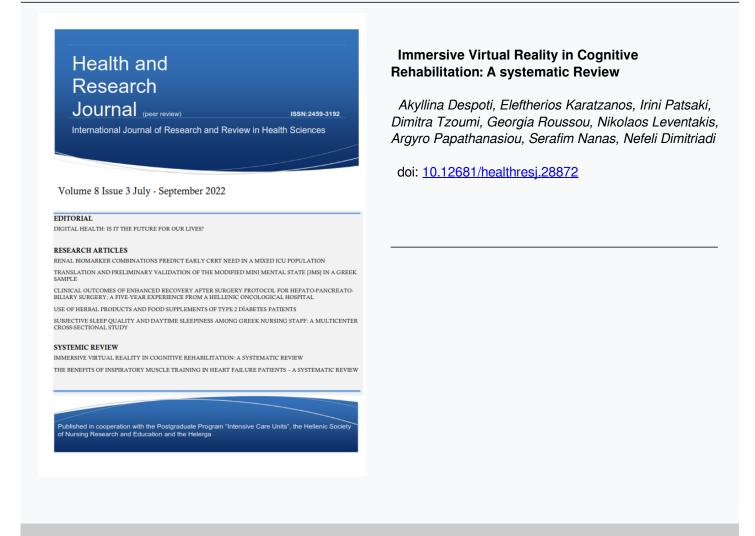




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Systematic Review

IMMERSIVE VIRTUAL REALITY IN COGNITIVE REHABILITATION: A SYSTEMATIC REVIEW

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Abstract

Background: Virtual Reality (VR) is a new technology used more and more in clinical trial.

Aim: The aim of this study is to investigate the effects of immersive VR as a rehabilitation approach of cognitive functions.

Method and Material: A systematic literature review was conducted in the electronic databases of PubMed, Cochrane, OTseeker and PsycINFO for articles published until August 2021. The main search terms were "immersive virtual reality," and "cognitive rehabilitation". The research was strictly limited in immersive technologies and adult patients suffering from neurological disorder or a traumatic injury or elderly with cognitive decline, and no reviews are included. Totally, 16 citations reviewed.

Results: All intervention studies reported improvements either in cognitive functions or in stress management and relaxation. In particular, most of the studies demonstrated improvement in attention (N=6) but also in executive functions (N=3), in memory (N=5) and in navigation skills (N=1). Regarding safety and feasibility, most of the participants in the studies completed successfully the tasks and did not report stimulation sickness.

Conclusions: The available limited data indicate that immersive VR environments can a) be feasible and safe and b) have a positive impact in cognitive functions in the dynamic process of rehabilitation. Further research is warranted in large-scale longitudinal clinical trials in various patients' groups in order to compare the effects of immersive and non-immersive VR interventions. Future studies should further investigate the long-term impact on cognitive functions in interventions using immersive VR.

Keywords: Immersive, virtual reality, rehabilitation, cognitive functions.

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INTRODUCTION

Even though virtual reality (VR) is a technology applied since 1980 in space and military (NASA- Virtual Interface Environment Workstation, 1980; Thomas A. Furness- Visually Coupled Airborne Systems Simulator, 1982), their use in medical rehabilitation is emerging the last decade.¹ Regarding, the field of clinical neuropsychology, VR has been used as a tool for the assessment (and rehabilitation of various cognitive functions, such as executive functions, memory, attention and visuospatial abilities, that have been degraded due to various neurological conditions and brain damage.²⁻⁵

Researchers claim that VR intervention methods have several advantages compared to traditional, face to face and paperand-pencil methods.⁶ More specifically, VR provides safe and engaging environment simulating the real world, and therefore high ecological validity. Their performance tracking is accurate, detailed and automated, and can record data which a human eve would not report eliminating the loss of important data due to the limitations of subjective observation. Furthermore, health care professionals thanks to VR systems own a great level flexibility and control over the tasks and they can offer personalization on the therapeutic protocols.

The VR technology can be presented in fully immersive, semiimmersive and non- immersive environments. High levels of immersion may provide a high sense of presence in the virtual world affecting both the physical and emotional reaction to the input from the VR system.⁷ The impact of immersion in rehabilitation using VR technologies needs to be assessed.

Immersive VR constitutes of a real-time three-dimensional virtual world where the user maintains a first-person view of the VR environment with which they interact, in a embodied experience, whilst in non-immersive or semi-immersive VR the "mirror" view can be used in a non-embodied experience with "mirror" view of the user, or with the use of two-dimensional (2D) graphics. The VR rehabilitation scenarios have been performed to either 2D or 3D graphics.⁸ A 3D environment is perceived to be more realistic and with higher sense of presence than a 2D environment.9

Spatial presence refers to "the sense of being in an environment".¹⁰ Higher levels of immersion have been linked to side Despoti et al.

effects as dizziness, nausea, discomfort, eye fatigue, disorientation or motion-sickness which is referred as VR sickness.¹¹ However, these symptoms have been reported to only 5% of the participants in a VR environment.¹²

The type of graphics can affect the participants' perception of the task and intentions.¹³ 2D and 3DVR-systems lead to different presence experiences and to different cortical activation patterns. In particular, presence experiences associated with activity of a fronto-parietal network, which is modulated by the Dorsolateral Prefrontal Cortex (DLPFC).¹⁰ Fully immersive 3D enriched-environment requires allocation of more brain and sensory resources for cognitive/motor tasks than 2D.¹⁴ However, the study of Lledó et al.,¹⁵ suggest that 2D VR environments may be a more efficient for post-stroke patients in rehabilitation of upper limb, mainly because of the accuracy in order to effectuate optimal kinematic trajectories.

There are more and more clinical trials that include VR. Most of the studies in cognitive rehabilitation, use semi or nonimmersive environments, mostly due to high economic software and hardware requirements or other development complications and issue related to the technologies interfacing and the three-dimensional graphics representation of the user in virtual space. The aim of this study is to review and investigate the effects of immersive VR as a rehabilitation approach of cognitive functions. Furthermore, safety and reliability will be also examined.

METHODOLOGY

The current review was conducted and reported with guidance of with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.

Data sources and search strategy

The electronic data bases of PubMed, Scopus, Cochrane, OTseeker and PsycINFO were systematically searched from inception until August of 2021. Keywords for strategy searching were: immersive virtual reality, cognitive rehabilitation and neuropsychological rehabilitation.

For example, a sample search strategy for the PubMed database was: ((((immersive virtual real*)) OR (immersive virtualreal*)) OR (immersive VR)) AND (((neuropsychological) OR (neuro rehab*)) OR ((cogn*) OR (CR))).

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Eligibility criteria and study selection

The inclusion criteria were the following: a) studies with immersive VR technologies published in English in peer-reviewed journals, b) studies with VR technologies that measure rehabilitation in cognitive functions (memory, attention and concentration, language, executive and visuospatial function, navigation), c) adult patients with diagnosis of neurological disorder or traumatic brain injury) (d) elderly with cognitive decline. The studies with psychiatric disorders were excluded. First, all articles were evaluated by two authors according to the title, abstract, and text. Then, all those who considered potentially eligible were fully read and initially analyzed. The last machine engine research was on 30 August 2021.

Data extraction

Extracted data of the studies were organized according to PICO process: (1) author and date of publication, (2) neurological disorder (3) sample size (4) experimental intervention, (5) control interventions (7) sessions details (number, duration and frequency), (8) outcomes, (9) type of study (Table 1). Furthermore, the neuropsychological outcome measures were arranged by cognitive functions: (1) attention/ concentration, (2) executive function, (3) (4) memory, visuospatial/orientation/navigation, (5) language and also stress (Table 2). Also, follow up sessions and ecological validly was also taken into account.

Quality assessment

Two authors (AD, EK) assessed the quality of the research of each RCT articles using the Physiotherapy Evidence Database (PEDro) Scale (Table 3). Total scores from 6 to 10 considered high quality, from 4-5 considered fair quality and \leq 3 considered poor quality. Two authors conducted a blinded rating of the methodological quality of the studies. Different rates and unclear issues were discussed.

Level of immersion

The level of immersiveness of VR technologies that were included on the studies was assessed using the criteria of Michael Heim (1998) by the 3ls: Immersion, Interaction and Information intensity, and the classification of sense of presence (SoP) in VR can be assessed by examination both of the interfaces and technologies used (360 stereoscopic view, interaction interfaces, embodiment of the user in virtual space) and the multimedia content (real-time three-dimensional graphics, interaction mechanisms, gamification techniques and real-world physics and properties simulation).

RESULTS

The selection process is summarized according to PRISMA guidelines as a flow chart (Fig. 1). Firstly, 468 records identified through databases searching. After deleting duplicate papers, 466 were screened by the authors to assess the inclusion criteria. A total number of 223 articles assessed full-text for eligibility. Consequently, 16 studies included in qualitative synthesis. For articles meeting inclusion criteria, data on study design, participant characteristics, and intervention outcomes were extracted by two of the authors (AD and EK). Disagreements between reviewers were resolved by consensus.

There were 16 studies selected that were relevant to the aim of this review (Table 1). Most of the studies were RCTs (N=6) and five feasibility and one reliability study. There were some lowlevel evidences including two case studies and two non- randomized controlled trials. All studies investigated immersive VR as rehabilitation tool in persons with neurological disorders (as stroke, Traumatic Brain Injury (TBI), Alzheimer Disease (AD)) MCI and elderly.

Participants

The number of participants ranged from 66 to 1 (mean= 26 persons). The total number of participants was 404 (Table 1). The majority of the studies¹⁶⁻²⁰ developed VR systems to train patients with traumatic brain injury (TBI). There were, four VR rehabilitation systems²¹⁻²⁴ practiced form elderly participants with cognitive decline. In addition, there are systems created aimed to train various cognitive functions for patients suffering from stroke,²⁵⁻²⁷ Alzheimer's disease²⁸ and mild cognitive impairment.²⁹⁻³¹

Aim of studies

The aim of the studies (Table 2) was either to test the feasibility of the VR systems,^{20,21,24,27,31} and the reliability¹⁶ or to train specific cognitive functions such as attention,^{18,19,20,29} executive functions,^{17,22} memory,²³ navigation,²⁸ general cognitive abilities and daily living,^{25,30} as well as stress relief and relaxation.²¹ One study compared screen displays as an alternative to HMD within virtual reality (VR)-based applications to train memory and attention functions.²⁶

Interventions

Some types of interventions concerned activities of the everyday life^{16,19,26,29,30} such as preparation of meal, interacting in a virtual store and accomplishing morning hygiene etc. Further, other scenarios included path finding and navigation^{19,23,24,26,28} and various kind of exercises such as card play and fishing,²⁵ fruit ninja,²² target detection in outdoor space such as garden²⁷ or Stroop tasks in VR Apartment and Classroom.¹⁷ One study uses scenes from nature for relaxation.²¹ Two studies^{18,20} designed simple interventions with minimal graphics such as just a black board with target and cursor or cancellation tasks, for patients with severe brain injuries on the early stages of recovery.

Comparison

Six out of the 15 studies^{22,25,26,29,30,23} included comparison group. In two studies^{23,29} the comparison group performed traditional, face to face training such as physical and cognitive rehabilitation or music therapy. Furthermore, in two study the experimental group was compared to non-immersive VR training,^{22,26} In two studies^{25,30} the comparison group submitted to computerized cognitive training.

Duration of interventions

Even though time of sessions was not included in every study, sessions lasted from two to 60 min (mean time = 30 min ca.), ranging from one to 60 sessions spread over the course of1 single day to 6 months. Feasibility studies consist the shorter trials, ranging from one to 8 sessions.

Measures

The intervention studies (Table 2) included pre and post measures of functions by using neuropsychological assessment tools such as Mini Mental State Examination (MMSE), Digit Span, Phonemic Verbal Fluency, Dual Task, Clock, Instrumental Activity of Daily Living (IADL), Stroop Color Test, Word Test, Montreal Cognitive Assessment (MOCA), Paced Auditory Serial Addition Task (PASAT), Delis-Kaplan Executive Function System (D-KEFS), Wechsler Memory Scale , Toulouse-PiéronTrail Making or behavioral scales such as Geriatric Depression Scale (GDS), Music in Dementia Assessment Scales, State-Trait Anxiety Inventory (STAI) questionnaire. Four studies contained computerized neurocognitive function test (CNFT)²⁵ and automated neuropsychological assessment metrics (ANAM),¹⁷ Korean version of the Consortium to Establish a Registry for Alzheimer's Disease (CERAD-K)³⁰ and the Dutch version of the Oxford Cognitive Screen (OCS-NL).²⁷ Additionally, two studies^{18,20} measured attention with kinematic analysis of movements, the performance data and observations of behavior. One study³¹ used custom-made hand motion tracking module and 3dimensional positions of the hands for assessing the finger tapping as an indication for attention and response time.

The feasibility of the VR systems was measured by observations, custom-developed Likert-scale questionnaire consisting of several open-ended questions regarding the VR experience and self-reported scales such as stress arousal checklist (SAC), simulator sickness questionnaire (SSQ), ITC sense of presence inventory (ITC-SOPI) and Borg rate of perceived exertion (RPE) scale.

Outcomes Feasibility

Regarding safety and feasibility^{20,21,24,27,31} most participants (N=134 out of 142 in total) completed successfully the tasks although the cognitive abilities varied from normal to severe. All the four studies conclude that VR is a safe, feasible, usable and engaging system for cognitive rehabilitation. Most of the participants did not face stimulation sickness from the immersive environment and had no negative side-effects such as dizziness, headache, disorientation. In addition, most participants experienced positive the iVR with low stress, enjoyment and high levels of engagement and tolerated well with the technology and the equipment of HMD.

Improvements of cognitive functions

All intervention studies reported improvements either in cognitive functions or in stress management and relaxation (Table 2). In particular, most of the studies (N=6) demonstrated improvement in attention.^{18,19,20,25,26,27} Better performance was also found in executive functions (N=3),^{17,22,29} in memory (N=5) ^{19,23,25,26,30} and in navigation skills (N=1).²⁸ One study referred to stress relief in older adults with various kind of cognitive abilities.²¹ As far as the studies with comparison groups^{22,23,25,29,30} when the control group performed traditional face to face cognitive training, in the one case²³ there was no improvements but progressive decline of cognitive functions of participants although iVR group had improvements in memory tests, especially in long-term recall. Furthermore, in the other case²⁹ even though both groups had significant improvements in Stroop test, only iVR group showed improvements in cognitive dualtask gait and more improvements in the TMT-B.

Immersive vs Non-immersive

In a study comparing iVR with computerized cognitive training²⁵ both groups demonstrated similar improvement. In the study of Park et al.,³⁰ in which they compared Mixed Reality with conventional computer-assisted cognitive training, even though experimental group showed significant more improvements than control group in visuospatial working memory and recall in visuospatial tasks, both groups did not improve significantly in the other cognitive domains.

Two studies^{22,26} compared immersive with non-immersive rehabilitation training, with mixed results. The study of Gamito et al.,³⁰ found improvements in working memory and sustained attention for both groups, regardless of the level of immersion. The study of Huang²² the experimental group improved significant in executive functions (Stroop Test and Trail Making Test). In advance, Huang²² supports that engaging in a more immersive environment may lead to a greater improvement of inhibitory control and task switching in older adults. Furthermore, when the participants felt located within an iVR and perceived the possibility of moving within the environment, they were more likely to improve their inhibitory control and tasks witching after experiencing presence.

Quality of RCT's

Six studies of the study were RCT's.^{22,23,25,26,29,30} The PEDro score for each study is reported in Table 3. The mean PEDro score of the studies included in the review was 7.2 with scores ranging from 6 to 8. In total, all included studied had high quality. The most common methodological weaknesses referred to the blinding of patients, therapists, and assessors. Furthermore, in most of the studies^{23,25,26,30} all patients received treatments as allocated, while two^{22,29} did not meet the criteria of "intention to treat".

DISCUSSION

The purpose of the present study was to systematically review and investigate the effects of immersive VR as a rehabilitation approach of cognitive functions in patients suffering from neurological disorder or a traumatic injury or elderly with cognitive decline. Furthermore, we also examined safety and feasibility. Of the 16 studies included, all intervention studies reported improvements in cognitive functions and in particular, in attention, executive functions, memory and in navigation skills. Furthermore, all conclude that immersive VR is feasible, safe and usable for neurorehabilitation of patients with cognitive impairments.

More specifically, in patients with stroke it was noted significant improvement in Computerized neurological test that examined visual and auditory attention along with verbal and visual memory in comparison when cognitive training was performed in a fully immersive environment,²⁵ in working memory and attention²⁶ and in neglect.²⁷ Most of the studies demonstrated improvement in attention.^{18,19,20,25,26} More RCTs have examined the beneficial effects of VR in elderly facing with cognitive challenges regarding executive functioning.^{22,29,30} Additionally, benefits were demonstrated even in navigational tasks,²⁸ and in memory.^{19,23,25,26} One study referred to stress relief in older adults with various kind of cognitive abilities.²¹

Regarding safety and feasibility, most of the participants completed successfully the tasks and did not report any stimulation sickness, dizziness or dissorientantion.^{20,21,24,27,31} Sakhare et al.,²⁴ having examined the feasibility of VR training in elderly noted high levels of arousal and low stress levels indicating a level of excitement and enjoinment. And even in patients with Traumatic Brain Injury the immersion was well tolerated.¹⁶⁻²⁰

Even though the available data is still limited, VR could promote neurorehabilitation in different pathologies, such as stroke. MCI, dementia and TBI. In recent years, more and more studies, support that VR interventions provoke neuroplasticity, by promoting the activation of different neuronal connections, such as the fronto-parietal network¹⁰ and by activating cortical reorganization.³²⁻³⁴ Hence, VR technology is leading to improvements in motor, cognitive and psychological functions. Immersive VR seems to be a promising tool in cognitive rehabilitation both for patients and for therapist as it can provide a feasible, safe, accurate, flexible and enjoyable training environment. Further research is warranted in large-scale longitudinal clinical trials in various patients' groups in order to investigate the long-term impact on cognitive functions in interventions using immersive VR. Longitudinal studies on cognitive VR interventions would provide better evidence of the VR efficacy on rehabilitation. Studies should also include follow-up to report the maintenance of cognitive improvements. Furthermore, immersive VR intervention could be combined with quantitative techniques such as EEG, eye-tracking, heart-rate etc. to provide useful tracks about psychophysiological responses. Additionally, we suggest more studies comparing different levels of immersion as the results are still mixed. Lastly, VR rehabilitation applications could be examined as telerehabilitation systems, to ensure accessibility and long-term improvements in the everyday life of the patients.

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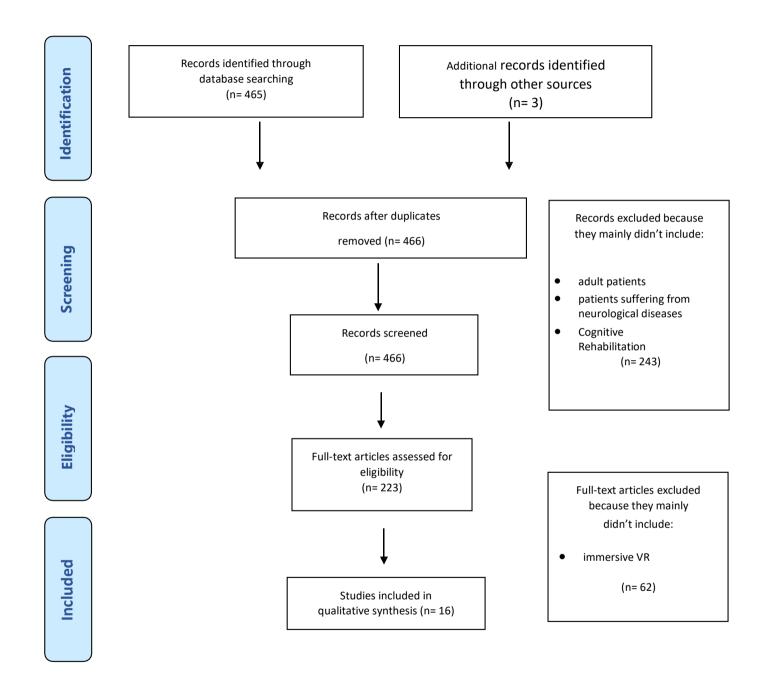
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ANNEX





Study	Participants	Population	Intervention	Comparison	Duration	Outcomes	Study Type
Cho &Lee, 2019	N=42 (EG=21, CG=21)	Stroke	VR (fishing, cards) + Computerized cogni- tive exercise (REHACOM)	•	4 weeks (5/week, for 30')	Attention, memory, per- formance of daily living improved in both groups	RCT
Gamito at al., 2014	N= 17 (EG=8, CG=9)	Stroke	HMD VR with 9 tasks of everyday life (such as morning hygiene and breakfast, find the way to minimarket, find a virtual character, a door number etc)		12 sessions (1/week)	Improved working memory and sustained attention regardless of the VR device	RCT
Huang, 2019	N=32 (EG=16, CG=17)	Elderly	Immersive Fruit Ninja VR	Non immersive Fruit Ninja (Ki- nect)		EG= significant effect on the Stroop Test and Trail Making Test. The feeling of presence could con- tribute to older adults' cognitive im- provement, and (b) the impacts of immersive exergame training on executive functions vary across individual do- mains	RCT
Optale et al., 2010	N=36 (EG=18, CG=18)	Elderly	VR training in path finding and in focused attention				RCT
Park et al., 2019	N=21 (EG=11, CG=10)	MCI	MR-based cognitive training based on eve- ryday tasks such as home setting, caring for a grandchild	computer- as-	sessions (3/week	EG= significant more improvements visuospa- tial working memory but no to other cognitive domain either for EG or CG	RCT

TABLE 1. Summary of the studies included.

	NL 24	MCI		Tuesditions	12	Deth manage in it.	DCT
Liao et al., 2019	N=34 (EG=18, CG=18)	MCI	VR-based cognitive training (VR) like met- ro, kitchen chef, store clerk, football, tai chi	-	12 weeks (3/week, 60', 36 sessions)	Both groups= significant improvements in the SCWT and single-task and motor dual-task gait performance measures. VR group= showed im- provements in cognitive dual- task gait, more improvements in the TMT-B and DTC of ca- dence with borderline signifi- cances.	RCT
Appel et al., 2020	EG=66	Elderly	VR nature scenes for relaxation and stress relief	-	1 session (3-20')	Feasible and safe to expose older adults with various levels of cognitive decline in VR	-
Huygelier et al., 2020	EG=7	Stroke	VR outdoor space: vegetable garden, lake and forest	-	6 sessions (30-45')	It is promising to us im- mersive VR for neglect rehabilitation.	Feasibility, non- randomized
Larson et al., 2011	EG=18	ТВІ	3D cancellation exercises in both visual and hap- tic (tactile) stimuli	-	12 block protocol over 2 days	parisons of target acqui-	Feasibility, Non- randomized
Sakhare et al., 2019	EG= 40 (older=20, younger=20)	Elderly	Navigating in aVR park while cycling stationary bike		1 session (4 trials)	Feasible and enjoyable in both younger and older adults	Feasibility, non- randomized
Yun et al., 2020	EG=11	MCI	Virtual harvest and cook games to im- prove various cognitive domains		1 session (30')	VR cognitive training system is feasible and usable in patients with MCI	

Christians	EG=30	TBI	VR Kitchen, meal prep-	-	2 times	There is adequate initial	Reliability,
en et al.,	20-50	101	aration with multiple		the	reliability	Non-
1998			steps		task (30	rendonity	randomized
1550			51005		steps)		randomized
					within 7-		
					10 days		
					TO Udys		
Dahdah et	FG-15	TBI	VR version of the		8	Significantly reduced	Non-
al., 2017	10-15	1 DI	Stroop in VR Apart-		sessions(3	response time on the	randomized
al., 2017			ment and Classroom		0-60')	word- reading condition	randomized
					0 00)	of VR Stroop and non-	
						significantly reduced re-	
						sponse time on the	
						interference condition.	
						Non- significant	
						improvements in	
						accuracy and inhibition were demonstrated on	
						the color-naming condi-	
						tion of VR Stroop.	
						Significantly improved	
						accuracy under time	
						pressure was found for	
						the ANAM, after VR in-	
Dation	FC 21	TDI			2 -1 (2	tervention	Nee
Dvorkin et	EG=21	TBI	Visuo-haptic VR, with	-	2 days (3	Patients were attentive	Non-
al., 2013			one target and cursor		conditions	to the task, although had	randomized
					-no haptic	attention loss both be-	
					feedback,	fore (prolonged initia-	
					a break-	tion) and during (pauses	
					through	during motion) a move-	
					force, and	ment.	
					haptic	Compared to no haptic	
					nudge- in	feedback, patients bene-	
					12, 4-	fited from haptic nudge	
					minute	cues but not	
					blocks	break-through forces.	
						Overall, patients im-	
						proved and increased	
						the number of targets	
Consistent	FC_1	трі	O tooleo of averation of the		10	acquired.	Casa Cture
Gamito et	EG=1	TBI	9 tasks of everyday life	-	10 online	Improvement in working	Case Study
al., 2011			(such as morning hy-		VR	memory and attention	
			giene and breakfast,		sessions		
			find				
			the way to minimarket,				
			find a virtual character,				
			a door number etc)				

White&M	EG=1	AD	Navigate to targets in	 7 weeks	Learned to perfectly nav-	Case Study
oussavi,			a symmetric, landmark-		igate, skill at navigating	
2016			less virtual building.		while driving improved	
					noticeably and that he	
					enjoyed cognitive im-	
					provement in	
					his daily life at home.	

N= Number of Participants, EG= Experimental Group, CG= Control Group, MCI= Mild Cognitive Impairment, TBI=Traumatic Brain Injury,

AD=Alzheimer's Disease, VR=Virtual Reality, RCT=Randomized Control Trial

Study	Participants		Aim	Measures/ Assessment	Attention & Concentration	Executive functions		Visuospat ial, Orientati on, Navigati on	
Optale et al., 2010	36 (EG=18, CG=18)	Elderly	Lessen cog- nitive de- cline and improve memory functions	MMSE, Digit Span, Pho- nemic Verbal Fluency, Dual Task, Clock, IADL, GDS			~		20
Cho &Lee, 2019	42 (EG=21, CG=21)	Stroke	Impact of cognitive function and activity of daily living	Computerized Neurocogni- tive Function Test (CNT)	~		~		
Gamito et al., 2014	17 (EG=8, CG=9)	Stroke	Compare HMD vs non-HMD VR in memory and attention rehabilitatio n	Wechsler Memory Scale, Tou- Iouse- Piéron	~		~		
Huygelier et al., 2020	EG=7	Stroke	Feasibility of VR rehabili- tation game for neglect	The Dutch version of the Oxford Cog- nitive Screen (OCS-NL), Behavioral Inattention Test (BIT) let- ter cancela- tion task and fig- ure copy task	~				
Liao et al., 2019 Despoti et al.	34 (EG=18, CG=18)	MCI	Cognitive training on executive function and dual- task gait perfor- mance in older adults with MCI, as well as to compare VR-based cognitive training	Stroop Color and Word Test (SCWT) 238		✓			

TABLE 2. Summary of the cognitive function improved in studies

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		OTOL

				1	1	1	<u> </u>	Т	<u> </u>
			with						
			traditional						
	21/50 11		F((14					
Park et al.,	21 (EG=11,	MCI	Effective-	Korean ver-			\checkmark		
2019	CG=10)		ness in gen-	sion of the					
			eral cogni-	Consortium					
			tion of an	to Establish					
			MR-based	a Registry					
			cognitive	for Alz-					
			training	heimer's					
				Disease					
				(CERAD-K)					
	50.00								
Appel et al.,	EG=66	Elderly	Provide en-	State-Trait					\checkmark
2020			joy-	Anxiety In-					
			ment/relaxa	ventory,					
			tion and	Music in					
			reduce anxi-	Dementia					
			ety and de-	Assessment					
			pressive	Scales, mod-					
			symptoms.	ified STAI					
			symptoms.						
				questionnaire					
Dahdah et	EG=15	тві	Whether	Woodcock-		~			
al., 2017			immersive	Johnson, 3rd					
			VR treat-	Edition (WJ-					
			ment in-	III), Delis-					
			terven-	Kaplan Ex-					
			tions im-	ecutive					
			prove ex-	Function					
			ecutive						
				System (D-					
			dysfunc-	KEFS), Au-					
			tion in pa-	tomated					
			tients with	Neuropsy-					
			brain inju-	chological					
			ry and	Assessment					
			whether	Metrics					
			perfor-						
			mance is	(ANAM),					
			stronger on	Simulator					
			a VR version	Sickness					
				Questionnaire					
			of the						
			Stroop than	(SSQ)					
			traditional						
			Stroop						
White&Mo	EG=1	AD	Learn to	MOCA				\checkmark	
ussavi,			navigate in						
2016			a simple						
2010			VR naviga-						
			tion (VRN)						
			environ-						
			ment and						
			whether						
			that train-						
			ing could						
			also bring						
			real-life						
			cognitive						
			benefits						
Gamito, et	EG=1	ТВІ	Train	PASAT	\checkmark		\checkmark		
al., 2011			memory and	(Paced Audi-					
ai., 2011			attention						
			attention				1	İ	1

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			outside clin-	tory Serial				
			ic premises	Addition				
				Task)				
Dvorkin et al., 2013	EG=21	ТВІ	Attention training in early stages of recovery from severe TBI	Kinematic analysis of arm movements and analy- sis of the effect of force type on perfor- mance (i.e., the number of targets ac- quired in a block of trials)	•			
Larson et al., 2011	EG=18	TBI	Feasibility of VR and robotics technolo- gy to im- prove at- tention in patients with severe TBI in the early stages of recovery.	Performance data (i.e., time) and ob- servations of behavior,	✓			
Huang, 2019	EG=16, CG=17	Elderly	Exergaming and virtual reality (VR)- based train- ing for executive functions in older adults	Stroop Test, Trail Making Test Digit Span		✓		

EG= Experimental Group, CG= Control Group, MCI= Mild Cognitive Impairment, TBI=Traumatic Brain Injury, AD=Alzheimer's Disease, VR=Virtual Reality, MMSE= Mini Mental State Examination, MOCA= Montreal Cognitive Assessment, IADL= Instrumental Activities of Daily Living Scale, GDS= The Geriatric Depression Scale

Study	Random	Conceale	Baseline	Blinded	Blinded	Blinded	Follow-	"Intenti	Between-	Point	Total
	allocatio	d	comparab	subjects	therapists	assessors	up	on to	group	estimates	Score
	n	allocation	ility					treat"	analysis	and	PEDro
										variability	Scale
Cho	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	8/10
&Lee,											
2019											
Gamito	Yes	No	Yes	No	No	Yes	Yes	Yes	Yes	Yes	7/10
at al.,											
2014											
Huang,	Yes	Yes	Yes	No	No	Yes	Yes	No	Yes	Yes	7/10
2019											
Optale	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	8/10
et											
al.,											
2010											
Park et	Yes	No	Yes	No	No	No	Yes	Yes	Yes	Yes	6/10
al.,											
2019											
Liao et	Yes	Yes	Yes	No	No	Yes	Yes	No	Yes	Yes	7/10
al.,											
2019											

TABLE 3. PEDro score for RCT's included in the systematic review