 2022). Since the VR training in this study did not include physical exercise components, the exercise intervention produced higher alpha connectivity and more significant DAR improvement post-intervention. VR training can improve resting-state brain function indicators related to attention and cognitive control in elderly MCI patients, but when training content includes only cognitive components, its effects on inter-regional connectivity may be inferior to traditional exercise training.

In addition to EEG results, Kang et al. (2021) used fMRI to investigate brain functional connectivity in elderly patients with subjective cognitive decline and diagnosed MCI. The experimental group underwent immersive VR training twice weekly for four weeks, including eight task types targeting attention, memory, executive function, calculation, and visuospatial orientation, with game elements incorporated. Both experimental and control groups took dementia-preventive medication during the intervention. fMRI results revealed significantly increased connectivity in visuospatial function-related brain regions, including connections from right lateral visual cortex to left cingulate gyrus, right cingulate gyrus, left frontal pole, left superior frontal gyrus, anterior cingulate cortex, and white matter, as well as connections from medial visual cortex to right insular cortex, right frontal pole, right frontal cortex, right caudate nucleus, left caudate nucleus, right thalamus, left insular cortex, and white matter. Compared to the control group, increased functional connectivity in cortical and white matter regions in the VR group was associated with improved performance on the copy task of the Rey Complex Figure Test, indicating that VR training improved functional connectivity in brain regions related to visual function in elderly MCI patients.

4.2 Effects of VR Training on Task-State Brain Function Task state refers to brain activity during specific tasks such as memory, recognition, and movement. Research shows that cognitive training causes brain functional reorganization in older adults during task states, manifested as decreased or increased brain activity, or both (霍丽娟 et al., 2018).

Some studies observed reduced brain activation intensity or narrowed activation range following cognitive training in older adults (Brehmer et al., 2011; Vermeij et al., 2017), with similar phenomena observed in elderly MCI patients after VR training. In Liao et al. (2020), elderly MCI patients in the experimental group received immersive VR combined training while the control group underwent physical and cognitive training in real-world settings. After 12 weeks, researchers used 16-channel fNIRS to measure brain activation during MoCA assessment. Results showed significantly reduced activation in channels 7 and 13, left prefrontal cortex, right prefrontal cortex, and bilateral prefrontal cortex in the experimental group, while the control group showed significant reduction only in channel 10 and right prefrontal cortex. Researchers interpreted reduced post-training brain activation as improved neural efficiency due to intervention. Enhanced neuronal processing efficiency requires fewer neurons to perform the same tasks, representing more efficient neural representation and more precise neural circuits (Brehmer et al., 2011). Combined with neuropsychological performance, the VR training group showed significant improvement in overall cognitive function, executive function, immediate memory, delayed memory, and IADL, while the control group showed improvement only in executive function and immediate memory scores, with fewer brain regions showing reduced activation. This further demonstrates that non-virtual cognitive and physical training can improve cognitive function in elderly MCI patients, but with less pronounced effects than VR training.

Some studies found enhanced activation in local brain regions following cognitive training. The compensatory model posits that the aging brain maintains optimal cognitive function by increasing activation in specific regions and recruiting additional brain networks (Lustig et al., 2009), with similar phenomena observed in elderly MCI patients. Belleville et al. (2011) used fMRI to demonstrate increased activation in frontal, temporal, and parietal regions in elderly MCI patients following non-virtual memory training, including both pretraining activated regions and newly recruited alternative regions. Maintaining optimal memory function depends not only on increased activation of specific regions but also on newly activated brain areas (Cabeza, 2002; Reuter-Lorenz, 2002; Stern et al., 2005). Similar increased activation levels were observed under VR training conditions. Tian et al. (2023) conducted a pre-post experiment using 18-channel near-infrared spectroscopy to sample resting-state and task-state data in elderly MCI patients during a single VR game session. Seventeen participants played the 10-minute VR game "Beat Saber" with similar music and identical difficulty settings. Upon task completion, participants were divided into task completers (n=6) and non-completers (n=11). Analysis of six brain regions (left prefrontal, right prefrontal, left occipital, right occipital, left motor, and right sensorimotor) revealed statistically significant differences in right occipital lobe (ROL) and left occipital lobe (LOL) between groups, with non-completers showing higher activation levels in both resting and task states. From the compensatory model perspective, non-completers required stronger brain activation to maintain cognitive function. However, this study lacked a non-VR intervention control group, preventing determination of whether activation differences were attributable to VR training itself.

Furthermore, different virtual environment settings affect brain activation levels and whole-brain connectivity in cognitively impaired populations. Qu et al. (2023) used fNIRS to investigate brain activation in elderly participants during resting state and two VR task conditions (urban and natural environments). Wavelet amplitude (WA) results showed that VR intervention primarily affected the right motor cortex and right occipital lobe in cognitively impaired populations: right motor cortex WA significantly decreased under both VR conditions, while right occipital lobe WA significantly increased only in the natural environment condition. VR intervention also enhanced whole-brain connectivity, mostly bidirectional information connections, with natural environment tasks exerting more significant effects on brain network connectivity than urban environment tasks. Overall results indicated that VR natural environments provide greater brain stimulation than urban environments, supplementing details on brain function changes during task states in elderly cognitively impaired populations and offering new insights for future VR training content design.

5 Problems and Prospects

VR training can produce positive effects on various cognitive functions in elderly MCI patients and is gaining global popularity. However, the magnitude of benefits, mechanisms through which different factors influence intervention effects, and dose-response relationships remain unclear. Few follow-up reports after intervention completion make it difficult to determine long-term effects. Existing research has focused only on VR training effects on brain function in elderly MCI patients, lacking investigation of brain structural changes and other neurophysiological activities, leaving neural mechanism exploration incomplete and requiring further deepening.

5.1 Clarify Intervention Differences and Optimize VR Training Whether VR training effects on cognitive function in elderly MCI patients are equivalent or superior to traditional environment interventions remains controversial. Regarding overall cognitive function, empirical studies indicate VR training superiority, with two immersive VR combined training studies showing better effects than traditional combined training (Liao et al., 2020; Kwan et al., 2021) and one non-immersive VR motor training study demonstrating superiority over traditional motor training (Choi & Lee, 2019). For memory, two studies obtained equivalent improvement effects, with Ji-Hyuk Park et al. (2018) comparing semi-immersive VR motor training to computer-based cognitive training, and Liu et al. (2022) comparing immersive VR cognitive training to traditional cognitive training. For attention, studies show considerable variation: the aforementioned memory study by Ji-Hyuk Park et al. (2018) found significantly greater attention improvement in the VR group, while Liu et al. (2022) found no significant between-group differences. For executive function, studies also show substantial variation: Amjad et al. (2019) compared semi-immersive VR combined training to real-world motor training, finding significant executive function improvement only in the VR group. Another study comparing non-immersive VR cognitive training to conventional cognitive rehabilitation found executive function improvement in both groups, with superior improvement in the VR group compared to the control group performing desktop activities in real-world settings (J. S. Park et al., 2020). In Liu et al. (2022), immersive VR cognitive training and traditional cognitive training produced equivalent working memory improvement. Notably, some studies employed substantially different task forms between virtual and traditional environments, such as cognitive versus motor training (Ji-Hyuk Park & Jin-Hyuck Park, 2018) or combined versus motor training (Amjad et al., 2019). Additionally, research indicates that natural and urban virtual environments differentially affect brain network connectivity in older adults, with natural virtual environments providing greater brain stimulation (Qu et al., 2023). Therefore, whether differences between VR and traditional intervention effects stem from intervention modality or environment requires further clarification.

Virtual environments can be created through real-scene filming or modeling technology, with content derived from the real world or entirely from imagination and hypothesis, offering considerable flexibility. Compared to real environments, advantages include higher controllability—allowing rapid adjustment of weather, lighting, sound, and scene furnishings—while disadvantages include lack of sensory information beyond visual and auditory modalities and more restricted activity range, amplitude, and flexibility. VR training is designed based on virtual environment characteristics. The inherent limitations of this environment, along with unreasonable task design, low completion rates, and poor technology acceptance among participants, may explain why VR training did not produce ideal effects in some studies. Additionally, methods for enhancing intervention efficacy in traditional settings may be applicable to VR training. Research indicates that exercise programs containing at least two of aerobic, resistance, or balance training components are most effective for protecting overall cognition and executive function in MCI patients (Huang et al., 2022). Therefore, designing multi-component exercise in VR motor training may produce superior effects to single-modality exercise, though this requires appropriately designed control groups to exclude confounding factors.

5.2 Define Immersion Levels and Reveal Influence Mechanisms Current research shows that VR training immersion levels differentially affect improvement of specific cognitive functions in elderly MCI patients, but the reasons for these differences remain unclear. A meta-analysis by Yu et al. (2023) of 14 randomized controlled studies using VR training to improve cognition in elderly MCI patients found that semi-immersive VR interventions produced significantly better effects on cognitive flexibility than fully immersive and non-immersive VR interventions. For other cognitive functions, although no significant differences emerged among the three VR types, certain trends were observed: non-immersive VR subgroups achieved more significant improvements in overall cognitive function and short-term memory, while fully immersive VR showed slight advantages for attention intervention effects. Subgroup analysis from another meta-analysis indicated that semi-immersive VR produced more significant improvement in overall cognitive function in elderly MCI patients compared to immersive VR (边继萍 et al., 2023).

Result discrepancies may stem from different classification of VR device types. For example, a randomized controlled trial included in both studies (J. S. Park et al., 2020) used the MOTOCOG system with hardware including a touchscreen monitor and devices such as doorknobs, buttons, and steering wheels, with participants performing driving, cooking, and shopping activities in a 2D screen-displayed virtual environment. Yu et al. (2023) classified this as non-immersive VR, while 边继萍 et al. (2023) classified it as semi-immersive VR. Clear, unified standards for defining these two VR device categories using 2D screens are currently lacking. Altering VR training immersion levels can affect task engagement, ecological validity, and user experience, thereby influencing training efficacy. However, the mechanisms through which this factor affects intervention outcomes for specific cognitive functions require further investigation.

5.3 Clarify Dose-Response Relationships and Explore Long-Term Effects Researchers typically implement long-term VR training lasting 4–12 weeks, with 2–3 sessions per week, each lasting 15–100 minutes, though VR intervention intensity currently lacks clear definition. Limitations of existing research include small sample sizes, unclear long-term effects, and failure to consider sex differences. Dose-response relationship research remains scarce, with only Amjad et al. (2019) comparing effects of single-session versus long-term (30 sessions) semi-immersive VR combined training: after six weeks of intervention, changes in delta and theta waves during eyes-closed and eyes-open states were greater than after single-session intervention; beta-2 waves, which showed no change after single-session intervention, demonstrated significant enhancement after long-term intervention; furthermore, EEG complexity in both states was higher after long-term intervention. Research indicates that Alzheimer's disease patients show more regular EEG patterns and reduced complexity compared to age-matched controls (Monllor et al., 2021). Long-term intervention produced more significant effects on the brains of elderly MCI patients, but the dose producing maximal effects remains undetermined.

Few studies have reported long-term effects of VR training. Mirelman et al. (2016) implemented six weeks of non-immersive VR motor training in older adults, with the experimental group showing improved executive function and attention to a slightly lesser degree than the control group receiving traditional environment motor training—effects that were statistically comparable. Six months post-intervention, follow-up assessments revealed that both groups maintained cognitive performance above post-training levels, with the VR group showing lower executive function but higher attention performance compared to the control group. However, only 43 of the 282 older adult participants in this study had MCI, and no subgroup analysis was conducted; thus, whether these long-term effects apply to elderly MCI patients remains undetermined. Future research should expand sample sources using appropriate sampling methods to ensure representativeness and generalizability, optimize experimental design considering trial duration and intensity, clarify dose-response relationships for VR training effects on cognitive function in elderly MCI patients, and conduct continuous tracking and follow-up after intervention to determine long-term effects.

5.4 Explore Brain Changes and Reveal Neural Mechanisms Brain imaging and electrophysiological techniques including fMRI, EEG, and fNIRS are used to observe objective indicators such as brain region activation and inter-regional connectivity associated with cognitive function improvement in elderly MCI patients. During resting state, immersive VR cognitive training positively affected attention-related brain activity and improved functional connectivity in brain regions related to visual function. EEG results showed significantly reduced theta waves and decreased TBR in parietal and temporal regions of the VR group (Thapa et al., 2020). In some studies, these improvements were significantly greater than in traditional exercise training control groups, though control groups showed significantly greater improvement in some power ratios (DAR and TBR) and higher resting-state alpha connectivity in prefrontal cortex, anterior cingulate cortex, temporal, and parietal regions post-intervention (Yang et al., 2022). fMRI results showed that immersive VR cognitive training improved functional connectivity in visuospatial function-related brain regions in elderly MCI patients (Kang et al., 2021). During task state, immersive VR combined training produced significantly reduced activation in channels 7 and 13, left prefrontal cortex, right prefrontal cortex, and bilateral prefrontal cortex, indicating improved neural efficiency, while the control group receiving combined training in traditional environments showed reduced activation only in channel 10 and right prefrontal cortex, suggesting VR training may produce superior brain function improvement effects compared to traditional interventions (Liao et al., 2020). However, due to small sample sizes and substantial heterogeneity in VR training immersion levels, task modalities and content, duration, and frequency across existing studies, the generalizability of conclusions remains limited, requiring caution when applying findings to broader contexts.

Current neuroscience research findings primarily focus on resting-state brain function changes, with relatively insufficient results on task-state brain activity, while effects of VR training on brain structure and other neurophysiological activities in elderly MCI patients remain unclear. Research indicates that cognitive training can increase cortical gray matter volume and enhance white matter fiber connections in older adults (霍丽娟 et al., 2018); whether VR training can produce similar effects on the brains of elderly MCI patients awaits confirmation. Future research should expand sample sizes, continue exploring VR training effects on brain function in elderly MCI patients, and examine brain structure and other neurophysiological activities to further reveal the neural mechanisms through which VR training affects cognitive function in elderly MCI patients.

References:

边继萍, 刘晓凤, 魏利荣, 刘云, 王申. (2023). 虚拟现实技术用于轻度认知障碍患者康复的 Meta 分析. 护理学杂志, 38(21), 96–102.

董宣如. (2020). 轻度认知障碍人群认知特点及随访研究 (博士学位论文), 华东师范大学, 上海.

霍丽娟, 郑志伟, 李瑾, 李娟. (2018). 老年人的脑可塑性: 来自认知训练的证据. 心理科学进展, 26(05), 846–858.

田金洲, 解恒革, 秦斌, 时晶, 王荫华, 王新平, … 王鲁宁. (2016). 中国简短认知测试在痴呆诊断中的应用指南. 中华医学杂志, 96(37), 2945–2959.

Ahn, I. S., Kim, J. H., Kim, S., Chung, J. W., Kim, H., Kang, H. S., … Kim, D. K. (2009). Impairment of instrumental activities of daily living in patients with mild cognitive impairment. Psychiatry Investigation, 6(3), 180–184.

Amjad, I., Toor, H., Niazi, I. K., Pervaiz, S., Jochumsen, M., Shafique, M., … Ahmed, T. (2019). Xbox 360 Kinect cognitive games improve slowness, complexity of EEG, and cognitive functions in subjects with mild cognitive impairment: A randomized control trial. Games for health, 8(2), 144.

Angelidis, A., van der Does, W., Schakel, L., & Putman, P. (2016). Frontal EEG theta/beta ratio as an electrophysiological marker for attentional control and its test-retest reliability. Biological Psychology, 121(Pt A), 49–52.

Ban, J. Y., Park, H. K., & Kim, S. K. (2020). Effect of glycyrrhizic acid on scopolamine-induced cognitive impairment in mice. International Neurourology Journal, 24(Suppl 1), S48–S55.

Bamodu, O., & Ye, X. M. (2013). Virtual reality and virtual reality system components. Advanced Materials Research, 765−767, 1169−1172.

Belleville, S., Clement, F., Mellah, S., Gilbert, B., Fontaine, F., & Gauthier, S. (2011). Training-related brain plasticity in subjects at risk of developing Alzheimer's disease. Brain (London, England : 1878), 134(Pt 6), 1623−1634.

Brehmer, Y., Rieckmann, A., Bellander, M., Westerberg, H., Fischer, H., … Bäckman, L. (2011). Neural correlates of training-related working-memory gains in old age. Neuroimage, 58(4), 1110−1120.

Bruderer-Hofstetter, M., Rausch-Osthoff, A. K., Meichtry, A., Münzer, T., & Niedermann, K. (2018). Effective multicomponent interventions in comparison to active control and no interventions on physical capacity, cognitive function and instrumental activities of daily living in elderly people with and without mild impaired cognition − A systematic review and network meta-analysis. Ageing Research Reviews, 45, 1−14.

Burton, R. L., O'Connell, M. E., & Morgan, D. G. (2018). Cognitive and neuropsychiatric correlates of functional impairment across the continuum of no cognitive impairment to dementia. Archives of Clinical Neuropsychology, 33(7), 795−807.

Cabeza, R. (2002). Hemispheric asymmetry reduction in older adults: The HAROLD model. Psychology and Aging, 17(1), 85−100.

Carrieri, M., Petracca, A., Lancia, S., Basso, M. S., Brigadoi, S., Spezialetti, M., … Quaresima, V. (2016). Prefrontal cortex activation upon a demanding virtual hand-controlled task: A new frontier for neuroergonomics. Frontiers in Human Neuroscience, 10, 53.

Choi, W., & Lee, S. (2019). The effects of virtual kayak paddling exercise on postural balance, muscle performance, and cognitive function in older adults with mild cognitive impairment: A randomized controlled trial. Journal of Aging and Physical Activity, 27(6), 861−870.

Christman, S., Bermudez, C., Hao, L., Landman, B. A., Boyd, B., Albert, K., … Taylor, W. D. (2020). Accelerated brain aging predicts impaired cognitive performance and greater disability in geriatric but not midlife adult depression. Translational psychiatry, 10(1), 317.

Ciesielska, N., Sokołowski, R., Mazur, E., Podhorecka, M., Polak-Szabela, A., … Kędziora-Kornatowska, K. (2016). Is the Montreal Cognitive Assessment (MoCA) test better suited than the Mini-Mental State Examination (MMSE) in mild cognitive impairment (MCI) detection among people aged over 60? Meta-analysis. Psychiatria Polska, 50(5), 1039−1052.

Clarke, A. R., Barry, R. J., Karamacoska, D., & Johnstone, S. J. (2019). The EEG theta/beta ratio: A marker of arousal or cognitive processing capacity? Applied Psychophysiology and Biofeedback, 44(2), 123−129.

Diamond, A. (2013). Executive functions. Annual Review of Psychology, 64, 135−168.

Doniger, G. M., Beeri, M. S., Bahar-Fuchs, A., Gottlieb, A., Tkachov, A., Kenan, H., … Plotnik, M. (2018). Virtual reality-based cognitive-motor training for middle-aged adults at high Alzheimer's disease risk: A randomized controlled trial. Alzheimers & Dementia (New York, N. Y.), 4, 118−129.

Faria, A. L., Andrade, A., Soares, L., & I, B. S. (2016). Benefits of virtual reality based cognitive rehabilitation through simulated activities of daily living: A randomized controlled trial with stroke patients. Journal of NeuroEngineering and Rehabilitation, 13(1), 96.

Ferreira-Brito, F., Fialho, M., Virgolino, A., Neves, I., Miranda, A. C., Sousa-Santos, N., … Santos, O. (2019). Game-based interventions for neuropsychological assessment, training and rehabilitation: Which game-elements to use? A systematic review. Journal of Biomedical Informatics, 98, 103287.

Finnigan, S., Wong, A., & Read, S. (2016). Defining abnormal slow EEG activity in acute ischaemic stroke: Delta/alpha ratio as an optimal QEEG index. Clinical Neurophysiology, 127(2), 1452−1459.

García-Betances, R. I., Arredondo, W. M., Fico, G., & Cabrera-Umpiérrez, M. F. (2015). A succinct overview of virtual reality technology use in Alzheimer's disease. Frontiers in Aging Neuroscience, 7, 80.

Garcia, L., Kartolo, A., & Méthot-Curtis, E. (2012). A discussion of the use of virtual reality in dementia. In C. Eichenberg (Ed.), Virtual reality in psychological, medical and pedagogical applications (pp.123-136). Rijeka: Intech.

Goumopoulos, C., Skikos, G., & Frounta, M. (2023). Feasibility and effects of cognitive training with the COGNIPLAT game platform in elderly with mild cognitive impairment: Pilot randomized controlled trial. Games for Health Journal, 12(5), 414−425.

Haense, C., Kalbe, E., Herholz, K., Hohmann, C., Neumaier, B., Krais, R., … Heiss, W. D. (2012). Cholinergic system function and cognition in mild cognitive impairment. Neurobiology of Aging, 33(5), 867−877.

Hassandra, M., Galanis, E., Hatzigeorgiadis, A., Goudas, M., Mouzakidis, C., Karathanasi, E. M., … Theodorakis, Y. (2021). A virtual reality APP for physical and cognitive training of older people with mild cognitive impairment: Mixed methods feasibility study. JMIR Serious Games, 9(1), e24170.

Herold, F., Hamacher, D., Schega, L., & Müller, N. G. (2018). Thinking while moving or moving while thinking − concepts of motor-cognitive training for cognitive performance enhancement. Frontiers in Aging Neuroscience, 10, 228.

Hu, M., Wu, X., Shu, X., Hu, H., Chen, Q., Peng, L., … Feng, H. (2021). Effects of computerised cognitive training on cognitive impairment: A meta-analysis. Journal of Neurology, 268(5), 1680−1688.

Huang, X., Zhao, X., Li, B., Cai, Y., Zhang, S., Wan, Q., … Yu, F. (2022). Comparative efficacy of various exercise interventions on cognitive function in patients with mild cognitive impairment or dementia: A systematic review and network meta-analysis. Journal of Sport and Health Science, 11(2), 212—223.

Iliadou, P., Paliokas, I., Zygouris, S., Lazarou, E., Votis, K., Tzovaras, D., … Tsolaki, M. (2021). A comparison of traditional and serious game-based digital markers of cognition in older adults with mild cognitive impairment and healthy controls. Journal of Alzheimers Disease, 79(4), 1747—1759.

Jahn, F. S., Skovbye, M., Obenhausen, K., Jespersen, A. E., & Miskowiak, K. W. (2021). Cognitive training with fully immersive virtual reality in patients with neurological and psychiatric disorders: A systematic review of randomized controlled trials. Psychiatry Research, 300, 113928.

Kang, J. M., Kim, N., Lee, S. Y., Woo, S. K., Park, G., Yeon, B. K., … Cho, S. J. (2021). Effect of cognitive training in fully immersive virtual reality on visuospatial function and frontal-occipital functional connectivity in predementia: Randomized controlled trial. Journal of Medical Internet Research, 23(5), e24526.

Kennedy, R. S., Fowlkes, J. E., & Lilienthal, M. G. (1993). Postural and performance changes following exposures to flight simulators. Aviation Space and Environmental Medicine, 64(10), 912—920

Kwan, R. Y. C., Liu, J. Y. W., Fong, K. N. K., Qin, J., Leung, P. K., Sin, O. S. K., … Lai, C. K. Y. (2021). Feasibility and effects of virtual reality motor-cognitive training in community-dwelling older people with cognitive frailty: Pilot randomized controlled trial. JMIR Serious Games, 9(3), e28400.

Lai, F. H., Tong, A. Y., Fung, A. W., Yu, K. K., Wong, S. S., Lai, C. Y., … Man, D. W. (2022). Information communication technology as instrumental activities of daily living for aging-in-place in Chinese older adults with and without cognitive impairment: The validation study of advanced instrumental activities of daily living scale. Frontiers in Neurology, 13, 746640.

Lauenroth, A., Ioannidis, A. E., & Teichmann, B. (2016). Influence of combined physical and cognitive training on cognition: A systematic review. BMC Geriatrics, 16, 141.

Lejko, N., Larabi, D. I., Herrmann, C. S., Aleman, A., & Ćurčić-Blake, B. (2020). Alpha power and functional connectivity in cognitive decline: A systematic review and meta-analysis. Journal of Alzheimers Disease, 78(3), 1047—1088.

Li, X., Li, K., Zhu, Z., Jin, Y., Gao, Z., Xu, J., … Zhang, L. (2022). Exercise regulates the metabolic homeostasis of methamphetamine dependence. Metabolites, 12(7), 606.

Liao, Y., Tseng, H., Lin, Y., Wang, C., & Hsu, W. (2020). Using virtual reality-based training to improve cognitive function, instrumental activities of daily living and neural efficiency in older adults with mild cognitive impairment. European Journal of Physical and Rehabilitation Medicine, 56(1), 47–57.

Liu, Z., He, Z., Yuan, J., Lin, H., Fu, C., Zhang, Y., … Jia, J. (2022). Application of immersive virtual-reality-based puzzle games in elderly patients with post-stroke cognitive impairment: A pilot study. Brain Sciences, 13(1), 79.

Llinas-Regla, J., Vilalta-Franch, J., Lopez-Pousa, S., Calvo-Perxas, L., Torrents Rodas, D., … Garre-Olmo, J. (2017). The trail making test: Association with other neuropsychological measures and normative values for adults aged 55 years and older from a Spanish-speaking population-based sample. Assessment, 24(2), 183–196.

Lustig, C., Shah, P., Seidler, R., & Reuter-Lorenz, P. A. (2009). Aging, training, and the brain: A review and future directions. Neuropsychology Review, 19(4), 504–522.

Lv, H., Wang, Z., Tong, E., Williams, L. M., Zaharchuk, G., Zeineh, M., … Wintermark, M. (2018). Resting-state functional MRI: Everything that nonexperts have always wanted to know. American Journal of Neuroradiology, 39(8), 1390–1399.

Maeng, S., Hong, J. P., Kim, W., Kim, H., Cho, S., Kang, J. M., … Cho, S. (2021). Effects of virtual reality-based cognitive training in the elderly with and without mild cognitive impairment. Psychiatry Investigation, 18(7), 619–627.

Mirelman, A., Rochester, L., Maidan, I., Del Din, S., Alcock, L., Nieuwhof, F., … Hausdorff, J. M. (2016). Addition of a non-immersive virtual reality component to treadmill training to reduce fall risk in older adults (V-TIME): A randomised controlled trial. Lancet (London, England), 388(10050), 1170–1182.

Mondellini, M., Arlati, S., Gapeyeva, H., Lees, K., Maritz, I., Pizzagalli, S. L., … Teder-Braschinsky, A. (2022). User experience during an immersive virtual reality-based cognitive task: A comparison between Estonian and Italian older adults with MCI. Sensors (Basel, Switzerland), 22(21), 8249.

Monllor, P., Cervera-Ferri, A., Lloret, M. A., Esteve, D., Lopez, B., Leon, J. L., … Lloret, A. (2021). Electroencephalography as a non-invasive biomarker of Alzheimer's disease: A forgotten candidate to substitute CSF molecules? International Journal of Molecular Sciences, 22(19), 10889.

Moulaei, K., Sharifi, H., Bahaadinbeigy, K., & Dinari, F. (2024). Efficacy of virtual reality-based training programs and games on the improvement of cognitive disorders in patients: A systematic review and meta-analysis. BMC Psychiatry, 24(1), 116.

Mrakic-Sposta, S., Di Santo, S. G., Franchini, F., Arlati, S., Zangiacomi, A., Greci, L., … Vezzoli, A. (2018). Effects of combined physical and cognitive virtual reality-based training on cognitive impairment and oxidative stress in MCI patients: A pilot study. Frontiers in Aging Neuroscience, 10, 282.

Park, J. H. (2022). Effects of virtual reality-based spatial cognitive training on hippocampal function of older adults with mild cognitive impairment. International Psychogeriatrics, 34(2), 157–163.

Park, J. H., & Park, J. H. (2018). Does cognition-specific computer training have better clinical outcomes than non-specific computer training? A single-blind, randomized controlled trial. Clinical Rehabilitation, 32(2), 213−222.

Park, J. H., Liao, Y., Kim, D. R., Song, S., Lim, J. H., Park, H., … Park, K. W. (2020). Feasibility and tolerability of a culture-based virtual reality (VR) training program in patients with mild cognitive impairment: A randomized controlled pilot study. International Journal of Environmental Research and Public Health, 17(9), 3030.

Park, J. S., Jung, Y. J., & Lee, G. (2020). Virtual reality-based cognitive-motor rehabilitation in older adults with mild cognitive impairment: A randomized controlled study on motivation and cognitive function. Healthcare (Basel, Switzerland), 8(3), 335.

Perry, R. J., Watson, P., & Hodges, J. R. (2000). The nature and staging of attention dysfunction in early (minimal and mild) Alzheimer's disease: Relationship to episodic and semantic memory impairment. Neuropsychologia, 38(3), 252−271.

Petersen, R. C. (Ed.). (2003). Mild cognitive impairment: aging to Alzheimer's disease. Oxford University Press.

Petersen, R. C., Lopez, O., Armstrong, M. J., Getchius, T., Ganguli, M., Gloss, D., … Rae-Grant, A. (2018). Practice guideline update summary: Mild cognitive impairment: Report of the guideline development, dissemination, and implementation subcommittee of the American Academy of Neurology. Neurology, 90(3), 126−135.

Potmesilova, P., Potmesil, M., & Mareckova, J. (2023). Basal stimulation as developmental support in at-risk newborns: A literature review. Children (Basel, Switzerland), 10(2), 389.

Prichep, L. S., John, E. R., Ferris, S. H., Rausch, L., Fang, Z., Cancro, R., … Reisberg, B. (2006). Prediction of longitudinal cognitive decline in normal elderly with subjective complaints using electrophysiological imaging. Neurobiology of Aging, 27(3), 471−481.

Putman, P., Verkuil, B., Arias-Garcia, E., Pantazi, I., & van Schie, C. (2014). EEG theta/beta ratio as a potential biomarker for attentional control and resilience against deleterious effects of stress on attention. Cognitive Affective & Behavioral Neuroscience, 14(2), 782−791.

Qu, J., Zhang, Y., & Bu, L. (2023). Functional near-infrared spectroscopy in the assessment of rehabilitation efficacy of virtual reality products for people with cognitive disorders. International Journal of Industrial Ergonomics, 97, 103500.

Raimondo, L., Oliveira, Ĺ., Heij, J., Priovoulos, N., Kundu, P., Leoni, R. F., … van der Zwaag, W. (2021). Advances in resting state fMRI acquisitions for functional connectomics. Neuroimage, 243, 118503.

Reason, J. T. (1978). Motion sickness adaptation: A neural mismatch model. Journal of The Royal Society of Medicine, 71(11), 819−829.

Reuter-Lorenz, P. (2002). New visions of the aging mind and brain. Trends in Cognitive Sciences, 6(9), 394.

Roberts, R. O., Knopman, D. S., Mielke, M. M., Cha, R. H., Pankratz, V. S., Christianson, T. J., … Petersen, R. C. (2014). Higher risk of progression to dementia in mild cognitive impairment cases who revert to normal. Neurology, 82(4), 317−325.

Salatino, A., Zavattaro, C., Gammeri, R., Cirillo, E., Piatti, M. L., Pyasik, M., … Ricci, R. (2023). Virtual reality rehabilitation for unilateral spatial neglect: A systematic review of immersive, semi-immersive and non-immersive techniques. Neuroscience and Biobehavioral Reviews, 152, 105248.

Sánchez-Moguel, S. M., Alatorre-Cruz, G. C., Silva-Pereyra, J., González-Salinas, S., Sanchez-Lopez, J., Otero-Ojeda, G. A., … Fernández, T. (2017). Two different populations within the healthy elderly: Lack of conflict detection in those at risk of cognitive decline. Frontiers in Human Neuroscience, 11, 658.

Stern, Y., Habeck, C., Moeller, J., Scarmeas, N., Anderson, K. E., Hilton, H. J., … van Heertum, R. (2005). Brain networks associated with cognitive reserve in healthy young and old adults. Cerebral Cortex, 15(4), 394−402.

Suffczynski, P., Kalitzin, S., Pfurtscheller, G., & Lopes, D. S. F. (2001). Computational model of thalamo-cortical networks: Dynamical control of alpha rhythms in relation to focal attention. International Journal of Psychophysiology, 43(1), 25−40.

Thapa, N., Park, H. J., Yang, J. G., Son, H., Jang, M., Lee, J., … Park, H. (2020). The effect of a virtual reality-based intervention program on cognition in older adults with mild cognitive impairment: A randomized control trial. Journal of Clinical Medicine, 9(5), 1283.

Tian, M., Cai, Y., & Zhang, J. (2023). The impact of virtual reality-based products on mild cognitive impairment senior subjects: An experimental study using multiple sources of data. Applied Sciences-Basel, 13(4),

Torpil, B., Sahin, S., Pekcetin, S., & Uyanik, M. (2021). The effectiveness of a virtual reality-based intervention on cognitive functions in older adults with mild cognitive impairment: A single-blind, randomized controlled trial. Games for Health Journal, 10(2), 109−114.

Tortora, C., Di Crosta, A., La Malva, P., Prete, G., Ceccato, I., Mammarella, N., … Palumbo, R. (2024). Virtual reality and cognitive rehabilitation for older adults with mild cognitive impairment: A systematic review. Ageing Research Reviews, 93, 102146.

Tseng, K. C., & Giau, D. T. N. (2022). A feasibility study of using virtual reality as a pre-occupancy evaluation tool for the elderly. Automation in Construction, 134, 104037.

Tuena, C., Pedroli, E., Trimarchi, P. D., Gallucci, A., Chiappini, M., Goulene, K., … Stramba-Badiale, M. (2020). Usability issues of clinical and research applications of virtual reality in older people: A systematic review. Frontiers in Human Neuroscience, 14, 93.

Van Son, D., De Blasio, F. M., Fogarty, J. S., Angelidis, A., Barry, R. J., … Putman, P. (2019). Frontal EEG theta/beta ratio during mind wandering episodes. Biological Psychology, 140, 19−27.

Vermeij, A., Kessels, R., Heskamp, L., Simons, E., Dautzenberg, P., … Claassen, J. (2017). Prefrontal activation may predict working-memory training gain in normal aging and mild cognitive impairment. Brain Imaging and Behavior, 11(1), 141−154.

Walsh, E. I., Smith, L., Northey, J., Rattray, B., & Cherbuin, N. (2020). Towards an understanding of the physical activity-BDNF-cognition triumvirate: A review of associations and dosage. Ageing Research Reviews, 60, 101044.

Winblad, B., Palmer, K., Kivipelto, M., Jelic, V., Fratiglioni, L., Wahlund, L. O., … Petersen, R. C. (2004). Mild cognitive impairment − beyond controversies, towards a consensus: Report of the International Working Group on Mild Cognitive Impairment. Journal of Internal Medicine, 256(3), 240−246.

Xie, J., Zhang, W., Shen, Y., Wei, W., Bai, Y., Zhang, G., … Wang, M. (2023). Abnormal spontaneous brain activity in females with autism spectrum disorders. Frontiers in Neuroscience, 17, 1189087.

Yan, M., Zhao, Y., Meng, Q., Wang, S., Ding, Y., Liu, Q., … Chen, L. (2022). Effects of virtual reality combined cognitive and physical interventions on cognitive function in older adults with mild cognitive impairment: A systematic review and meta-analysis. Ageing Research Reviews, 81, 101708.

Yang, J., Thapa, N., Park, H., Bae, S., Park, K. W., Park, J., … Park, H. (2022). Virtual reality and exercise training enhance brain, cognitive, and physical health in older adults with mild cognitive impairment. International Journal of Environmental Research and Public Health, 19(20), 13300.

You, S. H., Jang, S. H., Kim, Y. H., Hallett, M., Ahn, S. H., Kwon, Y. H., … Lee, M. Y. (2005). Virtual reality-induced cortical reorganization and associated locomotor recovery in chronic stroke: An experimenter-blind randomized study. Stroke, 36(6), 1166−1171.

Yu, D., Li, X., & Lai, F. H. (2023). The effect of virtual reality on executive function in older adults with mild cognitive impairment: A systematic review and meta-analysis. Aging & Mental Health, 27(4), 663−673.

Zhao, T., Huang, H., Li, J., Shen, J., Zhou, C., Xiao, R., … Ma, W. (2023). Association between erythrocyte membrane fatty acids and gut bacteria in obesity-related cognitive dysfunction. AMB Express, 13(1),

Zhu, K., Zhang, Q., He, B., Huang, M., Lin, R., … Li, H. (2022). Immersive virtual reality-based cognitive intervention for the improvement of cognitive function, depression, and perceived stress in older adults with mild cognitive impairment and mild dementia: Pilot pre-post study. JMIR Serious Games, 10(1), e32117.

Zhu, S., Sui, Y., Shen, Y., Zhu, Y., Ali, N., Guo, C., … Wang, T. (2021). Effects of virtual reality intervention on cognition and motor function in older adults with mild cognitive impairment or dementia: A systematic review and meta-analysis. Frontiers in Aging Neuroscience, 13, 586999.

Note: Figure translations are in progress. See original paper for figures.