Systemic Literature Review of the Use of Virtual Reality for Rehabilitation in Parkinson Disease

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Background: Functional rehabilitation is important when managing Parkinson disease (PD). Virtual reality (VR) therapy is a noninvasive, potential alternative or adjunct to conventional therapies used during rehabilitation.

Observations: The authors searched for articles in Google Scholar, PubMed, Physiotherapy Evidence Database Score (PEDro), and Cochrane after setting specific requirements starting in July 2019. Methodologic quality was assessed by PEDro for randomized controlled trials. Among 89 studies identified, 28 included in this review evaluated VR therapy for use during rehabilitation for PD: 7 used immersive VR and 21 used nonimmersive VR. Among the immersive

VR studies, 6 showed improvement in primary outcomes after adding VR therapy. Among the nonimmersive VR studies, 5 showed improvement with VR therapy when compared with conventional therapy, 9 showed improvement with VR and conventional therapy with no between group difference, and the remaining 7 showed improvement in primary outcomes after adding VR intervention. The quality and diversity of studies was a major limitation.

Conclusion: VR therapy is a promising rehabilitation modality for PD but more studies are needed. Additional investigations of VR therapy and PD should include direct comparisons between immersive and nonimmersive VR therapies.

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Parkinson disease (PD) is the second most common neurodegenerative disorder after Alzheimer disease.[1] Age-standardized incidence rates of PD in population-based studies in Europe and the United States range from 8.6 to 19.0 per 100,000 individuals, using a strict diagnostic criterion for PD.[2] The negative impact of PD on health-related quality of life imposes a heavy burden on veterans. According to the US Department of Veterans Affairs (VA) National Parkinson's Disease Consortium, the VA has as many as 50,000 patients with PD under its care. Because of this demand, the VA has strived to revolutionize available services for veterans with PD and related movement disorders.[3]

The classic motor symptoms of resting tremors, bradykinesia, postural instability, and rigidity of this progressive neurodegenerative disorder is a significant cause of functional limitations that lead to increased falls and inability to perform activities of daily living that challenges the individual and caregiver.[4] Rehabilitation has been considered as an adjuvant to surgical and medical treatments for PD to maximize function and minimize complications. High-intensity multimodal exercise boot camps and therapy that focuses on intensely exercising high-amplitude movements, have been shown to improve motor performance in PD.[5,6] Available evidence has shown that exercise-dependent plasticity is the main mechanism underlying the effects of physiotherapy because it increases synaptic strength and affects neurotransmission.[7] Although there is no

consensus on the optimal approach for rehabilitation, innovative techniques have been proposed and studied. One such approach involves virtual reality (VR), which has begun to attract attention for its potential use during rehabilitation.[8]

VR is a simulated experience created by computer-based technology that grants users access to a virtual environment. There are 2 categories of VR: immersive and nonimmersive. Immersive VR is the most direct experience of virtual environments and usually is implemented through a head-mounted display. These displays have monitors in front of each eye, which can provide monocular or biocular imaging with the most common display being small liquid crystal display (LCD) panels.

Nonimmersive VR typically allows a participant to view a virtual environment by using standard high-resolution monitors rather than a headset or an immersive screen room. Many systems are readily available to the general public as electronic interactive entertainment (ie, video games). Interaction with the virtual world happens through interfaces such as keyboards and controllers while viewing a television or computer monitor. These systems often are more accessible and affordable when compared with immersive VR, although this is changing rapidly.

VR therapy is a noninvasive therapeutic alternative modality for PD. This review aims to study the use of VR to treat PD from a rehabilitative standpoint. Although not the only review on the topic, this systematic review is the first

to examine the differences between immersive and nonimmersive VR rehabilitation for PD. VR technology is evolving rapidly and the research behind its clinical applications is steadily growing, especially as accessibility improves. This review also is an updated summary of the current literature on the effectiveness of VR therapy during PD rehabilitation.

METHODS

Starting in July 2019, the authors searched several databases (PubMed, Google Scholar, Cochrane, and the Physiotherapy Evidence Database [PEDro]) for articles by using the keyword "Parkinson's disease" combined with either "virtual reality" or "video games." To find studies specific to rehabilitation, searches included the additional keyword: "rehabilitation." After compiling an initial set of 89 articles, titles were reviewed to eliminate duplicates. The authors then read the abstracts to exclude study protocols, systematic reviews, and studies that used VR but did not focus on PD or any therapeutic outcome.

Articles were sorted into immersive or nonimmersive virtual reality categories. To be included as immersive VR, studies had to use any type of VR headset or full-scale VR room. Anything less immersive or similar to a traditional video game was included in the nonimmersive VR category. Articles that met inclusion criteria were selected for the systematic review. Criteria for inclusion in this review were: (1) English language; (2) included a study population focused on PD; (3) used some form of VR therapy; and (4) assessed potential rehabilitation by quantitative outcome measures. Only articles published in peer-reviewed journals were included.

Data were extracted into 2 tables specifically modified for this review: immersive and nonimmersive VR. Extracted data included study author name and publication date, study design, methodologic quality, sample size and group allocation, symptom progression via the Hoehn and Yahr Scale (1 to 5), VR modality, presence of control groups, primary outcomes, and primary findings.

Two of the authors (AS, BC) assessed the quality of each study by using the 11-point PEDro scale for randomized controlled trials (RCTs) (Table 1). Most criterion relate to the design and conduct of the study, but 3 focus on eligibility criteria (item 1), between-group statistical comparisons (item 10), and measures of vari-

TABLE 1 Physiotherapy Evidence Database Scale Elements

Items	Descriptions
1	Eligibility criteria specified[a]
2	Subjects randomly allocated to groups
3	Allocation concealed
4	The groups similar at baseline regarding the most important prognostic indicators
5	Blinding of all subjects
6	Blinding of all therapists administering therapy
7	Blinding of all assessors who measured ≥ 1 key outcome
8	Measures of ≥ 1 key outcome obtained from > 85% of subjects initially allocated to groups
9	All subjects with available outcome measures received treatment or control condition as allocated or, data for ≥ 1 key outcome was analyzed by intention to treat
10	Between-group statistical comparison results reported for ≥ 1 key outcome
11	Both point measures and measures of variability provided for ≥1 key outcome

[a]Does not contribute to total score.

ability (item 11). The total possible score was 10 because only 2 out of the 3 items on reporting quality contributed points to the total score (eligibility criteria specified did not).[9]

RESULTS

This review is reported according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines (PRISMA).[10] After screening and assessment, 28 articles met inclusion criteria for this review: 7 using immersive VR and 21 using nonimmersive VR (Figure). The immersive studies included 2 RCTs (both with PEDro scores of 5), 1 controlled study with a PEDro score of 5, 1 prepost pilot study, and 3 cohort studies (Table 2). The nonimmersive studies included 13 RCTs with an average PEDro score of 5.8; 2 pre-post pilot studies, 1 repeated measures study with a historic control, 1 non-RCT, 2 pre-post prospective studies, and 2 cohort studies (1 retrospective and 1 prospective) (Table 3).

Several outcome and assessment tools were used; the most common measures were related to gait, balance, kinematics, and VR feasibility. Studies varied in VR modalities and protocol,

TABLE 2 Immersive Virtual Reality Studies

Source Study design (PEDro score)	Participants, No. (H&Y) Study Groups: No.	VR Modality and Duration	Control	Outcomes	Primary Findings
Janeh et al, 2019[11] Pre/post pilot	15 (2-3)	Unity3D with GAITRite electronic walkway system; HTC Vive headset	Same procedure without VR	Spatio-temporal gait parameters via GAITRite walkway system	VR manipulation tasks significantly increased step width and swing time variability for both body sides; there was no carryover after VR
Ma et al, 2011[12] RCT (5)	33 (2-3) Control: 16 Experimental: 17	Polarized glasses plus projection-based VR system with motion tracking; 60 trials of reaching for fast-moving virtual balls with dominant hand	60 trials turning pegs with nondominant hand	Success rates and kinematic data	VR group became faster and more forceful when reaching for stationary balls; no significant difference in success rate or kinematics with moving balls
Robles-Garcia et al, 2016[13] RCT (5)	16 Control: 8 Experimental: 8	VR avatar via head mounted display; three 25 to 35 min-sessions/wk for 4 wks	Same VR system, but lacked imitation	Self-paced movement features and cortico-spinal excitability	Movement amplitude increased significantly in the experimental group
Ma et al, 2012[35] Controlled (5)	24 (1-3) Control: 24 without PD Experimental: 24	Polarized glasses plus projection-based VR system with motion tracking; 5 trials of both physical and virtual reality	Physical reality	Trunk and arm movement times, trunk-arm coordination, index-desynchrony score	VR induced shorter trunk MTs, shorter offset intervals, and lower desynchrony scores
Griffin et al, 2011[36] Repeated measure cohort	26 (2-4)	VRG (might be more consistent with augmented reality glasses; unable to confirm specifics of glasses)	Same procedure without VR	Task completion time, gait, FoG frequency; FoF	Only visual-flow VRG stimuli showed improvement in task completion time; VRG rhythmic cueing impaired overall walking
Espay et al, 2010[37] Prospective cohort crossover	13	Virtual (augmented) reality goggles containing built-in LCD screen 2 wks of twice daily (30-min duration)	Same procedure without VR	Gait velocity, stride length, cadence, and FOGQ	Virtual device significantly enhanced velocity and stride length; overall improvement in FOGQ
Espay et al, 2013[38] Prospective cohort	13, 2 completed study	Virtual (augmented) reality goggles containing built-in LCD screen; 4 wks at-home use	None	UPDRS3 and FOGQ	Improved FOGQ and UPDRS3 in 1 of 2 participants

Abbreviations: FoF, fear of falling; FoG, freezing of gait; FOGQ, Freezing of Gait Questionnaire; H&Y, Hoehn and Yahr Scale; LCD: liquid crystal display; MT, movement time; PD, Parkinson disease; PEDro, Physiotherapy Evidence Database score; RCT, randomized controlled trial; UPDRS3, Third part of Unified Parkinson's Disease Rating Scale; VR, virtual reality; VRG, virtual reality glasses.

ranging from 21 sessions of Nintendo Wii Fit gaming for 7 weeks to 1 session of VR headset use.

Immersive VR

There were fewer immersive VR studies and these studies had lower mean PEDro scores when compared with nonimmersive VR studies. The VR modalities in the immersive studies used a VR headset or a multisensory immersive system that included polarized glasses. All the studies showed positive improvement in primary outcomes with the exception of Ma and colleagues, which showed no difference in success rates or kinematics with moving balls, and only showed improvement in reaching for stationary balls.[11] The mean number of participants in the studies was 18.4.

All 7 studies had each participant complete tasks without VR then with the VR therapy. None of the studies compared immersive VR therapy with more conventional therapies. Robles-Garcia and colleagues compared 2 VR groups where the experimental group imitated an avatar's finger tapping in the VR system while the control group lacked this imitation.[12] The authors found that adding that imitation to the VR group lead to an increase in movement amplitude.

Among the immersive VR studies, only Janeh and colleagues commented on possible adverse effects (AEs) and found that VR was a safe method without AEs of discomfort or simulator sickness.[13] The other 6 studies did not make any mention or discussion of AEs related to the training.

Nonimmersive VR

VR modalities used in nonimmersive studies included consumer video gaming systems. Nintendo Wii and Microsoft Xbox Kinect were most commonly used. Among the 21 studies, 14 compared VR therapy with a type of traditional exercise (eg, treadmill training, stretching exercises, balance training). The mean number of participants of the studies was 28.3.
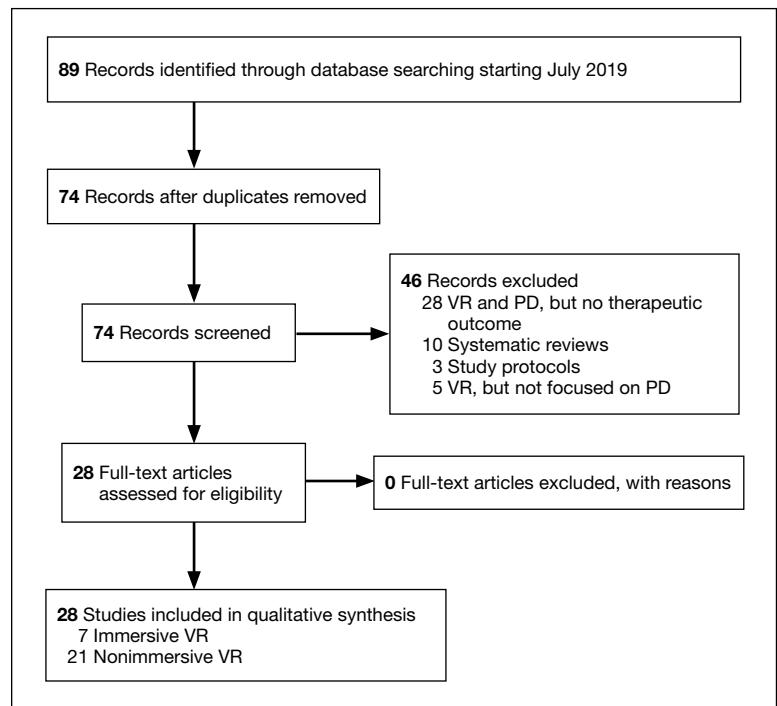
Five studies showed a difference between the VR and traditional training groups.[14-18] However, 9 studies showed positive improvement in both groups and found no between-group differences.[19-25] Among the remaining 7 studies, all showed improvement in primary outcomes after adding VR interventional therapy. In 1 RCT, 3 groups were compared (no intervention, Nintendo Wii, and Xbox Kinect) for gait tests, anxiety levels, memory, and attention.[26] The authors found that only the Nintendo Wii group showed improvement in outcomes. A prospective cohort study was the only one to compare different doses of VR therapy (10 sessions vs 15 sessions of Nintendo Wii Fit).[27] The authors found that both groups demonstrated the same amount of improvement on balance performances with no group effect.

Ten studies reported no AEs during the training, but also did not define what was considered an AE.[15,16,19,22-25,27-29] Eight studies did not make any mention of AEs.[14,17,21,26,27,30-32] Yen and colleagues reported no AEs during training except for the patients' tendency to fall.[20] However, therapists supervised the patients to avoid falls and no falls occurred. Nuic and colleagues reported 3 serious AEs, unrelated to the training: severe pneumonia (n = 1) and deep-brain stimulation generator replacement (n = 2).[33] During the video game training sessions no specific AEs occurred. Only Pompeu and colleagues defined an AE as any untoward medical occurrence such as convulsion, syncope, dizziness, vertigo, falls, or any medical condition that required hospitalization or disability.[34] One researcher registered the occurrence of any AE; however, none occurred during the study period.

DISCUSSION

This systematic review demonstrates that VR therapy is a promising addition to rehabilitation for PD. Evidence supporting VR therapy is limited, but is continually expanding, and current evidence has shown improvement in assessments and rehabilitative outcomes involving

FIGURE PRISMA Screening and Review Process Flow Diagram

Abbreviations: PD, Parkinson disease; VR, virtual reality.

PD. Most nonimmersive studies have shown that VR therapy does not lead to better outcomes when compared with traditional therapy but also is not harmful and does provide similar improvement. Immersive VR studies, on the other hand, have not compared therapy with conventional training extensively, and tend to focus more on time for task completion or movement.

There were fewer immersive VR studies than nonimmersive VR studies. This could be because of the increased technological difficulty and demand to correctly execute immersive VR modalities, as well as the—until recently—substantial expense. This might be another reason why the mean PEDro scores for immersive VR RCTs were lower than the mean scores found in nonimmersive RCTs.

Limitations

This review was limited by several factors related to the included studies. A variety of rating scales were used in the immersive and nonimmersive VR studies. Although there was some general overlap with common measurements such as gait, balance, kinematics, and VR feasibility, no studies had the same primary and

TABLE 3 Nonimmersive Virtual Reality Studies Reviewed

Source Study design (PEDro score)	Participants, No. (H&Y) Study Groups: No.	VR Modality and Duration	Control	Outcomes	Primary findings
Pelosin et al, 2019[14] RCT (5)	24 (2-3) 15 OA Control: 14 PD + 8 OA Experimental: 10 PD + 7 OA	Nonimmersive VR environment with treadmill training; three 45-min sessions/wk for 6 wks	Treadmill training without VR	Primary: No. falls and SAI magnitude; Secondary: Gait parameters	Increase in inhibition of SAI protocol on cortical excitability, improved obstacle negotiation performance, and reduction of number of falls in VR group
Liao et al, 2015[15] RCT (7)	36 (1-3) Control: 12 Traditional exercise: 12 VR: 12	Wii Fit VR exercise; two 1-h sessions/wk for 6 wks	Traditional exercise or only fall-prevention education (control)	Primary: Obstacle crossing performance and dynamic balance Secondary: SOT, PDQ-39, FES-I, TUG	VR group showed greater improvement in obstacle crossing velocity, crossing stride length, dynamic balance, and secondary outcomes
Mirelman et al, 2010[16] Repeated measures study with historical control	20 (2-3)	Treadmill testing with virtual environment; 3 sessions/wk for 6 wks	Historical active group of PD patients who followed similar protocol without VR	Gait measures and Trail Making Test times	Gait speed significantly improved overall; Trail Making Test times improved
Lee et al, 2015[17] RCT (4)	20 Control: 10 Experimental: 10	K-Pop Dance Festival for Nintendo Wii + NDT and FES; five 45-min session/wk for 6 wks	NDT and FES without Wii	Balance, ADLs, and depressive disorder status	Significant improvement in balance, ADLs, and depressive disorder status in experimental group
Feng et al, 2019[18] RCT (8)	28 (2.5-4) Control: 14 Experimental: 14	Standard television VR device; five 45-min sessions/wk for 12 wks	Conventional physical therapy	BBS, TUGT, UPDRS3, FGA	Significant improvement in BBS, TUGT, and FGA; no significant difference in UPDRS3
Gandolfi et al, 2017[19] RCT (7)	76 (2.5-3) Control: 38 Experimental: 38	Nintendo Wii Fit; three 50-min sessions/wk for 7 wks	SIBT	Primary: BBS Secondary: ABC scale, 10-MWT, DGI, PDQ-8	Significant improvement in BBS; no significant between-group differences in secondary outcomes
Yen et al, 2011[20] RCT (7)	42 (2-3) Control: 14 CBT: 14 VR: 14	VR-augmented balance training with 3D VR games; two to three 30-min sessions/wk for 6 wks	Untrained or CBT	Equilibrium scores, sensory ratios, and VRT	No significant difference between VR and CBT groups; equilibrium scores in VR and CBT group improved compared with control
Yang et al, 2016[21] RCT (7)	23 (2-3) Control: 12 Experimental: 11	VR balance training on touch-screen computer; two 50-min sessions/wk for 6 wks	CBT	Primary: BBS Secondary: DGI, TUG, PDQ, motor score of UPDRS	Both groups performed better in BBS, DGI, TUGT, PDQ, without significant differences between groups
Pompeu et al, 2012[22] RCT (7)	32 (1-2) Control: 16 Experimental: 16	Global exercise + Wii Fit VR; two 1-h sessions/wk for 7 wks	Global exercise plus balance exercise	Primary: UPDRS (section II) Secondary: BBS	Both groups showed improvement in section II of UPDRS; no additional advantages with Wii-based training
Heuvel et al, 2014[23] RCT (7)	33 (2-3) Control: 16 Experimental: 17	Interactive balance games with explicit augmented visual feedback (VFT); two 1-h sessions/wk for 5 wks	Conventional training	Primary: Functional reach test Secondary: Balance and gait	No significant difference found in functional reach test
Liao et al, 2015[24] RCT (7)	36 (1-3) Control: 12 Traditional exercise: 12 VR: 12	VR-based Wii Fit 12 sessions in 6 wks	Traditional exercise or only fall-prevention education (control)	Lower extremity muscle strength, sensory integration ability, walking velocity, stride length, and functional gait assessment	Significant improvement in level walking velocity, stride length, functional gait assessment, muscle strength, and vestibular integration in VR and traditional exercise group

Source Study design (PEDro score)	Participants, No. (H&Y) Study Groups: No.	VR Modality and Duration	Control	Outcomes	Primary findings
Fundaro et al, 2018[25] Retrospective cohort	20 (2-3) Control: 10 Experimental: 10	42-inch flat screen with virtual avatar in virtual landscape; Five 30-min sessions/wk for 4 wks	Conventional gait training	UPDRS, FIM, 10-MWT	All patients showed significant improvement in UPDRS and FIM scores; significantly better improvement in UPDRS in VR group
Alves et al, 2019[26] RCT (6)	27 (1-3) Control: 9 Experimental: 9 (Wii) and 9 (Kinect)	Nintendo Wii; Xbox Kinect Two 45-60 min sessions/wk	No intervention	Single and dual task gait tests (TUG, 10MWT, and 30SWT), anxiety levels, memory, and attention	Only Wii group showed significant improvement in single and dual task gait tests, decreased anxiety, and improved memory and attention
Negrini et al, 2016[27] Prospective cohort	27 Control: 11 Experimental: 16	Nintendo Wii Fit three 30-min sessions/wk for 5 wks	Nintendo Wii Fit two 30-min sessions/wk for 5 wks	FRT, PST, BBS, and Tinetti scale	Both groups showed significant improvement on balance performances
van Beek et al, 2019[28] Pre/post pilot	10 (2-4)	Exergaming system (Leap Motion Controller) Two 30-min sessions/wk for 4 wks	N/A	Primary: Feasibility and usability (SUS and PRPS) Secondary: 9HPT, DexQ-24, PDQ-39, UPDRS)	Significant improvement in PRPS; those with impaired dexterity had significant improvement in 9HPT and PDQ-39
Palacios-Navarro et al, 2015[29] Pre-post prospective	7	Microsoft Kinect; 4 sessions/wk for 5 wks	N/A	Completion time score and 10MWT	Significant improvement in completion time score and 10MWT
Mendes et al, 2012[30] Non-RCT	16 (1-2) Control: 11 healthy older people	Nintendo Wii; 10 games 2 sessions/wk for 7 wks	Healthy older people	Scores of 10 Wii Fit games and functional reach test	Scores of PD group depends on demands of games involved; significant improvement in functional reach test posttraining
Lameira de Melo et al, 2018[31] RCT (7)	37 (1-3) Control: 12 Treadmill: 13 VR: 12	Kinect Xbox 360; Three 20-min sessions/wk for 4 wks	Conventional training (control) and treadmill training; Three 20-min sessions/wk for 4 wks	Clinical measures, gait variables, and 6MWT	Longer distance on 6MWT and faster gait speed in VR and treadmill groups; VR group had more intense heart rate
Maidan et al, 2018[32] RCT (4)	64 (2–3) Control: 34 Intervention: 30	Treadmill training with virtual obstacles on screen in front of treadmill; Three 45-min sessions/wk for 6 wks	Treadmill training; Three 45-min sessions/wk for 6 wks	Prefrontal activation	Significant reduction in prefrontal activation in both groups, greater decrease in interventional
Nuic et al, 2018[33] Pre/post pilot	10 (≥ 3)	Kinect motion sensor 18 sessions over 6 or 9 wks	N/A	Feasibility and acceptability of video game rehabilitation and its effects on parkinsonian disability, gait, and balance disorders	High feasibility, acceptability, and satisfaction scores; FOGQ, GABS, and axial score significantly decreased and ABC-scale increased
Pompeu et al, 2013[34] Pre/post prospective	7 (2-3)	Kinect Adventures Fourteen 1-h sessions, 3 sessions/wk	N/A	Feasibility and safety outcomes, 6MWT, BESTest, DGI, PDQ-36	Improvement in game scores and no adverse events; improvements seen in 6MWT, BESTest, DGI, and PDQ-39

Abbreviations: 6MWT, 6-minute walk test; 9HPT, Nine-Hole Peg Test; 10MWT, 10-Meter Walk Test; 30SWT, 30-Seconds Walk Test; ABC, activity balance confidence; ADLs, activities of daily living; BBS, Berg Balance Scale; BESTest, Balance Evaluation System Test; CBT, conventional balance training; DexQ-24, Dexterity Questionnaire-24; DGI, Dynamic Gait Index; FES-I, fall efficacy scale; FES, functional electrical stimulation; FGA, Functional Gait Assessment; FOGQ, Freezing of Gait Questionnaire; GABS, gait and balance scale; H&Y, Hoehn and Yahr; MDS-UPDRS, Movement Disorders Society Unified Parkinson's Disease Rating Scale; N/A, not applicable; NDT, neurodevelopment treatment; PD, Parkinson's disease; PDQ, Parkinson's Disease Questionnaire; PEDro, Physiotherapy Evidence Database score; PRPS, Pittsburgh Rehabilitation Participation Scale; RCT, randomized controlled trial; SAI, short-latency afferent inhibition; SIBT, sensory integration balance training; SOT, sensory organization test; SYS, System Usability Scale; TUGT, Timed Up and Go Test; UPDRS, Unified Parkinson's Disease Rating Scale; VR, virtual reality; VRT, verbal reaction time.

secondary outcomes. Such heterogeneity in protocols and outcomes limited our ability to draw conclusions from these differing studies. Additionally, the average number of participants of both immersive and nonimmersive studies were small and the statistical significance of findings should be interpreted with caution. Finally, VR devices and systems differed between studies, further limiting comparisons. Although these factors limit this systematic review, we can still identify treatment and research implications. Adequately powered future studies with standardized protocols would further improve the available evidence and support for VR as an intervention.

CONCLUSIONS

VR therapy is a promising rehabilitation modality for PD. Additional investigations of VR therapy and PD should include direct comparisons between immersive and nonimmersive VR therapies. It could be hypothesized that the greater immersion and engagement potential of immersive VR would demonstrate greater functional improvement compared with nonimmersive VR, but there is no data to support this for PD. VR therapy for PD appears to be a relatively safe alternative or adjunct to traditional therapy with a potentially positive impact on a variety of symptoms and is growing as an innovative therapeutic approach for PD patients.

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