

## Neuropsychological rehabilitation of spatial memory: A systematic review

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### ABSTRACT

**Background:** Spatial memory is defined as the cognitive ability that enables individuals to encode, store, and retrieve information related to the location of objects in the environment. This function may be compromised by aging or neurodegenerative disorders. Consequently, the development of interventions aimed at its stimulation and rehabilitation is imperative.

**Objective:** This study aimed to review empirical work on the neuropsychological rehabilitation of human spatial memory.

**Methods:** A systematic search was conducted in PubMed, Scopus, and Web of Science. Studies were included if they involved spatial memory rehabilitation or training programs assessing pre- and post-intervention outcomes. Eight studies met the inclusion criteria and were evaluated in terms of sample characteristics, intervention design, and spatial memory measures.

**Results:** Across studies, post-intervention improvements were observed in tasks assessing visuospatial recall, route learning, and navigation efficiency, measured using instruments such as the Corsi Block-Tapping Test, Rey-Osterrieth Complex Figure, and virtual navigation tasks. Moderate to large effect sizes (Cohen's  $d = 0.5-0.9$ ) were reported for allocentric and active navigation training, particularly in immersive virtual reality and multimodal interventions. Improvements in visuospatial working memory, route learning, and allocentric navigation were broader in healthy older adults and more specific and compensatory in individuals with mild cognitive impairment. The observed benefits were influenced by variables such as immersion level, type of spatial cues, and baseline cognitive performance.

**Conclusions:** Neuropsychological interventions represent effective strategies for enhancing and maintaining spatial memory. These findings emphasize the need to adapt intervention protocols to individual characteristics and task demands to optimize rehabilitation outcomes.

### Glossary

2D 2-dimension  
3D 3-dimension  
AD Alzheimer's disease  
CBTT Corsi Block-Tapping Test  
DMST Delayed Matching to Sample Task  
MCI Mild Cognitive Impairment  
PRISMA Preferred Reporting Items for Systematic reviews and Meta-Analyses  
ROCF Rey-Osterrieth Complex Figure

VR Virtual reality  
WoS Web of Science

### 1. Introduction

Spatial memory is defined as the cognitive ability that allows individuals to encode, store, and retrieve information related to the location of objects in the environment (Piber, 2021).

This skill enables the retention of spatial information and facilitates the recognition of previously visited places (Piber, 2021). In everyday life, spatial memory is essential, aiding in the recollection of misplaced

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objects such as keys or the navigation back home after a walk (England et al., 2015). This ability relies on three processes: object processing (the recognition of the perceived object), place processing (the encoding of the object's position in space), and the binding of the object with its specific location (the association and integration of the object's identity with its location) (England et al., 2015; Postma et al., 2008).

Recent systematic reviews have provided a comprehensive overview of the assessment of spatial memory and orientation, highlighting the diversity of paradigms currently used to evaluate this ability and their implications for intervention design. Tragantzopoulou and Giannouli (2024) summarized the main tools currently used to evaluate spatial orientation in older adults, emphasizing the importance of distinguishing between egocentric and allocentric frameworks when evaluating navigation and memory performance, as well as between real-world and virtual assessments, to improve the ecological validity of rehabilitation outcomes. Similarly, Costa et al. (2020) demonstrated the moderate to high accuracy of spatial orientation tasks for the early diagnosis of mild cognitive impairment (MCI). These findings highlight the necessity of integrating standardized neuropsychological assessments with ecologically valid tasks, such as virtual navigation and real space paradigms, to obtain a comprehensive evaluation of spatial memory in research and clinical settings.

Spatial memory demonstrates a pattern of evolution across the lifespan, exhibiting both developmental gains and age-related decline (Ruggiero et al., 2016). Evidence from studies of both humans and non-human primates suggests that spatial abilities, including symmetry perception, spatial organization, and visual orientation, are supported by networks of perception and attention (Ekstrom et al., 2017; Epstein & Baker, 2019; Giannouli, 2013). These visual-spatial capacities contribute to the formation and updating of internal representations of space, which are essential for navigation and environmental interaction.

A growing body of research has explored different strategies to enhance visuospatial memory across the lifespan. Cognitive and neuropsychological interventions, including multimodal interventions engaging both cognitive and emotional domains may yield long-term benefits in maintaining visuospatial efficiency across aging (Giannouli et al., 2024; Toril et al., 2016).

Spatial memory is reflected in navigation and orientation abilities, which are required for proper movement through space (Montana et al., 2019). It relies on a network of interconnected cortical and subcortical regions that encode, store, and retrieve spatial information for environmental navigation (Baumann et al., 2009). Key structures include the parahippocampal gyrus, posterior parietal cortex, hippocampus, and striatum, whose coordinated activity supports spatial representation and orientation strategies (Baumann et al., 2009). The brain activation pattern of navigation networks varies depending on the strategy employed and the individual's familiarity with the environment, suggesting that the engagement of these brain regions is context-dependent (Bocchia et al., 2014).

The predominant brain structure involved in spatial memory is the hippocampus (Burgess et al., 2002). This structure, located in the medial temporal lobe and part of the limbic system, is associated with episodic memory consolidation and spatial representation through the creation of cognitive maps (Burgess et al., 2002; Xiong, 2008). Its spatial function depends on an extended circuit comprising specialized cells (place, grid, and head-direction cells) that encode location, distance, and orientation (Burgess et al., 2002). Physical exercise can enhance the volume of the hippocampus, which in turn leads to improvements in spatial memory accuracy (Boecker et al., 2024). This finding serves to reinforce the proposed structural-functional link between hippocampal plasticity and performance in spatial tasks. In addition, it demonstrates the potential of non-pharmacological interventions to enhance cognitive function.

The hippocampal system and its associated regions facilitate the organization of information through two complementary frames of reference: egocentric and allocentric (Burgess et al., 2002; Tuena, Mancuso, et al., 2021). The egocentric frame organizes sensory

information according to the relative position of objects in relation to the individual's body, while the allocentric frame establishes relationships between objects or reference points regardless of the individual's position in the environment, enabling orientation and route planning from different locations and perspectives. Effective navigation requires the combination of these systems in accordance with the environmental demand. Both systems are susceptible to the effects of normal aging and pathological conditions, which can result in impaired spatial memory and navigation ability (Tuena, Serino, et al., 2021).

The functional architecture of spatial memory networks and their cellular components provides a foundation for understanding how different intervention approaches may influence specific neurobiological and cognitive systems. Active navigation and allocentric training primarily enhance plasticity in the hippocampus and entorhinal cortex, strengthening the place and grid cell coding mechanisms that underlie spatial encoding and consolidation (Boecker et al., 2024). Body-based and vestibular-proprioceptive enrichment promotes multisensory integration processes that improve spatial updating and orientation accuracy (Frissen et al., 2011). Attentional and working memory training engages the frontoparietal control networks that are responsible for maintaining and manipulating spatial representations (Purg Suljić et al., 2024; Rizza et al., 2024). Finally, aerobic exercise supports neurotrophin release and plasticity in the hippocampal subfields, acting as a complementary pathway to cognitive training and facilitating overall network adaptability (Farhani et al., 2022). These mechanisms illustrate how interventions may engage the neural systems supporting spatial memory.

Spatial memory impairments have been observed in both MCI and Alzheimer's disease (AD), particularly in tasks requiring the memorization of specific locations and spatial orientation (Poos et al., 2021; Tuena et al., 2024; Tuena, Serino, et al., 2021). These difficulties are associated with damage to the hippocampus and entorhinal cortex (Braak & Braak, 1991), regions that are especially vulnerable to neurodegenerative processes (Poos et al., 2021). Given the vulnerability of spatial memory to both aging and neurodegenerative conditions, several cognitive interventions have been developed to support its rehabilitation. At the core of these interventions is the principle of neuroplasticity, which refers to the brain's ability to undergo structural and functional reorganization in response to damage (Kleim, 2011). This adaptive capacity encompasses synaptic changes, including long-term potentiation and depression, as well as structural modifications, such as neurogenesis and dendritic growth, particularly in the hippocampus (Cassilhas et al., 2016).

While the majority of research has centered on aging, MCI and AD, spatial memory deficits have also been documented in other neurological and medical populations, including individuals with traumatic brain injury (Skelton et al., 2000), Parkinson's disease (García-Navarra et al., 2025), vestibular dysfunction (Zhang et al., 2022), Williams syndrome (Bostelmann et al., 2017) and cancer (Gates et al., 2022). These conditions are characterized by disruptions within the hippocampal, parietal, and vestibular circuits, resulting in impairments in orientation, navigation, and spatial updating. Consequently, the development of spatial memory rehabilitation programs holds relevance across a broad range of clinical populations, extending beyond the domains of aging and neurodegenerative disorders.

Recent technological advances, particularly the implementation of virtual reality (VR), have led to significant advancements in the therapeutic approach for spatial memory rehabilitation (Montana et al., 2019). The incorporation of these tools has opened innovative pathways for designing more realistic, interactive, and personalized therapeutic environments (Cheung et al., 2014). VR has been demonstrated to create immersive environments that integrate bodily cues and multisensory stimuli, enhancing engagement and supporting the encoding of spatial information (Riva et al., 2016; Tuena, Serino, et al., 2021). Research indicates that VR-based interventions may promote experience-dependent plasticity, improve navigation strategies, and possibly

facilitate functional recovery in both healthy aging and conditions such as MCI and AD (Montana et al., 2019; Riva et al., 2016).

Despite these promising developments, a clear consensus regarding the most effective intervention protocols has yet to be reached. Differences in training design, frequency, task type, and immersion level make it difficult to determine which factors contribute most to rehabilitation success. Furthermore, few reviews have systematically examined how these methodological variables influence spatial memory outcomes.

Addressing this gap, the present systematic review synthesizes current evidence on neuropsychological interventions targeting spatial memory. It evaluates the strategies, tools, and outcome measures used across studies and examines whether these interventions are associated with structural or functional brain changes. Such an effort is essential to clarify which intervention formats, tools, and environmental contexts are most beneficial for preserving or enhancing spatial memory in both healthy and clinical populations. These insights will help identify best practices for rehabilitating spatial memory and develop more targeted clinical applications.

## 2. Methods

A systematic review of the existing scientific literature on the neuropsychological rehabilitation of spatial memory was conducted. This review was carried out in accordance with the PRISMA (2020) guidelines (Page et al., 2021).

### 2.1. Inclusion and exclusion criteria

The inclusion criteria adopted in this review were: (1) experimental studies conducted on human participants; (2) implementation of specific intervention programs; (3) evaluation of the intervention using neuropsychological tests; and (4) assessment of spatial memory, operationally defined as the cognitive ability to encode, store, and retrieve information about spatial relationships and environmental layouts, related constructs such as spatial navigation, visuospatial memory, topographical orientation, and wayfinding were also included under this definition. On the other hand, the exclusion criteria were: (1) studies conducted on animals; (2) articles not written in English or Spanish; (3) review articles, conference abstracts, or book chapters; (4) single-case studies; and (5) studies that did not report outcomes related to spatial memory.

### 2.2. Information search

The literature search was conducted in the PubMed, Scopus, and Web of Science (WoS) databases. The selection of these three databases was made on the basis of their complementary coverage and relevance to the research scope. PubMed provides extensive indexing of biomedical and neurocognitive studies, ensuring inclusion of clinical and experimental evidence related to brain function and rehabilitation. Scopus includes a wide range of interdisciplinary and applied psychology literature, capturing studies at the intersection of neuroscience, cognition, and therapy. WoS provides comprehensive access to interdisciplinary publications across cognitive neuroscience, neuropsychology, and rehabilitation research. Collectively, these databases ensure a balanced and systematic retrieval of peer-reviewed studies across clinical, psychological, and neuropsychological domains related to spatial memory rehabilitation.

Searches were completed on December 17th, 2024. A variety of terms were utilized for each key concept, with the objective of maximizing the retrieval of relevant articles, including: “spatial memory”, “rehabilitation”, “neurorehabilitation”, “neuropsychological rehabilitation”, “cognitive rehabilitation”, “intervention”, “neuropsychological intervention”, “cognitive intervention”, and “cognitive training”. Specifically, the search string that was applied across all three databases is as follows: “spatial memory” AND (“rehabilitation” OR

“neurorehabilitation” OR “neuropsychological rehabilitation” OR “cognitive rehabilitation” OR “intervention” OR “neuropsychological intervention” OR “cognitive intervention” OR “cognitive training”). Additional filters were applied to refine the results: in PubMed, the filters “Clinical Trial” and “Randomized Controlled Trial” were used; in Scopus, the search was limited to the subject areas of “Neuroscience”, “Psychology”, “Multidisciplinary”, and “Health Professions”; and in WoS, the filters “Article” and “Clinical Trial” were applied. The filters “Clinical Trial” and “Randomized Controlled Trial” were applied to ensure the inclusion of studies with stronger methodological control, enhancing the quality and interpretability of the evidence regarding intervention efficacy. No date restrictions were applied in any database.

For the screening process, the search outputs from PubMed, Scopus, and WoS were compiled into an Excel spreadsheet, and duplicate records were eliminated. Two researchers independently screened titles and abstracts to exclude irrelevant studies, followed by a full-text review to confirm eligibility based on the inclusion and exclusion criteria. Any discrepancies were resolved through discussion and consensus, with a third reviewer consulted when agreement could not be reached.

### 2.3. Study selection

The selection process based on PRISMA is presented in Fig. 1. The search in PubMed, Scopus, and WoS databases using the aforementioned keywords and search string yielded a total of 1588 records: 46 from PubMed, 668 from Scopus, and 874 from WoS. After removing 331 duplicate entries, 1257 records remained for initial screening. Based on the title and abstract, 1198 records were excluded for not meeting the inclusion criteria or for meeting one or more exclusion criteria. The remaining 59 articles were reviewed in full text for eligibility, leading to the exclusion of 51 articles for the following reasons: studies conducted in animals, review articles, studies that did not evaluate spatial memory, studies that did not implement a neuropsychological rehabilitation program, or studies not written in English. Consequently, a total of eight studies were included in this systematic review.

Data were extracted using a standardized template that included

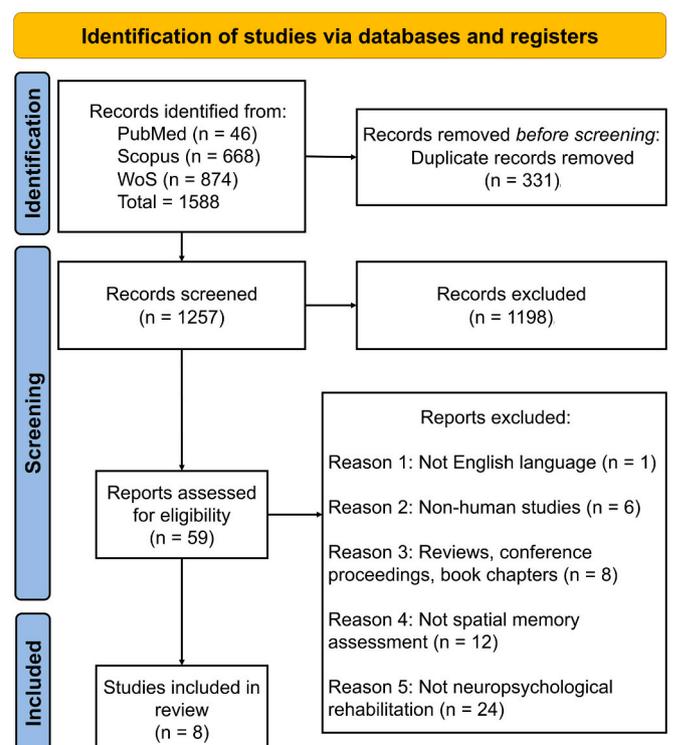


Fig. 1. PRISMA flow-process diagram.

study design, sample characteristics, intervention details, outcome measures, and main results. The extracted information was synthesized descriptively and organized in both tabular and narrative formats to identify methodological patterns and intervention outcomes across studies. Despite the absence of a meta-analysis, due to the heterogeneity of the included studies, the methodological quality of each study was evaluated based on the clarity of the intervention, the control conditions, the pre-post assessments, and the completeness of the reporting.

### 3. Results

#### 3.1. Study characteristics

Table 1 offers a concise synopsis of the sample characteristics, study aims, spatial memory assessment methods, rehabilitation programs employed, and the main findings of the reviewed studies. Fig. 2 presents a conceptual overview of the principal spatial memory intervention types, their key components, and the mechanisms they target or improve.

##### 3.1.1. Sociodemographic characteristics

The mean age of participants ranged from 25.2 years (Palermo et al., 2017) to 75.5 years (Tuena et al., 2024), with the majority of studies including samples with an average age exceeding 68 years (Clemenson et al., 2020; Merriman et al., 2022; Serweta-Pawlik et al., 2023; Stramba-Badiale et al., 2024; Tagliabue et al., 2022; Tuena et al., 2024). The majority of studies had sample sizes between 15 and 60 participants (Clemenson et al., 2020; Hötting et al., 2013; Merriman et al., 2022; Serweta-Pawlik et al., 2023; Tuena et al., 2024). The smallest sample size was reported by Stramba-Badiale et al. (2024), who included seven participants, while the largest sample size was reported by Tagliabue et al. (2022), who included 104 participants. With respect to the distribution of participants by sex, 50% of the studies reported a predominance of male participants (Palermo et al., 2017; Serweta-Pawlik et al., 2023; Tagliabue et al., 2022; Tuena et al., 2024). In contrast, 25% of the studies showed an overrepresentation of female participants (Clemenson et al., 2020; Merriman et al., 2022). Finally, two studies reported an equal distribution between sexes (Hötting et al., 2013; Stramba-Badiale et al., 2024).

With regard to participant profiles, the majority of investigations were conducted with healthy adults (Clemenson et al., 2020; Hötting et al., 2013; Merriman et al., 2022; Palermo et al., 2017; Tagliabue et al., 2022), although clinical populations were also included, such as patients with MCI (Stramba-Badiale et al., 2024; Tuena et al., 2024) and individuals undergoing cancer treatment (Serweta-Pawlik et al., 2023). Furthermore, some studies provided relevant data concerning the educational levels of the participants (Clemenson et al., 2020; Serweta-Pawlik et al., 2023; Stramba-Badiale et al., 2024; Tuena et al., 2024). In this regard, the studies have reported a mean minimum of 10.7 years of schooling (Tuena et al., 2024) and a mean maximum of 16.53 years (Clemenson et al., 2020). In their study, Serweta-Pawlik et al. (2023) assessed education employing a scale ranging from 1 (below primary education) to 5 (post-secondary education), with level 3 (vocational education) being the most prevalent among the participants.

##### 3.1.2. Program and intervention characteristics

Despite methodological heterogeneity, consistent trends emerged in program duration and design. Most interventions lasted four to six weeks (Clemenson et al., 2020; Hötting et al., 2013; Merriman et al., 2022; Serweta-Pawlik et al., 2023), with sessions typically ranging between 30 and 60 min (Clemenson et al., 2020; Hötting et al., 2013; Merriman et al., 2022) and involving 5–10 total sessions (Hötting et al., 2013; Merriman et al., 2022; Tagliabue et al., 2022).

Interventions combined cognitive, sensorimotor, and immersive components, delivered either through 2D computerized tasks (Clemenson et al., 2020; Hötting et al., 2013; Merriman et al., 2022;

Palermo et al., 2017; Stramba-Badiale et al., 2024; Tagliabue et al., 2022; Tuena et al., 2024) and immersive VR tasks (Serweta-Pawlik et al., 2023; Stramba-Badiale et al., 2024; Tuena et al., 2024). Additionally, three studies employed technologies that enabled movement control in the rehabilitation tasks using participants' own body movements. Specifically, the Wii Balance Board (Merriman et al., 2022), 3dRudder (Stramba-Badiale et al., 2024), and a gyroscope for detecting head movements (Palermo et al., 2017) were utilized.

##### 3.1.3. Assessment tools

Spatial memory was assessed using a combination of standardized neuropsychological tests and task-specific measures. Common standardized neuropsychological tests included the Rey-Osterrieth Complex Figure (ROCF) for visuospatial recall (Clemenson et al., 2020), the Corsi Block-Tapping Test (CBTT) for visuospatial working memory (Serweta-Pawlik et al., 2023), and the Delayed Matching to Sample Task (DMST) for short-term spatial retention (Tagliabue et al., 2022). VR tasks simulated navigation, route learning, and object-location recall (Hötting et al., 2013; Merriman et al., 2022) through digital mazes or circular arenas inspired by the Morris Water Maze paradigm (Palermo et al., 2017; Stramba-Badiale et al., 2024; Tuena et al., 2024). Most of studies employed a combination of pre- and post-intervention measurements (Clemenson et al., 2020; Hötting et al., 2013; Merriman et al., 2022; Serweta-Pawlik et al., 2023; Tagliabue et al., 2022). One study incorporated a three-month follow-up assessment (Tagliabue et al., 2022).

#### 3.2. Main results

Despite the presence of variations in scope and methodology, the reviewed studies consistently demonstrated improvements in spatial learning, recall accuracy, and navigation efficiency following cognitive or immersive interventions. Across studies, gains were most significant when participants engaged in active exploration, received spatial feedback, or trained within embodied VR contexts that provided sensorimotor cues. Effect sizes are summarized in Table 1. Across interventions, the magnitude of improvement ranged from small ( $d = 0.26$ ;  $\eta^2 = 0.02$ ) to large ( $d \approx 0.9$ ;  $\eta^2 \approx 0.14$ ), reflecting moderate-to-substantial gains in spatial recall, route learning, and navigation accuracy. The largest effects were observed in programs that combined immersive or 3D environments with active navigation (Clemenson et al., 2020; Merriman et al., 2022) and in attentive individuation training targeting visuospatial working memory (Tagliabue et al., 2022). In contrast, smaller effects were reported for brief single-session or feasibility-based protocols (Palermo et al., 2017; Serweta-Pawlik et al., 2023; Stramba-Badiale et al., 2024; Tuena et al., 2024).

Interventions based on active navigation and cognitive training consistently demonstrated improvements in spatial learning and memory performance across the reviewed studies. Programs incorporating exploration within 3D or 2D spatially complex environments led to enhanced spatial recall, route learning, and orientation accuracy. These include screen-based computer tasks (Clemenson et al., 2020; Hötting et al., 2013; Merriman et al., 2022). Clemenson et al. (2020) trained participants through both 2D and 3D video games requiring spatial exploration and environmental mapping, which improved visuospatial recall as measured by the ROCF. These effects were attributed to hippocampal-dependent memory enhancement resulting from environmental enrichment. Similarly, Hötting et al. (2013) examined the effects of combined cognitive (spatial vs. perceptual) and physical (aerobic vs. non-aerobic) training on spatial learning. The spatial condition required participants to learn and retrieve landmark-path relations in a virtual maze task performed during active fMRI, thereby engaging both egocentric (path integration) and allocentric (perspective shifting) skills. Cognitive training, rather than perceptual exercises, improved participants' ability to learn landmarks and spatial relationships within a virtual maze. Neuroimaging results revealed reduced activation in hippocampal and parahippocampal regions, indicating greater neural

**Table 1**  
Characteristics and main findings of the reviewed studies.

Study	Sample characteristics	Objective	Spatial memory assessment	Rehabilitation program	Main results
Clemenson et al. (2020)	N = 51 (13 M, 38 F) Healthy older adults MA = 68.52 ± 5.87 EL = 16.53 ± 2.25 3 subgroups: 2D (n = 18; 4 M, 14 F; MA = 70.83 ± 5.98; EL = 15.94 ± 2.65) 3D (n = 18; 5 M, 13 F; MA = 67.5 ± 5.02; EL = 16.2 ± 2.3) AC (n = 15; 5 M, 10 F; MA = 68.73 ± 5.98; EL = 17.33 ± 1.23)	To determine the effectiveness of a video game-based cognitive training in healthy older adults.	ROCF. Pre- and post-intervention assessments.	Duration: 4 weeks. Frequency: daily. Session duration: 30–45 min. Total sessions: 28. Home-based autonomous training with a different video game depending on subgroup: 2D (training with an unfamiliar 2D video game); 3D (training with an unfamiliar 3D video game); AC (training with a familiar video game).	Post-intervention improvement in ROCF scores for the 2D and 3D subgroups. 3D vs AC $\Delta$ LDI = 0.097; Cohen's d = 0.47 (medium); 2D vs AC $\Delta$ LDI = 0.053; Cohen's d = 0.26 (small).
Hötting et al. (2013)	N = 33 (16 M, 17 F) Healthy adults MA = 48.9 ± 4.0 4 subgroups: Aer-Spa Aer-Perc NoAer-Spa NoAer-Perc	To explore the effects of cognitive and physical interventions on spatial learning in healthy adults.	Spatial learning task in MRI scanner. Pre- and post-intervention assessments.	Duration: 4 weeks. Frequency: not specified. Session duration: 45 min. Total sessions: 6. Cognitive conditions: Spa (perspective-shift (allocentric) and path integration (egocentric) tasks); Perc (visual discrimination task (control)). Physical conditions: Aer (aerobic training (cycling)); NoAer (stretching, strength, relaxation, coordination (control)).	Subgroups Aer-Spa and NoAer-Spa showed higher post- than pre-intervention scores ( $p < .001$ ). Lower frontal, parietal, temporal, and hippocampal activation in Aer-Spa and NoAer-Spa compared to Aer-Perc and NoAer-Perc. $\eta^2G = 0.067$ – $0.090$ (medium effects).
Merriman et al. (2022)	N = 56 (21 M, 35 F) Healthy older adults MA = 71.82 ± 4.64 3 subgroups: CityQuest (n = 21; MA = 69.27 ± 2.68) SpaNav (n = 20; MA = 73.10 ± 4.59) Obst (n = 15; MA = 73.67 ± 5.46)	To assess the efficacy of a 3D video game-based intervention on spatial memory performance in healthy older adults.	Route visualization in video for recalling route and object location. Four spatial navigation tasks: computerized object recognition and direction decision; 2D landmark location and object naming tasks; spatial strategy task in virtual maze. Pre- and post-intervention assessments.	Duration: 5 weeks. Frequency: 2/week. Session duration: 60 min. Total sessions: 10. CityQuest: locate 4 targets in virtual city (obstacles, difficulty levels). SpaNav: same without obstacles. Obst: collect objects avoiding obstacles.	Post-intervention improvements in object recognition and 2D landmark location tasks ( $ps \leq 0.008$ ). Post-intervention improvements in both egocentric and allocentric strategies ( $ps \leq 0.044$ ). CityQuest improved in 2D landmark location ( $p = .001$ ). Partial $\eta^2 \approx 0.08$ (medium effect; CIs not reported), qualitative improvement.
Palermo et al. (2017)	N = 60 (49 M, 11 F) Healthy young adults MA = 25.2 ± 4.5	To assess the effects of interface and navigation mode in a virtual environment on spatial memory in healthy young adults.	Object location task (Morris maze). Training system evaluated by questionnaire. Post-intervention assessment.	Duration: one individual session. Session duration: not specified. Variables: interface (mouse / gyroscope); navigation (active / passive).	No influence of interface or navigation mode on spatial memory performance. ES not reported; qualitative small-to-medium motivational effect.
Serweta-Pawlik et al. (2023)	N = 18 (11 M, 7 F) Head and neck cancer patients undergoing treatment MA = 64 ± 10.0 Age range = 38–76 Education range = 1–5	To assess the utility of immersive VR programs for spatial memory in cancer patients.	CBTT. Pre- and post-intervention assessments.	Duration: 6–7 weeks. Frequency: 3/week. Session duration: 15–30 min. Total sessions: $\approx 21$ . 23 immersive VR apps including adventure, exploration, meditation, simulation, or music genres.	28% of patients improved in post-test, whereas 11% of patients worsened. ES not reported; qualitative moderate individual gains.
Stramba-Badiale et al. (2024)	N = 7 (3 M, 4 F) MCI patients MA = 75 ± 4.62 EL = 12.86 ± 3.89 MMSE = 28.01 ± 1.36 Completed both conditions (n = 5); only immersive (n = 1); only semi-immersive (n = 1).	To explore the effect of technology type on spatial memory performance in MCI patients.	Spatial recall task (Morris maze). Object location via navigation.	Duration: one individual session. Session duration: 75 min. Conditions: immersive / semi-immersive. Navigation task phases: encoding (object collection) and recall (object placement).	No significant differences between conditions in object placement error or angular deviation. ES not reported; descriptive small differences favoring semi-immersive condition.
Tagliabue et al. (2022)	N = 104 (54 M, 50 F) Healthy older adults MA = 68.24 ± 4.81 SATURN $\geq 26$ 3 subgroups: Pas (n = 36; 21 M, 15 F; MA = 68.25 ± 2.73) Enum (n = 35; 17 M, 18 F; MA = 68.77 ± 3.40)	To assess the effects of different cognitive trainings on spatial memory in healthy older adults.	Online DMST. Pre-, post-intervention, and 3-month follow-up assessments.	Duration: 1 week. Frequency: daily. Session duration: not specified. Total sessions: 5. Self-administered online training (increasing difficulty): Pas (complete questionnaires); Enum (questionnaire + adaptive color dot counting task); DMST	Post-intervention improvements in low baseline performers in Enum and DMST ( $ps < 0.001$ ). Follow-up improvements compared to pre-intervention in low performers ( $ps \leq 0.028$ ), with greater improvement in DMST compared to Pas ( $p = .045$ ). Enum: high performers

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Table 1 (continued)

Study	Sample characteristics	Objective	Spatial memory assessment	Rehabilitation program	Main results
	DMST (n = 33; 16 M, 17 F; MA = 68.12 ± 3.29)			(questionnaire + adaptive DMST task).	outperformed low in all 5 sessions (p < .001). DMST: high performers outperformed low in the first 2 sessions (ps ≤ 0.024). $\eta^2p = 0.108$ (main effect), $\eta^2p = 0.066$ (interaction); medium to large effects.
Tuena et al. (2024)	N = 15 (9 M, 6 F) MCI patients MA = 75.5 ± 6.2 EL = 10.7 ± 4.2 MMSE = 26.69 ± 1.45	To explore the efficacy of different navigation aids on spatial memory in MCI patients.	Spatial navigation task in virtual circular environment (Morris maze). Encoding and immediate recall of 4 objects and locations. Distal and intra-maze cues. 4 trials per object (2 using an egocentric frame, 2 using an allocentric frame).	Duration: 1 week. Frequency: 2/week. Session duration: 75 min. Total sessions: 2. Conditions: Bod (immersive RV with directional cues); Vis (screen-based, no cues); IntAllo (screen-based, interactive map and directional cues); RedLoad (screen-based, attentional markers and directional cues); FreeNav (screen-based, no cues).	Significant effect of navigation aids on spatial memory task: Bod < Vis and FreeNav (ps ≤ 0.047); IntAllo < FreeNav (p = .021). Significant association between navigation type and average object placement error (p = .027): Bod and IntAllo linked to lower error; Vis and FreeNav linked to higher error. $\eta^2p = 0.02$ (small effect).

Note: 2D, 2-dimension; 3D, 3-dimension; AC, active control; Aer, aerobic; Bod, bodily; CBTT, Corsi Block-Tapping Test; DMST, Delayed Matching to Sample Task; EL, educational level; Enum, enumeration; F, female; FreeNav, free navigation without cues; IntAllo, interactive allocentric map; M, male; MA, mean age; MCI, Mild Cognitive Impairment; MMSE, Mini-Mental State Examination; MRI, Magnetic Resonance Imaging; NoAer, non-aerobic; NR, not reported; Obst, obstacles-only; Pas, passive; Perc, perceptual; RedLoad, reduced executive load; ROCF, Rey-Osterrieth Complex Figure; SATURN, Self-Administered Tasks Uncovering Risk of Neurodegeneration; Spa, spatial; SpaNav, spatial navigation-only; Vis, vision only; VR, virtual reality;  $\Delta$ LDI, change in Lure Discrimination Index (the improvement in hippocampal-dependent memory). Effect sizes are reported as available in the original publications. When quantitative values (e.g., Cohen's d,  $\eta^2$ , or partial  $\eta^2$ ) and 95% confidence intervals were not explicitly provided, qualitative estimates of magnitude are indicated based on reported statistics (small  $\approx$  Cohen's d 0.2,  $\eta^2$  0.01; medium  $\approx$  Cohen's d 0.5,  $\eta^2$  0.06; large  $\approx$  Cohen's d 0.8,  $\eta^2 \geq 0.14$ ). All values reflect pre–post or between-group differences related to spatial memory performance.

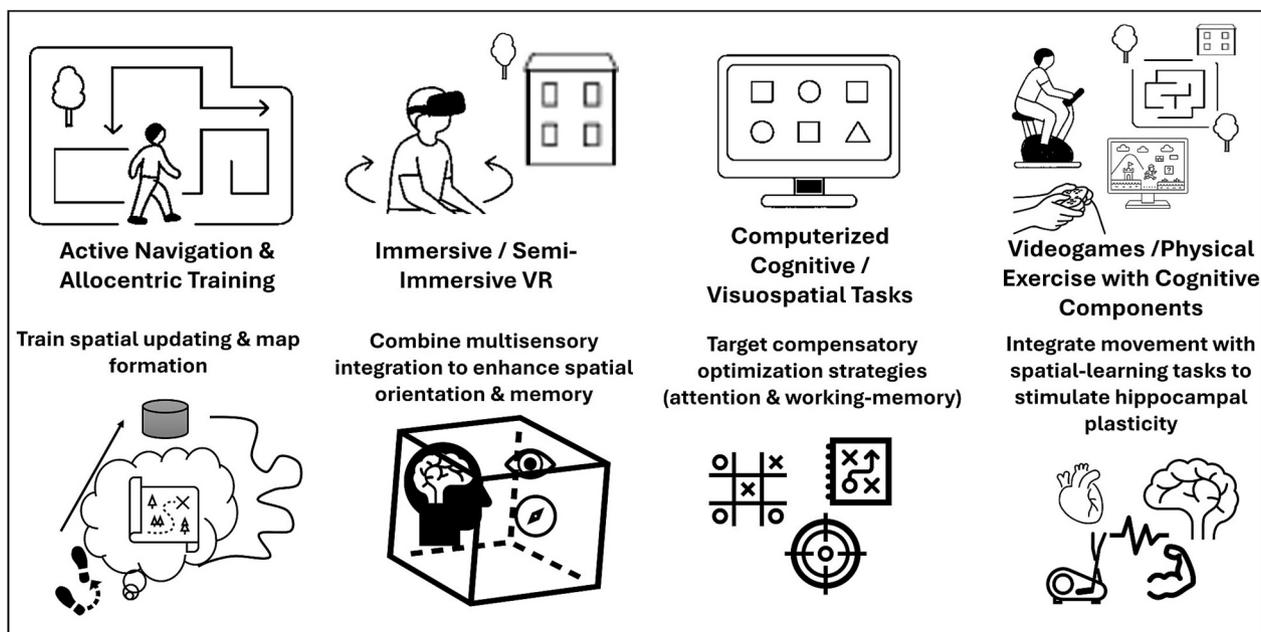


Fig. 2. Conceptual overview of spatial memory interventions illustrating their sensory–motor engagement, spatial–cognitive demands, and targeted cognitive and neurofunctional mechanisms.

efficiency following spatial learning. Merriman et al. (2022) employed the CityQuest task, a 3D interactive environment in which participants practiced route learning, obstacle avoidance, and landmark localization, requiring continuous spatial updating and balance control. Participants demonstrated significant improvements in landmark localization and route memory, favoring egocentric orientation strategies, a pattern consistent with the engagement of frontoparietal and vestibular systems during spatial navigation. These results suggest that interventions combining active exploration, spatial problem-solving, and sensorimotor engagement can effectively reinforce spatial memory through the

coordinated activation of hippocampal, parietal, and vestibular networks.

Interventions employing immersive and embodied VR also showed consistent benefits for spatial memory rehabilitation, particularly through the integration of multisensory feedback and bodily cues. These programs made use of immersive VR environments to enhance engagement, stimulate sensorimotor integration, and promote spatial updating processes. In a pilot study with oncology patients, Serweta-Pawlik et al. (2023) demonstrated that repeated exposure to commercial VR applications preserved or improved visuospatial working memory, as

assessed by the CBTT, in 88% of participants despite concurrent cancer treatment. Similarly, [Stramba-Badiale et al. \(2024\)](#) examined individuals with MCI using the ANTaging VR software under immersive and semi-immersive conditions. Both settings required active navigation and object relocation through body movement using the 3dRudder device. Although no significant differences in spatial accuracy emerged between the two modalities, patients rated the semi-immersive condition as more comfortable and usable, highlighting the importance of embodiment and interface design in neurorehabilitation contexts. Extending these findings, [Tuena et al. \(2024\)](#) investigated the use of navigation aids, including bodily cues, interactive allocentric maps, and reduced cognitive load strategies, to optimize spatial recall in patients with MCI, revealing that body-based cueing and interactive allocentric mapping resulted in superior spatial recall and lower localization errors relative to passive or unassisted navigation. These findings emphasize that combining vestibular–proprioceptive stimulation with visual-cognitive support strengthens encoding and recall processes, highlighting how sensory integration and spatial cueing can facilitate memory retrieval through vestibular and parietal engagement. While not strictly plasticity-based, this study contributes to understanding optimization-oriented approaches that complement plasticity-driven rehabilitation paradigms.

Interventions targeting attentional control and visuospatial working memory also demonstrated meaningful improvements in spatial performance, particularly among older adults with lower baseline cognitive levels. These programs emphasized the training of selective attention, working memory updating, and spatial maintenance, key processes that support spatial encoding and retrieval. In a large online study, [Tagliabue et al. \(2022\)](#) found that both attention-based enumeration training and DMST training significantly improved spatial working memory, especially in low-performing participants, with the DMST group maintaining these gains after three months, demonstrating the durability of process-based spatial training. Complementarily, [Palermo et al. \(2017\)](#) explored the impact of active and passive navigation, as well as the modality of interface in a virtual environment. Active navigation enhanced engagement and spatial awareness, reinforcing the attentional benefits of interactive exploration. These findings suggest that adaptive cognitive and attentional training, particularly when combined with interactive or embodied elements, strengthens frontoparietal control mechanisms underlying spatial working memory and supports adaptive improvements in navigation and recall across aging populations.

#### 4. Discussion

The aim of this systematic review was to evaluate the effectiveness of various neuropsychological interventions on spatial memory. The limited number of studies that met the inclusion criteria suggests a need for more systematic and methodologically rigorous research in this area. This observation highlights the importance of comprehensive reviews that synthesize existing evidence, identify methodological gaps, and guide the design of future intervention protocols. By consolidating empirical findings from a small but growing body of work, this review contributes to establishing a clearer framework for advancing the neuropsychological rehabilitation of spatial memory across both healthy and clinical populations.

The review considered the characteristics of the samples utilized, the intervention tools employed, the methodologies used to assess spatial memory, and the characteristics of the rehabilitation programs implemented in each study. The findings emphasize the efficacy of cognitive interventions in enhancing and preserving spatial memory in both healthy and clinical populations. They highlight the potential of VR as a promising methodology for spatial memory intervention and emphasize the influence of different variables, such as navigation conditions and the level of immersion, on performance in spatial memory tasks.

The sample sizes utilized in the reviewed studies exhibited heterogeneity. In less than 40% of the studies, the samples consisted of 18

participants or fewer ([Serweta-Pawlik et al., 2023](#); [Stramba-Badiale et al., 2024](#); [Tuena et al., 2024](#)), which hinders the extraction of reliable and robust conclusions. Furthermore, only two studies reported a balanced sex distribution among participants ([Hötting et al., 2013](#); [Stramba-Badiale et al., 2024](#)). This finding is of particular interest, as research has demonstrated that sex differences can influence performance in various memory and spatial ability tasks. Previous studies have reported sex-related differences in spatial strategy use and brain activation patterns ([Chai & Jacobs, 2010](#); [Chen et al., 2020](#); [Voyer et al., 1995](#)). Furthermore, only half of the studies provided information on participants' educational background, a variable frequently associated with memory performance ([Clemenson et al., 2020](#); [Serweta-Pawlik et al., 2023](#); [Stramba-Badiale et al., 2024](#); [Tuena et al., 2024](#)). Research has demonstrated a correlation between higher educational level and superior performance on spatial memory tasks ([Stramba-Badiale et al., 2024](#); [Tuena et al., 2024](#)). This phenomenon may be attributed to the potential influence of education on the development of more effective cognitive strategies or its role in contributing to cognitive reserve.

The duration of most rehabilitation programs ranged from four to five weeks ([Clemenson et al., 2020](#); [Hötting et al., 2013](#); [Merriman et al., 2022](#)). A four-week period is considered sufficient to observe cognitive improvements ([Nouchi et al., 2014](#)). The number of sessions is also critical in achieving lasting changes while avoiding participant fatigue ([Nouchi et al., 2014](#)). However, a significant challenge arises from the considerable variability in the number of sessions employed across the reviewed studies. This variability makes it difficult to draw meaningful comparisons between the results. In addition, methodological diversity, both in terms of the intervention format and the tools employed to assess spatial memory, limits the possibility of establishing direct comparisons across studies and highlights the need for greater uniformity in the design and evaluation of programs. Moreover, only one study incorporated follow-up data ([Tagliabue et al., 2022](#)), preventing a comprehensive evaluation of the long-term sustainability of intervention effects. This is a crucial aspect given the evidence that cognitive benefits tend to diminish without reinforcement or sustained integration into activities ([Willis et al., 2006](#)).

Studies have been conducted to evaluate the efficacy of rehabilitation programs in healthy adults ([Hötting et al., 2013](#)) and healthy older adults ([Clemenson et al., 2020](#); [Merriman et al., 2022](#); [Tagliabue et al., 2022](#)). These studies have reported significant improvements in spatial memory following intervention. Results suggest that the most efficacious programs incorporate active navigation ([Clemenson et al., 2020](#); [Merriman et al., 2022](#)), allocentric processing ([Hötting et al., 2013](#); [Tagliabue et al., 2022](#)), and enriched 3D environments ([Clemenson et al., 2020](#)). These findings reinforce the role of brain plasticity, even in healthy adult populations, as shown in previous research ([Johansson, 2004](#); [Mahncke et al., 2006](#)). In a recent study, [Serweta-Pawlik et al. \(2023\)](#) observed the maintenance and improvement of spatial memory in a significant number of cancer patients undergoing chemotherapy. Cognitive functions, including memory, are frequently impaired in these patients ([Ahles & Root, 2018](#)), and the study provides evidence of the efficacy of such rehabilitation programs in maintaining their quality of life and independence.

The reviewed evidence suggests that interventions targeting spatial memory activate and influence key neural systems that underlie spatial navigation and cognitive control. These approaches use neuroplastic mechanisms to improve the efficiency and flexibility of the hippocampal-entorhinal, frontoparietal, and multisensory integration networks. These mechanisms support restorative processes that facilitate the recovery of impaired functions and compensatory adaptations that optimize performance through alternative neural pathways.

Active navigation was a key component in five interventions ([Hötting et al., 2013](#); [Clemenson et al., 2020](#); [Merriman et al., 2022](#); [Tagliabue et al., 2022](#); [Palermo et al., 2017](#)), which typically involved self-directed movement within virtual or 3D spaces. Four of these interventions incorporated allocentric training elements ([Hötting et al.,](#)

2013; Clemenson et al., 2020; Tagliabue et al., 2022; Palermo et al., 2017), which facilitate the encoding of spatial relationships and map-based orientation. Programs that incorporate active navigation and allocentric training appear to promote plasticity within hippocampal–entorhinal circuits (Hötting et al., 2013), which support the encoding and consolidation of spatial maps (Ekstrom et al., 2017).

Interventions that emphasize body-based cues or vestibular–proprioceptive stimulation, such as those implemented by Tuena et al. (2024) and Hötting et al. (2013), engage multisensory integration networks, including the parietal and retrosplenial cortices, which coordinate spatial updating and self-motion processing (Frissen et al., 2011). Similarly, virtual navigation paradigms that simulate self-motion through optic flow and perspective shifts (Clemenson et al., 2020; Merriman et al., 2022) may recalibrate internal spatial representations and improve orientation accuracy, consistent with evidence linking vestibular input to spatial memory precision (Hitier et al., 2014; Schöberl et al., 2021).

Cognitive and attentional training approaches, such as those implemented by Tagliabue et al. (2022), Stramba-Badiale et al. (2024), and Serweta-Pawlik et al. (2023), target the frontoparietal control systems responsible for sustaining attention, maintaining working memory, and supporting goal-directed navigation (Purg Suljić et al., 2024; Rizza et al., 2024). This top-down modulation may improve the stability of spatial representations and promote compensatory mechanisms, particularly in aging and MCI (Lester et al., 2017).

Aerobic and combined physical–cognitive interventions (Hötting et al., 2013), can enhance neurotrophin release, particularly of brain-derived neurotrophic factor, and stimulate hippocampal subfield plasticity, promoting synaptic growth and network efficiency (Boecker et al., 2024; Cassilhas et al., 2016). Aerobic exercise contributes to angiogenesis, neurogenesis, and long-term potentiation within the hippocampal formation, which facilitates spatial encoding and consolidation (Ferrer-Uris et al., 2022). Similarly, cognitively enriched 3D navigation environments may mimic the effects of environmental enrichment by promoting experience-dependent structural remodeling in the hippocampus and entorhinal cortex (Clemenson & Stark, 2015).

The reviewed interventions can be broadly categorized as either plasticity-oriented or optimization-based training approaches. These approaches engage distinct yet complementary mechanisms of change. Plasticity-oriented interventions, such as repeated active navigation, allocentric training, and aerobic–cognitive programs (Clemenson et al., 2020; Hötting et al., 2013; Tagliabue et al., 2022), aim to induce lasting neural reorganization through sustained stimulation of hippocampal–entorhinal and frontoparietal circuits over time. In contrast, optimization-based approaches, including those employing navigational aids or body-based feedback (Merriman et al., 2022; Tuena et al., 2024), reduce cognitive load and improve encoding by enhancing sensory integration or externalizing spatial cues. Together, these complementary strategies demonstrate that spatial memory rehabilitation can operate both by driving neuroplastic adaptation or by supporting compensatory optimization, depending on the individual's cognitive status and neural integrity.

This theoretical distinction is further reflected in how specific design variables, such as immersion level, navigational aids, and baseline cognitive resources, shape the balance between plasticity- and optimization-based mechanisms across populations.

The studies that have examined the impact of particular variables on the performance of spatial memory in individuals with MCI have reported that better outcomes are often observed when tasks are conducted in non-immersive VR environments that provide discrete navigation aids, such as visual cues or stable spatial references (Stramba-Badiale et al., 2024; Tuena et al., 2024). High levels of immersion have been demonstrated to potentially compromise attentional resources, resulting in elevated error rates and a state of disorientation. Additionally, guided navigation tasks with structured spatial references exhibited superior performance in comparison to free-navigation tasks,

a phenomenon that can be attributed, at least in part, to the reduction in cognitive load. Therefore, lower levels of immersion, when combined with clear and stable visual aids, may facilitate spatial encoding and reduce cognitive demand. These findings are consistent with the optimization-based training framework, which proposes that external supports and environmental contingencies can facilitate performance by reducing processing demands when neural efficiency is reduced. Accordingly, lower levels of immersion, when combined with salient and stable visual aids, may maximize spatial encoding efficiency while preventing sensory or attentional overload.

Plasticity-oriented interventions, which involve repeated active exploration or unassisted navigation, may more effectively promote long-term neural reorganization in populations exhibiting preserved cognitive flexibility, such as healthy older adults (Clemenson et al., 2020; Hötting et al., 2013). Palermo et al. (2017) observed no significant differences in spatial memory performance across interfaces with different levels of immersion among healthy young adults. However, the participants indicated a preference for the gyroscope interface, rating it as more interesting and enjoyable, reflecting the motivational and experiential benefits associated with immersive training environment, which activated reward-related and attentional networks (Bediou et al., 2018; Riva et al., 2016). The absence of performance differences can be attributed to the sample's profile, which is characterized by elevated cognitive flexibility. This ability enables young adults to adapt effectively to diverse conditions (Westhoff et al., 2024). Immersive VR has also been demonstrated to be an effective and well-tolerated tool in cancer patients (Serweta-Pawlik et al., 2023). Prior research has shown that VR can support the rehabilitation of various cognitive functions, including spatial memory, when moderate immersion levels are employed to prevent sensory overload (Kim et al., 2019). Taken together, these findings are pertinent to the design of neuropsychological rehabilitation programs targeting spatial memory. They also support the feasibility of immersive VR as a tool in pathological conditions.

The combined effect of physical rehabilitation and cognitive training on spatial memory performance was assessed (Hötting et al., 2013), showing greater processing benefits following spatial training. Research has emphasized the role of physical exercise in memory performance (Mandolesi et al., 2018; Ramirez Butavand et al., 2023), supporting its inclusion in cognitive rehabilitation programs to optimize consolidation and retrieval processes. However, in Hötting et al. (2013), improvements were observed irrespective of aerobic exercise, suggesting that performance gains may primarily stem from cognitive stimulation, with physical activity playing a less critical role.

Tagliabue et al. (2022) observed that visual attention training alone was sufficient to improve performance in a visuospatial working memory task, without the need for retention-focused training. These results support the use of attentional tasks for training short-term and working spatial memory, although such tasks may be insufficient for improving long-term spatial memory. For longer delay intervals in spatial tasks, retention has been shown to improve with specific consolidation training (Graves et al., 2022). Furthermore, the study highlighted the relevance of initial performance levels, indicating that participants with low initial performance exhibited more substantial improvements following attentional training compared to those with high baseline performance. This pattern aligns with the findings of other studies (Heinzel et al., 2016), which indicate that high-performing individuals tend to experience more limited benefits from training.

Collectively, these findings suggest that the efficacy of spatial memory rehabilitation depends on the interaction between neural integrity and task demands (Lester et al., 2017; Tuena et al., 2024). Interventions that emphasize repeated practice and exploratory learning have been shown to enhance plasticity-driven gains by engaging the hippocampal–entorhinal and frontoparietal circuit, which are responsible for experience-dependent reorganization (Cassilhas et al., 2016; Clemenson et al., 2020; Hötting et al., 2013). Interventions incorporating aids, body-based feedback, or reduced immersion primarily foster

optimization-based compensatory outcomes, supporting spatial updating and orientation through multisensory and attentional pathways (Tuena et al., 2024; Stramba-Badiale et al., 2021; Frissen et al., 2011). These principles provide a framework for adapting rehabilitation protocols to individual cognitive profiles, ensuring that intervention design, particularly the level of immersion, presence of aids, and baseline cognitive performance, optimizes spatial learning and functional transfer.

These findings also have significant implications for clinical and applied neuropsychology. The differentiation between plasticity- and optimization-based approaches offers a practical framework for the selection and adaptation of interventions according to the individual's cognitive resources and neural integrity. In practice, plasticity-oriented training, involving repeated active navigation, exploratory learning, and multisensory engagement, appears most suitable for individuals with relatively preserved cognitive flexibility, such as healthy older adults, to strengthen hippocampal–entorhinal and frontoparietal circuits through sustained stimulation. Conversely, optimization-oriented programs that incorporate navigational aids, body-based feedback, or reduced immersion may be more beneficial for populations with cognitive decline or neural compromise, such as individuals with MCI. These programs promote compensatory processes while preventing cognitive overload. For clinicians, these insights are particularly salient, as they demonstrate the importance of calibrating immersion level and task complexity to the user's baseline attentional and spatial capacities, fostering engagement while avoiding disorientation or fatigue. For researchers, adopting this dual-framework perspective may enhance methodological consistency across trials, refine criteria for intervention dosage and transfer, and guide the systematic integration of VR-based protocols into multidisciplinary rehabilitation frameworks.

## 5. Conclusions

In summary, the findings of this systematic review indicate that spatial memory is a cognitive function that can be effectively targeted and enhanced through well-structured and evidence-based neuropsychological rehabilitation programs. The studies that have been reviewed have reported significant improvements following interventions that integrate active navigation, allocentric reference frames, and technologies such as VR, provided that immersion levels are carefully considered. Furthermore, the efficacy of neuropsychological intervention programs is evident not only in healthy older adults but also in individuals with MCI and cancer patients. These findings, when considered collectively, support the efficacy of neuropsychological interventions in the rehabilitation of spatial memory. However, it is essential that these interventions be implemented in a structured manner and tailored to the cognitive profiles of individual participants to ensure optimal outcomes.

This review identifies salient aspects that neuropsychological interventions of spatial memory must consider, such as the incorporation of follow-up assessments to evaluate the stability of intervention effects and the standardization of intervention and evaluation protocols. Besides, the improvement of study quality is also dependent on the collection and consideration of relevant sociodemographic and clinical information, as well as the incorporation of usability, adherence, and patient satisfaction measures.

## 6. Limitations

The present systematic review was based on studies retrieved exclusively from PubMed, Scopus, and WoS databases. Therefore, it is plausible that pertinent studies from alternative sources were omitted. Furthermore, despite the utilization of a wide array of cognitive intervention-related terminology in search queries, the heterogeneity in terminology employed by authors across disciplines may have constrained the identification of potentially pertinent studies that were not indexed under the selected search terms.

It is imperative to acknowledge that a multitude of health conditions have the potential to influence spatial memory performance, thereby contributing to variability across samples. Neurological disorders (e.g., Parkinson's disease, traumatic brain injury) and systemic conditions (e.g., diabetes) have been associated with spatial navigation deficits. However, these factors were not consistently reported or controlled for in the included studies. It is imperative that future research systematically account for such clinical and physiological variables when designing interventions or interpreting their cognitive outcomes.

The limited number of studies that met the inclusion criteria results in findings that are not widely applicable and highlights the necessity for additional systematic and methodologically rigorous investigations to establish a robust evidence base for spatial memory rehabilitation.

## CRedit authorship contribution statement

**Tania Llana:** Writing – original draft, Methodology, Investigation, Formal analysis, Data curation. **Sara Garcés-Arilla:** Visualization, Methodology, Data curation. **Marta Mendez:** Writing – review & editing, Supervision, Methodology, Investigation, Formal analysis, Data curation, Conceptualization.

## Declaration of Generative AI and AI-assisted technologies in the writing process

During the preparation of this work the authors used DeepL Write in order to correct and improve the English version of this manuscript. After using this tool the authors reviewed and edited the content as needed and takes full responsibility for the content of the published article.

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## Declaration of competing interest

The authors declare that they have no conflict of interest.

## Data availability

Data will be made available on request.

## References

- Ahles, T. A., & Root, J. C. (2018). Cognitive effects of cancer and cancer treatments. *Annual Review of Clinical Psychology*, 14(1), 425–451. <https://doi.org/10.1146/annurev-clinpsy-050817-084903>
- Baumann, O., Chan, E., & Mattingley, J. B. (2009). Dissociable neural circuits for encoding and retrieval of object locations during active navigation in humans. *NeuroImage*, 49(3), 2816–2825. <https://doi.org/10.1016/j.neuroimage.2009.10.021>
- Bediou, B., Adams, D. M., Mayer, R. E., Tipton, E., Green, C. S., & Bavelier, D. (2018). Meta-analysis of action video game impact on perceptual, attentional, and cognitive skills. *Psychological Bulletin*, 144(1), 77–110. <https://doi.org/10.1037/bul0000130>
- Boccia, M., Nemmi, F., & Guariglia, C. (2014). Neuropsychology of environmental navigation in humans: Review and meta-analysis of fMRI studies in healthy participants. *Neuropsychology Review*, 24(2), 236–251. <https://doi.org/10.1007/s11065-014-9247-8>
- Boecker, H., Daamen, M., Kunz, L., Geiß, M., Müller, M., Neuss, T., ... Maurer, A. (2024). Hippocampal subfield plasticity is associated with improved spatial memory. *Communications Biology*, 7(1), 271. <https://doi.org/10.1038/s42003-024-05949-5>
- Bostelmann, M., Fragnière, E., Costanzo, F., Di Vara, S., Menghini, D., Vicari, S., ... Lavenex, P. B. (2017). Dissociation of spatial memory systems in Williams syndrome. *Hippocampus*, 27(11), 1192–1203. <https://doi.org/10.1002/hipo.22764>
- Braak, H., & Braak, E. (1991). Neuropathological staging of Alzheimer-related changes. *Acta Neuropathologica*, 82(4), 239–259. <https://doi.org/10.1007/BF00308809>
- Burgess, N., Maguire, E. A., & O'Keefe, J. (2002). The human hippocampus and spatial and episodic memory. *Neuron*, 35(4), 625–641. [https://doi.org/10.1016/S0896-6273\(02\)00830-9](https://doi.org/10.1016/S0896-6273(02)00830-9)

- Cassilhas, R. C., Tufik, S., & De Mello, M. T. (2016). Physical exercise, neuroplasticity, spatial learning and memory. *Cellular and Molecular Life Sciences*, 73(5), 975–983. <https://doi.org/10.1007/s00118-015-2102-0>
- Chai, X. J., & Jacobs, L. F. (2010). Effects of cue types on sex differences in human spatial memory. *Behavioural Brain Research*, 208(2), 336–342. <https://doi.org/10.1016/j.bbr.2009.11.039>
- Chen, W., Liu, B., Li, X., Wang, P., & Wang, B. (2020). Sex differences in spatial memory. *Neuroscience*, 443, 140–147. <https://doi.org/10.1016/j.neuroscience.2020.06.016>
- Cheung, K. L., Tunik, E., Adamovich, S. V., & Boyd, L. A. (2014). Neuroplasticity and virtual reality. In P. L. Weiss, E. A. Keshner, & M. F. Levin (Eds.), *Virtual reality for physical and motor rehabilitation* (pp. 5–24). New York: Springer. [https://doi.org/10.1007/978-1-4939-0968-1\\_2](https://doi.org/10.1007/978-1-4939-0968-1_2)
- Clemenson, G. D., & Stark, C. E. (2015). Virtual environmental enrichment through video games improves hippocampal-associated memory. *Journal of Neuroscience: The Official Journal of the Society for Neuroscience*, 35(49), 16116–16125. <https://doi.org/10.1523/JNEUROSCI.2580-15.2015>
- Clemenson, G. D., Stark, S. M., Rutledge, S. M., & Stark, C. E. L. (2020). Enriching hippocampal memory function in older adults through video games. *Behavioural Brain Research*, 390, Article 112667. <https://doi.org/10.1016/j.bbr.2020.112667>
- Costa, R. Q. M. D., Pompeu, J. E., Viveiro, L. A. P., & Brucki, S. M. D. (2020). Spatial orientation tasks show moderate to high accuracy for the diagnosis of mild cognitive impairment: A systematic literature review. *Arquivos de Neuro-Psiquiatria*, 78(11), 713–723. <https://doi.org/10.1590/0004-282X202000043>
- Ekstrom, A. D., Huffman, D. J., & Starrett, M. (2017). Interacting networks of brain regions underlie human spatial navigation: A review and novel synthesis of the literature. *Journal of Neurophysiology*, 118(6), 3328–3344. <https://doi.org/10.1152/jn.00531.2017>
- England, H. B., Fyock, C., Meredith Gillis, M., & Hampstead, B. M. (2015). Transcranial direct current stimulation modulates spatial memory in cognitively intact adults. *Behavioural Brain Research*, 283, 191–195. <https://doi.org/10.1016/j.bbr.2015.01.044>
- Epstein, R. A., & Baker, C. I. (2019). Scene perception in the human brain. *Annual Review of Vision Science*, 5, 373–397. <https://doi.org/10.1146/annurev-vision-091718-014809>
- Farhani, F., Shahrbani, S., Auais, M., Hekmatikar, A. H. A., & Suzuki, K. (2022). Effects of aerobic training on brain plasticity in patients with mild cognitive impairment: A systematic review of randomized controlled trials. *Brain Sciences*, 12(6), 732. <https://doi.org/10.3390/brainsci12060732>
- Ferrer-Uris, B., Ramos, M. A., Busquets, A., & Angulo-Barroso, R. (2022). Can exercise shape your brain? A review of aerobic exercise effects on cognitive function and neuro-physiological underpinning mechanisms. *AIMS Neuroscience*, 9(2), 150–174. <https://doi.org/10.3934/Neuroscience.2022009>
- Frissen, I., Campos, J. L., Souman, J. L., & Ernst, M. O. (2011). Integration of vestibular and proprioceptive signals for spatial updating. *Experimental Brain Research*, 212(2), 163–176. <https://doi.org/10.1007/s00221-011-2717-9>
- García-Navarra, S., Llana, T., & Méndez, M. (2025). Spatial memory deficits in Parkinson's disease: Neural mechanisms and assessment. *American Journal of Neurodegenerative Disease*, 14(3), 67–81. <https://doi.org/10.62347/CKGV8650>
- Gates, P., Krishnasamy, M., Wilson, C., Hawkes, E. A., Doré, V., Perchyonok, Y., ... Gough, K. (2022). Cancer-related cognitive impairment in patients with newly diagnosed aggressive lymphoma undergoing standard chemotherapy: A longitudinal feasibility study. *Supportive Care in Cancer: Official Journal of the Multinational Association of Supportive Care in Cancer*, 30(9), 7731–7743. <https://doi.org/10.1007/s00520-022-07153-9>
- Giannouli, V. (2013). *Visual symmetry perception*. *Encephalos*, 50, 31–42.
- Giannouli, V., Yordanova, J., & Kolev, V. (2024). Can brief listening to Mozart's music improve visual working memory? An update on the role of cognitive and emotional factors. *Journal of Intelligence*, 12(6), 54. <https://doi.org/10.3390/jintelligence12060054>
- Graves, K. N., Sherman, B. E., Huberdeau, D., Damisah, E., Quraishi, I. H., & Turk-Browne, N. B. (2022). Remembering the pattern: A longitudinal case study on statistical learning in spatial navigation and memory consolidation. *Neuropsychologia*, 174, Article 108341. <https://doi.org/10.1016/j.neuropsychologia.2022.108341>
- Heinzel, S., Lorenz, R. C., Pelz, P., Heinz, A., Walter, H., Kathmann, N., ... Stelzel, C. (2016). Neural correlates of training and transfer effects in working memory in older adults. *NeuroImage*, 134, 236–249. <https://doi.org/10.1016/j.neuroimage.2016.03.068>
- Hitler, M., Besnard, S., & Smith, P. F. (2014). Vestibular pathways involved in cognition. *Frontiers in Integrative Neuroscience*, 8, 59. <https://doi.org/10.3389/fnint.2014.00059>
- Hötting, K., Holzschneider, K., Stenzel, A., Wolbers, T., & Röder, B. (2013). Effects of a cognitive training on spatial learning and associated functional brain activations. *BMC Neuroscience*, 14(1), 73. <https://doi.org/10.1186/1471-2202-14-73>
- Johansson, B. B. (2004). Brain plasticity in health and disease. *The Keio Journal of Medicine*, 53(4), 231–246. <https://doi.org/10.2302/kjm.53.231>
- Kim, O., Pang, Y., & Kim, J.-H. (2019). The effectiveness of virtual reality for people with mild cognitive impairment or dementia: A meta-analysis. *BMC Psychiatry*, 19(1), 219. <https://doi.org/10.1186/s12888-019-2180-x>
- Klein, J. A. (2011). Neural plasticity and neurorehabilitation: Teaching the new brain old tricks. *Journal of Communication Disorders*, 44(5), 521–528. <https://doi.org/10.1016/j.jcomdis.2011.04.006>
- Lester, A. W., Moffat, S. D., Wiener, J. M., Barnes, C. A., & Wolbers, T. (2017). The aging navigational system. *Neuron*, 95(5), 1019–1035. <https://doi.org/10.1016/j.neuron.2017.06.037>
- Mahncke, H. W., Connor, B. B., Appelman, J., Ahsanuddin, O. N., Hardy, J. L., Wood, R. A., ... Merzenich, M. M. (2006). Memory enhancement in healthy older adults using a brain plasticity-based training program: A randomized, controlled study. *Proceedings of the National Academy of Sciences*, 103(33), 12523–12528. <https://doi.org/10.1073/pnas.0605194103>
- Mandolesi, L., Polverino, A., Montuori, S., Foti, F., Ferraioli, G., Sorrentino, P., & Sorrentino, G. (2018). Effects of physical exercise on cognitive functioning and wellbeing: Biological and psychological benefits. *Frontiers in Psychology*, 9, 509. <https://doi.org/10.3389/fpsyg.2018.00509>
- Merriman, N. A., Roudaia, E., Ondřej, J., Romagnoli, M., Orvieto, I., O'Sullivan, C., & Newell, F. N. (2022). "CityQuest," a custom-designed serious game, enhances spatial memory performance in older adults. *Frontiers in Aging Neuroscience*, 14, Article 806418. <https://doi.org/10.3389/fnagi.2022.806418>
- Montana, J. I., Tuena, C., Serino, S., Cipresso, P., & Riva, G. (2019). Neurorehabilitation of spatial memory using virtual environments: A systematic review. *Journal of Clinical Medicine*, 8(10), 1516. <https://doi.org/10.3390/jcm8101516>
- Nouchi, R., Taki, Y., Takeuchi, H., Sekiguchi, A., Hashizume, H., Nozawa, T., Nouchi, H., & Kawashima, R. (2014). Four weeks of combination exercise training improved executive functions, episodic memory, and processing speed in healthy elderly people: Evidence from a randomized controlled trial. *AGE*, 36(2), 787–799. <https://doi.org/10.1007/s11357-013-9588-x>
- Page, M. J., McKenzie, J. E., Bossuyt, P. M., Boutron, I., Hoffmann, T. C., Mulrow, C. D., ... Moher, D. (2021). The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. *BMJ*, 372, Article n71. <https://doi.org/10.1136/bmj.n71>
- Palermo, E., Laut, J., Nov, O., Cappa, P., & Porfiri, M. (2017). Spatial memory training in a citizen science context. *Computers in Human Behavior*, 73, 38–46. <https://doi.org/10.1016/j.chb.2017.03.017>
- Piber, D. (2021). The role of sleep disturbance and inflammation for spatial memory. *Brain, Behavior, & Immunity – Health*, 17, Article 100333. <https://doi.org/10.1016/j.bbih.2021.100333>
- Poos, J. M., Van Der Ham, I. J. M., Leeuwis, A. E., Pijnenburg, Y. A. L., Van Der Flier, W. M., & Postma, A. (2021). Short digital spatial memory test detects impairment in Alzheimer's disease and mild cognitive impairment. *Brain Sciences*, 11(10), 1350. <https://doi.org/10.3390/brainsci11101350>
- Postma, A., Kessels, R., & Vanasselen, M. (2008). How the brain remembers and forgets where things are: The neurocognition of object-location memory. *Neuroscience and Biobehavioral Reviews*, 32(8), 1339–1345. <https://doi.org/10.1016/j.neubiorev.2008.05.001>
- Purg Suljić, N., Kraljić, A., Rahmati, M., Cho, Y. T., Slana Ozimić, A., Murray, J. D., ... Repovš, G. (2024). Individual differences in spatial working memory strategies differentially reflected in the engagement of control and default brain networks. *Cerebral Cortex*, 34(8), Article bhae350. <https://doi.org/10.1093/cercor/bhae350>
- Ramirez Butavand, D., Rodriguez, M. F., Cifuentes, M. V., Miranda, M., Bauza, C. G., Bekinschtein, P., & Ballarini, F. (2023). Acute and chronic physical activity improves spatial memory in an immersive virtual reality task. *iScience*, 26(3), Article 106176. <https://doi.org/10.1016/j.isci.2023.106176>
- Riva, G., Baños, R. M., Botella, C., Mantovani, F., & Gaggioli, A. (2016). Transforming experience: The potential of augmented reality and virtual reality for enhancing personal and clinical change. *Frontiers in Psychiatry*, 7, 164. <https://doi.org/10.3389/fpsyg.2016.00164>
- Rizza, A., Pedale, T., Mastroberardino, S., Olivetti Belardinelli, M., Van der Lubbe, R. H. J., Spence, C., & Santangelo, V. (2024). Working memory maintenance of visual and auditory spatial information relies on Supramodal neural codes in the dorsal Frontoparietal cortex. *Brain Sciences*, 14(2), 123. <https://doi.org/10.3390/brainsci14020123>
- Ruggiero, G., D'Errico, O., & Iachini, T. (2016). Development of egocentric and allocentric spatial representations from childhood to elderly age. *Psychological Research*, 80(2), 259–272. <https://doi.org/10.1007/s00426-015-0658-9>
- Schöberl, F., Pradhan, C., Grosch, M., Brendel, M., Jostes, F., Obermaier, K., Sowa, C., Jahn, K., Bartenstein, P., Brandt, T., Dieterich, M., & Zwergal, A. (2021). Bilateral vestibulopathy causes selective deficits in recombining novel routes in real space. *Scientific Reports*, 11(1), 2695. <https://doi.org/10.1038/s41598-021-82427-6>
- Serweta-Pawlik, A., Lachowicz, M., Żurek, A., Rosen, B., & Żurek, G. (2023). Evaluating the effectiveness of visuospatial memory stimulation using virtual reality in head and neck cancer patients—Pilot study. *Cancers*, 15(6), 1639. <https://doi.org/10.3390/cancers15061639>
- Skelton, R. W., Bukach, C. M., Laurance, H. E., Thomas, K. G., & Jacobs, J. W. (2000). Humans with traumatic brain injuries show place-learning deficits in computer-generated virtual space. *Journal of Clinical and Experimental Neuropsychology*, 22(2), 157–175. [https://doi.org/10.1076/1380-3395\(200004\)22:2:1-1:FT157](https://doi.org/10.1076/1380-3395(200004)22:2:1-1:FT157)
- Stramba-Badiale, C., Tuena, C., Goulene, K. M., Cipresso, P., Morelli, S., Rossi, M., ... Riva, G. (2024). Enhancing spatial navigation skills in mild cognitive impairment patients: A usability study of a new version of ANTagging software. *Frontiers in Human Neuroscience*, 17, Article 1310375. <https://doi.org/10.3389/fnhum.2023.1310375>
- Tagliabue, C. F., Varesio, G., & Mazza, V. (2022). Training attentive individuation leads to visuo-spatial working memory improvement in low-performing older adults: An online study. *Attention, Perception, & Psychophysics*, 84(8), 2507–2518. <https://doi.org/10.3758/s13414-022-02580-6>
- Toril, P., Reales, J. M., Mayas, J., & Ballesteros, S. (2016). Video game training enhances visuospatial working memory and episodic memory in older adults. *Frontiers in Human Neuroscience*, 10, 206. <https://doi.org/10.3389/fnhum.2016.00206>
- Tragantzopoulou, P., & Giannouli, V. (2024). Spatial orientation assessment in the elderly: A comprehensive review of current tests. *Brain Sciences*, 14(9), 898. <https://doi.org/10.3390/brainsci14090898>

- Tuena, C., Mancuso, V., Stramba-Badiale, C., Pedrolì, E., Stramba-Badiale, M., Riva, G., & Repetto, C. (2021). Egocentric and allocentric spatial memory in mild cognitive impairment with real-world and virtual navigation tasks: A systematic review. *Journal of Alzheimer's Disease*, 79(1), 95–116. <https://doi.org/10.3233/JAD-201017>
- Tuena, C., Serino, S., Goulene, K. M., Pedrolì, E., Stramba-Badiale, M., & Riva, G. (2024). Bodily and visual-cognitive navigation aids to enhance spatial recall in mild cognitive impairment. *Journal of Alzheimer's Disease*, 99(3), 899–910. <https://doi.org/10.3233/JAD-240122>
- Tuena, C., Serino, S., Pedrolì, E., Stramba-Badiale, M., Riva, G., & Repetto, C. (2021). Building embodied spaces for spatial memory neurorehabilitation with virtual reality in normal and pathological aging. *Brain Sciences*, 11(8), 1067. <https://doi.org/10.3390/brainsci11081067>
- Voyer, D., Voyer, S., & Bryden, M. P. (1995). Magnitude of sex differences in spatial abilities: A meta-analysis and consideration of critical variables. *Psychological Bulletin*, 117(2), 250–270. <https://doi.org/10.1037/0033-2909.117.2.250>
- Westhoff, M., Heshmati, S., Siepe, B., Vogelbacher, C., Ciarrochi, J., Hayes, S. C., & Hofmann, S. G. (2024). Psychological flexibility and cognitive-affective processes in young adults' daily lives. *Scientific Reports*, 14(1), 8182. <https://doi.org/10.1038/s41598-024-58598-3>
- Willis, S. L., Tennstedt, S. L., Marsiske, M., Ball, K., Elias, J., Koepke, K. M., ... Active Study Group, F. T. (2006). Long-term effects of cognitive training on everyday functional outcomes in older adults. *JAMA*, 296(23), 2805. <https://doi.org/10.1001/jama.296.23.2805>
- Xiong, H. (2008). Hippocampus and spatial memory. In H. E. Gendelman, & T. Ikezu (Eds.), *Neuroimmune Pharmacology* (pp. 55–64). Springer US. [https://doi.org/10.1007/978-0-387-72573-4\\_6](https://doi.org/10.1007/978-0-387-72573-4_6).
- Zhang, X., Huang, Y., Xia, Y., Yang, X., Zhang, Y., Wei, C., ... Liu, Y. (2022). Vestibular dysfunction is an important contributor to the aging of visuospatial ability in older adults-data from a computerized test system. *Frontiers in Neurology*, 13, Article 1049806. <https://doi.org/10.3389/fneur.2022.1049806>