

ENHANCING BALANCE IN PARKINSON'S DISEASE PATIENTS: A COMPREHENSIVE LITERATURE REVIEW ON THE EFFICACY OF EXERCISE IN AN ENRICHED ENVIRONMENT

Ana PONEBŠEK¹, Friderika KRESAL¹, Luka ŠLOSAR^{2,3}

¹ Visokošolski zavod Fizioterapevtika, Ljubljana, Slovenia

² Science and Research Centre Koper, Institute for Kinesiology Research, Koper, Slovenia

³ Alma Mater Europaea – ECM, Department of Health Sciences, Maribor, Slovenia

Corresponding author:

Ana PONEBŠEK

Visokošolski zavod Fizioterapevtika
Slovenska c. 58, 1000 Ljubljana, Slovenia
E-mail: ponebsekana99@gmail.com

ABSTRACT

Various physiotherapeutic methods and approaches play a significant role in the treatment of patients with Parkinson's disease, including the use of enriched environments. Virtual reality (VR) as a type of enriched environment has the potential to create multiple sensory experiences and feedback, influencing various aspects of the patient's information processing and response. The suitability for home use and the considerable impact on motivation highlight its advantages over alternative approaches. The objective of this review is to investigate the impact of VR-based exercise on balance outcomes among individuals with Parkinson's disease. The inclusion criteria consisted of randomized controlled trials (RCTs) that examined the effects of exercise in a VR environment on individuals' static and dynamic balance outcomes. In order to gather relevant studies, we conducted a comprehensive search across three databases. From a dataset of 625 records, we conducted a comprehensive full-text screening based on specific inclusion and exclusion criteria. This process resulted in the inclusion of 14 RCTs in our review. The emerging evidence regarding exercising in a VR environment does not definitively prove its superiority over standard exercise routines. However, studies have demonstrated that both the experimental and control groups showed comparable improvements in enhancing static and dynamic balance among individuals with

Parkinson's disease. The comparable improvements in balance observed between the experimental and control groups signify the potential effectiveness of VR-based exercises. This underscores the encouragement for further development in this technology, particularly focusing on fully immersive VR environments, which may yield superior effects in enhancing balance among individuals with Parkinson's disease.

Keywords: *virtual reality, Parkinson's disease, balance, rehabilitation.*

UČINKOVITOST VADBE V OBOGATENEM OKOLJU ZA IZBOLJŠANJE RAVNOTEŽJA PRI PACIENTIH S PARKINSONOVO BOLEZNIJO: PREGLED LITERATURE

IZVLEČEK

Pri zdravljenju Parkinsonove bolezni imajo pomembno vlogo različne fizioterapevtske metode in pristopi, med katere spada tudi uporaba obogatene okolja. Navidezna resničnost kot vrsta obogatene okolja ima potencial za ustvarjanje večkratnih senzoričnih izkušenj in povratnih informacij, ki vplivajo na različne vidike obdelave informacij in odzivov pacientov. Poleg tega je prednost vadbe v obogatenu okolju tudi v tem, da je primerna za domačo uporabo in deluje spodbudno. Namen tega dela je s pregledom literature ugotoviti, kakšni so učinki vadbe z navidezno resničnostjo na ravnotežje pri pacientih s Parkinsonovo boleznijo. Vključitvena merila vsebujejo randomizirane kontrolirane raziskave, ki proučujejo učinke vadbe v okolju navidezne resničnosti na statične in dinamične rezultate ravnotežja posameznikov. Za zbiranje relevantnih raziskav smo obsežno preiskali tri baze podatkov. Med 625 zapisi smo temeljito preverili celotna besedila, upoštevajoč določena merila za vključitev in izključitev. S pomočjo tega postopka smo dobili 14 raziskav, ki smo jih vključili v svoj pregled. Na podlagi vključenih raziskav smo ugotovili, da nimamo dovolj dokazov, da bi lahko trdili, da vadba v obogatenu okolju pomembno izboljša ravnotežje pri pacientih s Parkinsonovo boleznijo v primerjavi s tradicionalno vadbo. Raziskave so pokazale, da sta eksperimentalna in kontrolna skupina pokazali primerljive izboljšave v statičnem in dinamičnem ravnotežju pri posameznikih. Primerljive izboljšave v ravnotežju, opažene med eksperimentalno in kontrolno skupino, kažejo potencialno učinkovitost vadb v okolju navidezne resničnosti. To potrjuje potrebo po nadaljnjem razvoju te tehnologije, še posebej osredinjenost na imerzivno obliko navidezne resničnosti, ki ima potencial za izboljšanje ravnotežja pri posameznikih s Parkinsonovo boleznijo.

Ključne besede: *navidezna resničnost, Parkinsonova bolezen, ravnotežje, rehabilitacija*

INTRODUCTION

Parkinson's disease (PD) is a neurodegenerative disorder characterized by the degeneration of dopaminergic neurons in the substantia nigra of the basal ganglia (Hague, Klaffke, & Bandmann, 2005). This results in a dopamine deficiency that manifests itself in primary motor signs and symptoms such as the slowing of movements, tremor, and increased muscle tone that worsen over time and negatively affect patients' balance, gait, functional mobility, and consequently quality of life (Goldman & Tanner, 1998; Müller et al., 2019). The main motor features are bradykinesia, rigidity, tremor, and postural instability (Ball, Teo, Chandra, & Chapman, 2019; Roytman et al., 2023). Parkinson's disease is not only a motor disorder, but also presents a variety of non-motor symptoms (e.g., disturbances in mood, cognition, and sleep) that often affect quality of life more than motor symptoms (Postuma, 2017).

Physiotherapy plays an important role in the treatment of Parkinson's disease. The use of various physiotherapy methods can improve balance and help patients become more independent. In addition to traditional rehabilitation methods, virtual reality (VR) is becoming an increasingly popular method for Parkinson's patients (Schultheis & Rizzo, 2001). Traditional rehabilitation methods include various exercise programs involving balance exercises, such as standing on one leg with eyes closed/open, stepping exercises, dual-task exercises, seated and standing exercises, and exercises on a balance beam or other challenging surfaces. Later, balance exercises are supplemented with perturbation (Lewis & Rosie, 2012).

VR as a form of enriched environment holds the potential of a breakthrough technology for non-physical rehabilitation by providing multisensory information and more realistic simulations to improve patient rehabilitation outcomes (Šlosar, Peskar, Pišot, & Marusic, 2023; Meulenberg, de Bruin, & Marusic, 2022). This computer-generated environment is not static, but responds to the user's movements, gestures, and verbal commands, giving the user the feeling of really being in this virtual world (Lewis & Rosie, 2012). With devices that allow visual or audio interaction between a person and VR, the person can imagine being part of the virtual environment. It can appear in it in the form of an imaginary object. In response to the user's task (in the case of physical therapy, movement), the computer program generates changes in the virtual environment through its sensors that provide feedback on performance.

VR can stimulate the user's movement and cognitive processes, increasing the patient's chances of regaining lost motor skills. It can also be used for bal-

ance training and visual feedback (Mirelman, Maidan, & Deutsch, 2013). The use of VR has a long-term effect on patients, as it can prevent or slow the progression of movement disorders (Allen, Sherrington, Paul, & Canning, 2011). Originally designed for recreation and entertainment, the systems are now also used for therapeutic purposes due to their low cost, high availability, and portability (Kong et al., 2016). These devices include the Sony Playstation, Nintendo Wii, and Microsoft Xbox 360 Kinect, also known as exergames. VR encourages patients to make lifestyle changes and incorporate exercise into their daily lives. In addition, patients can use these devices at home. Due to their low cost, these devices are also suitable as rehabilitation aids for patients from lower socioeconomic backgrounds (Yong Joo et al., 2010). VR ranges from non-immersive to fully immersive, according to the degree of immersiveness provided (Piron et al., 2010). Non-immersive VR refers to a virtual experience through a computer, but also allows the user to remain aware of and in control of their physical environment (Henderson et al., 2013). Common technologies in this category include gaming consoles like PlayStation, Xbox 360, and Nintendo Wii, which integrate exercise actions with gaming mechanics. To simplify the study of the effects of these interventions, Šlosar et al. (2022) categorized them as PC-exergames. Research suggests that these systems hold promise in ameliorating symptoms in neurological disorders and fostering cognitive and motor improvements, including in Parkinson's disease (Maggio et al., 2019). On the other hand, fully immersive VR enables natural interaction with the environment by using the entire body of the user, who thus becomes an active part of the 3D environment (Tieri, Morone, Paolucci, & Iosa, 2018). The most common types of VR technologies are the HMD (Head-Mounted Display) and CAVE (Cave Automatic Virtual Environment) systems. When physical activity is incorporated into interventions within a fully immersive VR environment, Šlosar et al. (2022) suggested the term VR-exergames to name and further investigate these interventions.

For a more precise analysis of intervention effects, we applied the taxonomy introduced by Šlosar et al. (2022) to classify the studies we gathered. In recent years, significant progress has been made in the field of technology and rehabilitation methods. Therefore, a literature review is needed to update the results of the previous literature review, (Chen, Gao, He, & Bian, 2020; Lei et al., 2019) in the field of VR training to improve balance in patients with Parkinson's disease. The aim of this review is to and analyze the existing studies to determine whether exercises in enriched environments improve balance ability in patients with Parkinson's disease.

METHODS

A literature search was performed across PubMed, PEDro, and Google Scholar (first 100 results) utilizing various keywords including “virtual reality,” “VR,” “Parkinson’s disease,” “balance,” “rehabilitation,” and their synonymous terms to locate relevant articles. Supplement A includes the distinct search strings employed for each database.

The inclusion criteria to detect all the relevant articles were (i) The subjects of the study were Parkinson’s disease patients who had been formally diagnosed by a hospital or by internationally recognized diagnostic criteria. There were no restrictions on gender, course of disease, or severity of the disease; (ii) randomized controlled trials (RCTs); (iii) studies in which the experimental group underwent PC- or VR-based exercise interventions; (iv) studies in which outcomes were related to balance, i.e., RCTs that observed whether balance improved in the experimental group at the end of treatment. The exclusion criteria comprised publications prior to 2010, RCTs not available under open access, irrelevant findings, non-English language studies, and those lacking a control group. In line with the Schoneburg et al. (2013) study, balance function is associated to four posture systems: static balance, dynamic balance, reactive posture adjustment, and expected posture adjustment. Considering their substantial impact on balance among Parkinson’s patients, our primary emphasis was on assessing static and dynamic balance as the primary outcomes.

The screening process commenced by evaluating the titles and abstracts of the studies, identifying those most relevant to our topic. The second phase involved examining the full texts to ascertain if they met the aforementioned inclusion criteria. The retrieved studies were then classified based on the taxonomy proposed by Šlosar et al. (2022): PC-exergame – studies conducted in non-immersive environments involving movement; PC-no-exergame – studies conducted in non-immersive environments without movement; VR-exergame – interventions fully immersing participants in a virtual environment while involving movement; VR-no-exergame – studies wherein participants were fully immersed in a virtual environment without movement.

RESULTS

Study selection and characteristics of included studies

The initial search retrieved a total of 625 articles (480 from PubMed, 100 from Google Scholar, and 45 from PEDro). After deduplication, 35 articles were excluded. Subsequently, 27 articles were excluded based on titles and 3 based on abstracts, leaving 14 articles for thorough evaluation as potential inclusions. Figure 1 illustrates the comprehensive inclusion and exclusion process of the articles.

All participants were diagnosed with Parkinson's disease at different disease stages: 4 trials reported Hoehn and Yahr stages 1 to 3, 7 trials reported Hoehn and Yahr stages 2 to 3, 1 trial reported Hoehn and Yahr stages 2 to 4, and 2 trial did not report any stage. All retrieved studies (van den Heuvel et al., 2013; Lee et al., 2015; Shih, Wang, Cheng, & Yang, 2016; Yang, Wang, Wu, Lo, & Lin, 2016; Gandolfi et al., 2017; Ribas, Alves da Silva, Corrêa, Teive, & Valderramas, 2017; Santos, Machado, Santos, Ribeiro, & Melo, 2019; Tollár, Nagy, & Hortobágyi, 2019; Liao, Yang, Wu, & Wang, 2015; Liao, Yang, Cheng, et al., 2015; Pazzaglia et al., 2020; Yen et al., 2011; Shen & Mak, 2014) were categorized as PC-exergame studies, excluding Feng et al. (2019). Feng et al. (2019) lacked sufficient intervention details, such as specific performance methods, exercise intensity progression, and supervision information during training. As a result, we included 13 studies in the PC-exergames category, while no studies were found for the other categories.

Effects of virtual reality training on static and dynamic balance

In all 14 studies, outcome measures used for balance assessment included the Berg Balance Scale (BBS), Limits of Stability (LOS), One-Legged Stance Test (OLS), the Activities-Specific Balance Confidence Scale (ABC), and the Sensory Organization Test (SOT). The majority of the studies used the BBS as the primary outcome measure for functional balance. The results are shown in Table 1. Several studies (Feng et al., 2019; Lee et al., 2015; Gandolfi et al., 2017; Tollár et al., 2019; Liao, Yang, Cheng, et al., 2015; Pazzaglia et al., 2020) demonstrated significant improvements in static and dynamic balance among participants in the experimental group. Ribas et al. (2017) and Yen et al. (2011) also concluded that the experimental group exhibited statistically signif-

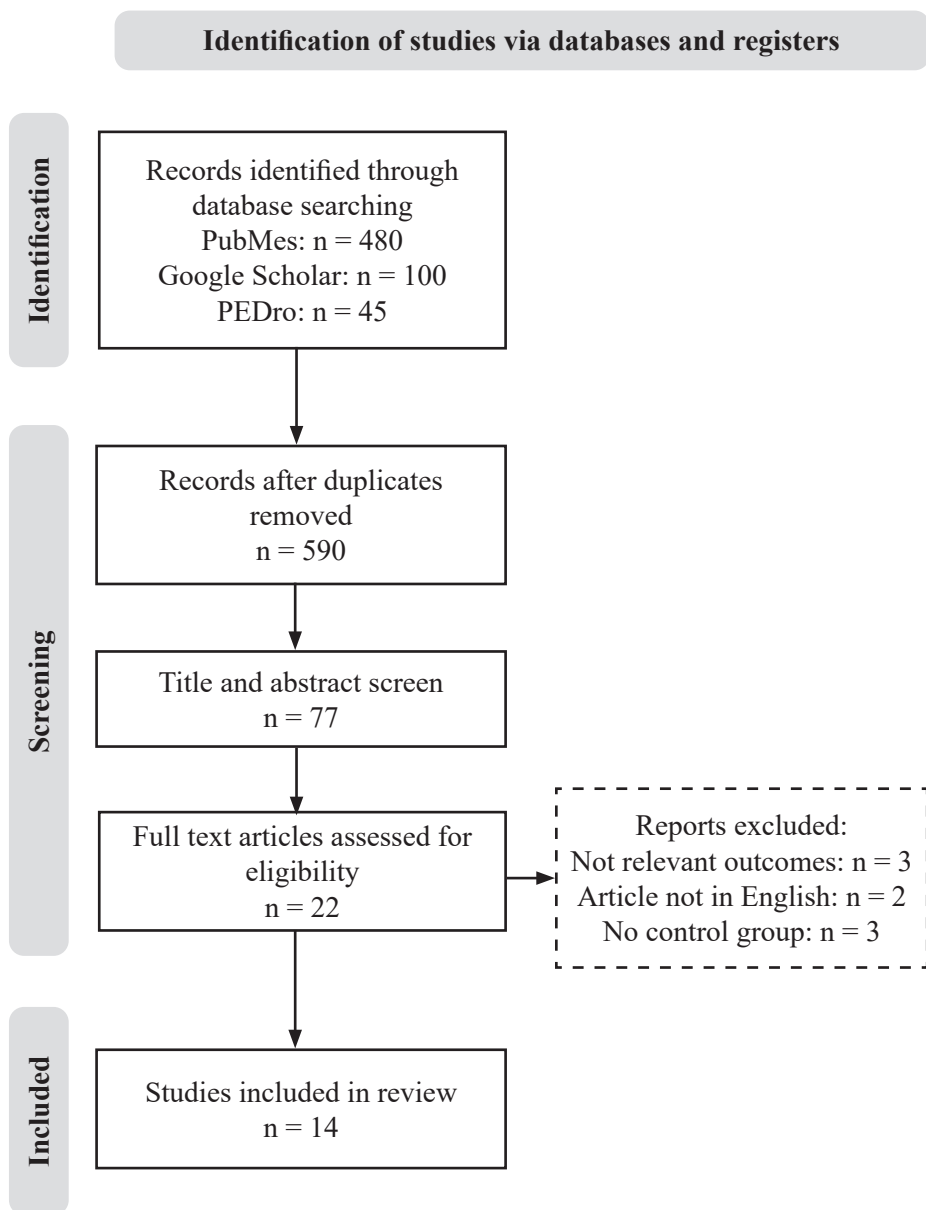


Figure 1: Flow chart depicting the selection process of identified articles

icant progress in maintaining balance compared to the control group; however, the progress was not sustained over time. Liao, Yang, Wu, et al. (2015) found significant improvements in balance among both the experimental group and the group that performed traditional exercises, when compared to the control group. Shen & Mak (2014) reported that participants in the experimental group showed a significantly increased level of self-confidence in maintaining balance, as assessed by the self-assessment ABC test. Shih et al. (2016) found that the experimental group achieved improved postural stability compared to the control group, which followed a traditional balance training program. Both exercise programs were effective in improving functional balance in patients with Parkinson's disease. In the study by van den Heuvel et al. (2013) the results did not show a significant improvement in balance among the participants. Similarly, Yang et al. (2016) found that balance improved equally in both groups, with no significant differences observed between them. Santos et al. (2019) also reported that a combination of traditional exercise and Nintendo Wii training, as well as each individual intervention with an equal amount of physiotherapy, led to balance improvement. However, when analyzing all the results, no statistically significant differences were found between the two groups.

Table 1: Summary of the 14 included studies

Study	Population	Intervention		Duration time	Outcomes and results
		Experimental group	Control group		
van den Heuvel et al. (2013)	n = 33	Visual feedback trainings, which was explicitly integrated in each workstation. Workstations consisted of a flat-panel LCD monitor connected to a PC containing, interactive dynamic balance exercises. (n = 17)	Conventional balance training (n = 16)	60 min / 10 treatment sessions / 5 weeks	There were no statistically significant differences between groups in change scores for BBS and SLS test.
N.-Y. Lee et al. (2015)	n = 20	Dance exercise with Nintendo Wii + neurodevelopment treatment + functional electrical stimulation (n = 10).	Neurodevelopment treatment + functional electrical stimulation (n = 10).	30 min / 5 times per week / 6 weeks	Balance had significantly improved in the EXP group while CON group showed no significant improvement. Balance was measured by BBS.
Shih et al. (2016)	n = 20	Balance-based exergaming intervention using the Kinect sensor. (n = 10)	Conventional balance training (n = 10)	50 min / 2 times per week / 8 weeks	Both training programs improved functional balance in people with PD according to the results of BBS tests. There were no significant differences between the groups.
Yang et al. (2016)	n = 23	Home-based balance training system included touchscreen computer and a wireless balance board. (n = 11)	Conventional balance training (n = 12)	50 min / 2 times per week / 6 weeks	After training, both groups performed better in the BBS at post-test and follow-up than at pretest. No significant differences were found between these two groups at post-test and follow-up.

Study	Population	Intervention		Duration time	Outcomes and results
		Experimental group	Control group		
Gandolfi et al. (2017)	n = 76	Balance training with Nintendo Wii and balance board. (n = 38)	Sensory Integration Balance Training (n = 38)	50 min / 3 days per week / 7 weeks	Significant between-group differences were found for BBS scores. EXP group – progress, according to the BBS
Ribas et al. (2017)	n = 20	The exergaming intervention consisted of Wii Fit games. The device used was a Nintendo video game console with a Wii Balance Board (n = 10)	Conventional exercise program (Warming, stretching active and resistance exercises) (n = 10)	30 min / 2 times per week / 12 weeks	Significant improvement in balance relative to BBS in the EXP group; this benefit was not sustained after the 60-day follow-up.
Santos et al. (2019)	n = 45	EXP1 group: Training with Nintendo Wii (n=15) EXP2 group: Training with Nintendo Wii + active assisted and resisted movements, based on the PNF. (n = 15)	CON group: active assisted and resisted movements, based on the PNF and gait training. (n = 15)	50 min / 2 a week / 8 weeks	There was no statistically significant difference between EXP1, EXP2 group and CON group according to the BBS.
Feng et al. (2019)	n = 28	Balance training with Microsoft Xbox 360 Kinect (n = 14)	Traditional rehabilitation training (warm up exercises, balance exercises, exercises for physical condition and coordination) (n = 14)	45 min / 5 times per week / 12 weeks	Significant improvement in BBS scores in both groups; BBS were better in EXP group than in CON group.

Study	Population	Intervention		Duration time	Outcomes and results
		Experimental group	Control group		
Tollár et al. (2019)	n = 74	EXP1 group: Exergames used the visual feedback modules of the Xbox 360 core system. (n = 25)	CON group: Wait-listed CON group continued with their habitual activity. (n = 24)	60 min / 5 times per week / 5 weeks	EXP1 group: patients had better results in BBS score compared to the EXP2 group.
		EXP2 group: stationary cycling (CYC) patients participated in a spinning class. (n = 25)			
Liao, Yang, Wu, et al. (2015)	n = 36	EXP1 group: Training with Nintendo Wii (strength and balance exercises) (n = 12)	CON group: did not undergo the structured exercise program but received fall-prevention education instead. (n = 12)	60 min / 2 times per week / 6 weeks	Both the EXP1 and EXP2 groups showed significant improvements in SOT test.
		EXP2 group: Traditional exercises such as stretching, strengthening, balance exercise, and treadmill training (n = 12)			
Liao, Yang, Cheng, et al. (2015)	n = 36	EXP1 group: Training with Nintendo Wii (strength and balance exercises) (n = 12)	CON group: fall-prevention education (n = 12)	60 min / 2 times per week / 6 weeks	Patients in the EXP1 group had better results in the LOS and SOT test than participants in control group.
		EXP2 group: traditional exercise (stretching, strengthening and balance exercises) (n = 12)			

Study	Population	Intervention		Duration time	Outcomes and results
		Experimental group	Control group		
Pazzaglia et al. (2020)	n= 51	Exercise to improve balance with the NIRVANA system. (n = 25)	Conventional rehabilitation program (exercises of motor coordination, balance training, start and stop exercises, and walking training) (n = 26)	40 min / 3 times per week / 6 weeks	EXP group improvement in balance according to BBS scale scores compared to the CON group.
Yen et al. (2011)	n = 42	EXP1 group: The hardware system for balance training includes dynamic balance board LCD screen, and a personal computer. (n = 14) EXP2 group: conventional balance training. (n = 14)	CON group: They did not receive any physical therapy (n = 14)	30 min / 2 times per week / 6 weeks	According to the SOT test, the EXP1 group made a significant improvement compared to the CON group, but this improvement was not sustained.
Shen & Mak, (2014)	n = 51	A computerized dancing system (KSD Technology Co. Ltd., Shenzhen, China) (n = 26)	Training that emphasized improving the strength of the hip (flexion, extension, and abduction) and knee (flexion and extension) (n = 25)	15–60 min / 5 times per week / 12 weeks	The ABC scale analysis showed that there were no significant differences between the two groups. The EXP group performed better on the SLS test.

Legend: BBS – Berg Balance Scale, ABC – activities-specific balance confidence scale, SLS – Single Leg Stance, SOT – Sensory Organization Test, LOS – Limits of Stability, EXP – experimental group, CON – control group, PNF – proprioceptive neuromuscular facilitation, PD – Parkinson disease

DISCUSSION

The literature review examining the impact of VR-based exercises on the static and dynamic balance outcomes of Parkinson's disease patients indicates that existing studies lack definitive evidence to establish the superiority of exercise in a virtual environment over standard exercise. The considerable variability in exercise methods makes it difficult to draw firm conclusions regarding the effect of PC-exergame training on the balance ability of Parkinson's disease patients.

Although most studies did not demonstrate the superiority of PC-exergames over standard exercise, a study by Liao, Yang, Cheng, et al. (2015) revealed that Wii Fit-based exercises were more effective than traditional exercise in improving dynamic balance. One potential explanation for improved balance lies in personalized therapy protocols tailored to meet individual therapeutic needs and preferences. Wii Fit exercises provide external feedback during training in both auditory and visual forms. The participants were able to make corrections based on feedback to enhance their motor performance. Some of the Wii Fit exercises require either attention or problem-solving ability. Lee et al. (2015) observed a similar positive impact when introducing an innovative training method for elderly individuals diagnosed with Parkinson's disease, employing Nintendo Wii dance games. Compared to the control group, balance of the experimental group was significantly enhanced. The experimental group received 30 more minutes of treatment per session comparing to control group and the difference in training time probably influenced the results. Another potential confounding factor in the study is that participants received traditional physiotherapy accompanied with Nintendo Wii. It is challenging to determine whether changes in clinical trials should be attributed to traditional balance training or VR.

Unlike the previously mentioned studies, van den Heuvel et al. (2013) did not integrate Nintendo Wii into their setup. Instead, they employed a mobile workstation setup equipped with a force plate for the intervention within the experimental group. However, this approach did not demonstrate superior effectiveness compared to conventional therapy.

The diversity of devices utilized in these studies poses a challenge in reaching definitive conclusions. Devices ranged from common gaming consoles like Nintendo Wii and Xbox Kinect to specialized rehabilitation systems such as the NIRVANA and the computerized dancing system (KSD Technology Co. Ltd., Shenzhen, China). Moreover, the varied frequency (ranging from 2 to 5 times per week) and duration (lasting 5 to 12 weeks) of training sessions add complexity in establishing effective protocols. This wide array of intervention

types and frequencies significantly contributes to result heterogeneity, presenting difficulties in establishing conclusive findings. To reduce variability in results, future studies should research tailored interventions for different disease stages. It is well known that Parkinson's disease patients often have a preserved ability to cycle (Licen, Rakusa, Bohnen, Manganotti, & Marusic, 2022). This represents a unique aspect of their motor function that must be considered when designing research studies. If the ability to cycle is preserved in Parkinson's disease, comparing the effectiveness of exergame / VR interventions with traditional cycling could be problematic because of the potential overlap in benefits and the need for differentiated evaluation methods to distinguish the respective effects.

Reviewing the literature it emerges that the PC-exergame technology for home-based training can be an effective option, particularly for individuals with limited access to rehabilitation centers and hospitals and could be used as a low-supervision home-base technology to obtain a therapeutic effect independently (Yang et al., 2016). However, a notable concern with home-based exercise lies in the possibility of users adopting compensatory movements to boost game performance. This inclination might lead patients to prioritize achieving high game scores over enhancing movement quality, potentially diminishing the genuine training effects. Before introducing computer games at home, it's essential to prevent compensatory movements from affecting game performance. Supervised exercises by a physiotherapist can ensure safety and discourage compensatory actions. This supervision is especially vital for older adults unfamiliar with new technologies.

Literature review is subject to certain limitations that should be considered. A significant limitation is the inclusion of various forms of exercise in the VR-exergaming category. In the future, as more studies become available, it would be advisable to perform sub-analyses that differentiate between different types of exercises. For instance, the Shen & Mak (2014) study incorporated dancing, while others focused on strength and balance exercises.

We included studies involving participants clinically diagnosed with Parkinson's disease, without any limitations on gender, age, disease duration or severity, and these studies exhibited variations in the types of technology employed and the duration of interventions. These factors may have introduced biases in the results and hindered direct comparisons. Future studies with improved technology and research methodologies are necessary to address the limitations and provide clearer insights into the effectiveness of exercise in enriched environments. Additionally, these future investigations should incorporate innovative technologies that enable a holistic understanding of motor control strategies in

Parkinson's disease (Marusic et al., 2023), thus advancing our comprehension of the condition's intricacies.

CONCLUSIONS

The literature review encompasses scientific publications that explore the use of VR as a treatment modality for individuals with Parkinson's disease, specifically focusing on the impact of training in an enriched environment on balance improvement. Some findings (although limited) suggest that exercise in an enriched environment can yield comparable outcomes to standard rehabilitation approaches, making it a viable option for balance rehabilitation in clinical settings. Additionally, it can serve as an adjunctive technology in the overall treatment plan for individuals with Parkinson's disease, aiming to enhance balance outcomes.

REFERENCES

- Allen, N., Sherrington, C., Paul, S., & Canning, C. (2011).** Balance and falls in Parkinson's Disease: a meta-analysis of the effect of exercise and motor training. *Movement Disorders: Official Journal of The Movement Disorder Society*, 26(9), 1605–1615. <https://doi.org/10.1002/mds.23790>.
- Ball, N., Teo, W.-P., Chandra, S., & Chapman, J. (2019).** Parkinson's Disease and the Environment. *Frontiers in Neurology*, 10, 218. <https://doi.org/10.3389/fneur.2019.00218>.
- Chen, Y., Gao, Q., He, C.-Q., & Bian, R. (2020).** Effect of virtual reality on balance in individuals with Parkinson disease: A systematic review and meta-analysis of randomized controlled trials. *Physical Therapy*, 100(6), 933–945. <https://doi.org/10.1093/ptj/pzaa042>.
- Feng, H., Li, C., Liu, J., Wang, L., Ma, J., Li, G., ... Wu, Z. (2019).** Virtual Reality Rehabilitation Versus Conventional Physical Therapy for Improving Balance and Gait in Parkinson's Disease Patients: A Randomized Controlled Trial. *Medical Science Monitor*, 25, 4186–4192. <https://doi.org/10.12659/MSM.916455>.
- Gandolfi, M., Geroin, C., Dimitrova, E., Boldrini, P., Waldner, A., Bonadiman, S., ... Smania, N. (2017).** Virtual reality telerehabilitation for postural instability in Parkinson's disease: a multicenter, single-blind, randomized, controlled trial. *Biomed Research International*, 2017, 1–11. <https://doi.org/10.1155/2017/7962826>.
- Goldman, S. M., & Tanner, C. (1998).** Etiology of Parkinson's disease. In J. Jankovic & E. Tolosa (Eds), *Parkinson's Disease and Movement Disorders* (pp. 133–158). London, UK: Williams and Wilkins.

- Hague, S. M., Klaffke, S., & Bandmann, O. (2005). Neurodegenerative disorders: Parkinson's disease and Huntington's disease. *Journal of Neurology, Neurosurgery, and Psychiatry*, 76(8), 1058–1063. <https://doi.org/10.1136/jnnp.2004.060186>.
- Henderson, E. J., Lord, S. R., Close, J. C. T., Lawrence, A. D., Whone, A., & Ben-Shlomo, Y. (2013). The ReSPonD trial—Rivastigmine to stabilise gait in Parkinson's disease a phase II, randomised, double blind, placebo-controlled trial to evaluate the effect of rivastigmine on gait in patients with Parkinson's disease who have fallen. *BMC Neurology*, 13, 188. <https://doi.org/10.1186/1471-2377-13-188>.
- Kong, K.-H., Loh, Y.-J., Thia, E., Chai, A., Ng, C.-Y., Soh, Y.-M., ... Tjan, S.-Y. (2016). Efficacy of a virtual reality commercial gaming device in upper limb recovery after stroke: a randomized, controlled study. *Topics in Stroke Rehabilitation*, 23(5), 333–340. <https://doi.org/10.1080/10749357.2016.1139796>.
- Lee, N.-Y., Lee, D.-K., & Song, H.-S. (2015). Effect of virtual reality dance exercise on the balance, activities of daily living, and depressive disorder status of Parkinson's disease patients. *Journal of Physical Therapy Science*, 27(1), 145–147. <https://doi.org/10.1589/jpts.27.145>.
- Lei, C., Sunzi, K., Dai, F., Liu, X., Wang, Y., Zhang, B., ... Ju, M. (2019). Effects of virtual reality rehabilitation training on gait and balance in patients with Parkinson's disease: A systematic review. *Plos One*, 14(11), e0224819. <https://doi.org/10.1371/journal.pone.0224819>.
- Lewis, G. N., & Rosie, J. A. (2012). Virtual reality games for movement rehabilitation in neurological conditions: How do we meet the needs and expectations of the users? *Disability and Rehabilitation*, 34(22), 1880–1886. <https://doi.org/10.3109/09638288.2012.670036>.
- Liao, Y.-Y., Yang, Y.-R., Cheng, S.-J., Wu, Y.-R., Fuh, J.-L., & Wang, R.-Y. (2015). Virtual reality-based training to improve obstacle-crossing performance and dynamic balance in patients with Parkinson's Disease. *Neurorehabilitation and Neural Repair*, 29(7), 658–667. <https://doi.org/10.1177/1545968314562111>.
- Liao, Y.-Y., Yang, Y.-R., Wu, Y.-R., & Wang, R.-Y. (2015). Virtual reality-based wii fit training in improving muscle strength, sensory integration ability, and walking abilities in patients with Parkinson's Disease: a randomized control trial. *International Journal of Gerontology*, 9(4), 190–195. <https://doi.org/10.1016/j.ijge.2014.06.007>.
- Licen, T., Rakusa, M., Bohnen, N. I., Manganotti, P., & Marusic, U. (2022). Brain dynamics underlying preserved cycling ability in patients with Parkinson's disease and freezing of gait. *Frontiers in Psychology*, 13, 847703. <https://doi.org/10.3389/fpsyg.2022.847703>.
- Maggio, M. G., Maresca, G., De Luca, R., Stagnitti, M. C., Porcari, B., Ferrera, M. C., ... Calabrò, R. S. (2019). The growing use of virtual reality in cognitive rehabilitation: Fact, fake or vision? A scoping review. *Journal of the National Medical Association*, 111(4), 457–463. <https://doi.org/10.1016/j.jnma.2019.01.003>.
- Marusic, U., Peskar, M., Šömen, M., Kalc, M., Holobar, A., Gramann, K., ... Manganotti, P. (2023). Neuromuscular assessment of force development, postural, and gait performance under cognitive-motor dual-tasking in healthy older adults and early Parkinson's disease patients: Study protocol for a cross-sectional Mobile Brain/Body Imaging (MoBI) study [version 3; peer review: 2 approved]. *Open Research Europe* 3(58). <https://doi.org/10.12688/openreseurope.15781.3>.

- Meulenberg, C. J. W., de Bruin, E. D., & Marusic, U. (2022).** A Perspective on Implementation of Technology-Driven Exergames for Adults as Telerehabilitation Services. *Frontiers in Psychology, 13*, 840863. <https://doi.org/10.3389/fpsyg.2022.840863>.
- Mirelman, A., Maidan, I., & Deutsch, J. E. (2013).** Virtual reality and motor imagery: Promising tools for assessment and therapy in Parkinson's disease. *Movement Disorders, 28*(11), 1597–1608. <https://doi.org/10.1002/mds.25670>.
- Müller, M. L. T. M., Marusic, U., van Emde Boas, M., Weiss, D., & Bohnen, N. I. (2019).** Treatment options for postural instability and gait difficulties in Parkinson's disease. *Expert Review of Neurotherapeutics, 19*(12), 1229–1251. <https://doi.org/10.1080/14737175.2019.1656067>.
- Pazzaglia, C., Imbimbo, I., Tranchita, E., Minganti, C., Ricciardi, D., Lo Monaco, R., ... Padua, L. (2020).** Comparison of virtual reality rehabilitation and conventional rehabilitation in Parkinson's disease: A randomised controlled trial. *Physiotherapy, 106*, 36–42. <https://doi.org/10.1016/j.physio.2019.12.007>.
- Piron, L., Turolla, A., Agostini, M., Zucconi, C. S., Ventura, L., Tonin, P., & Dam, M. (2010).** Motor learning principles for rehabilitation: A pilot randomized controlled study in poststroke patients. *Neurorehabilitation and Neural Repair, 24*(6), 501–508. <https://doi.org/10.1177/1545968310362672>.
- Postuma, R. B. (2017).** Nonmotor aspects of Parkinson's Disease-how do they help diagnosis? *International Review of Neurobiology, 133*, 519–539. <https://doi.org/10.1016/bs.irm.2017.04.002>.
- Ribas, C. G., Alves da Silva, L., Corrêa, M. R., Teive, H. G., & Valderramas, S. (2017).** Effectiveness of exergaming in improving functional balance, fatigue and quality of life in Parkinson's disease: A pilot randomized controlled trial. *Parkinsonism & Related Disorders, 38*, 13–18. <https://doi.org/10.1016/j.parkreldis.2017.02.006>.
- Roytman, S., Paalanen, R., Griggs, A., David, S., Pongmala, C., Koeppe, R. A., ... Bohnen, N. I. (2023).** Cholinergic system correlates of postural control changes in Parkinson's disease freezers. *Brain: A Journal of Neurology, 146*(8), 3243–3257. <https://doi.org/10.1093/brain/awad134>.
- Santos, P., Machado, T., Santos, L., Ribeiro, N., & Melo, A. (2019).** Efficacy of the Nintendo Wii combination with Conventional Exercises in the rehabilitation of individuals with Parkinson's disease: A randomized clinical trial. *NeuroRehabilitation, 45*(2), 255–263. <https://doi.org/10.3233/NRE-192771>.
- Schoneburg, B., Mancini, M., Horak, F., & Nutt, J. G. (2013).** Framework for understanding balance dysfunction in Parkinson's disease. *Movement Disorders: Official Journal of the Movement Disorder Society, 28*(11), 1474–1482. <https://doi.org/10.1002/mds.25613>.
- Schultheis, M., & Rizzo, A. (2001).** The application of virtual reality technology in rehabilitation. *Rehabilitation Psychology, 46*(3), 296–311. <https://doi.org/10.1037/0090-5550.46.3.296>.
- Shen, X., & Mak, M. K. Y. (2014).** Balance and gait training with augmented feedback improves balance confidence in people with Parkinson's disease: a randomized controlled trial. *Neurorehabilitation and Neural Repair, 28*(6), 524–535. <https://doi.org/10.1177/1545968313517752>.

- Shih, M.-C., Wang, R.-Y., Cheng, S.-J., & Yang, Y.-R. (2016).** Effects of a balance-based exergaming intervention using the Kinect sensor on posture stability in individuals with Parkinson's disease: A single-blinded randomized controlled trial. *Journal of Neuroengineering and Rehabilitation*, *13*(1), 78. <https://doi.org/10.1186/s12984-016-0185-y>.
- Šlosar, L., Voelcker-Rehage, C., Paravlič, A.-H., Abazovic, E., de Bruin, E.-D., & Marusic, U. (2022).** Combining physical and virtual worlds for motor-cognitive training interventions: Position paper with guidelines on technology classification in movement-related research. *Frontiers in Psychology*, *13*. <https://doi.org/10.3389/fpsyg.2022.1009052>.
- Šlosar, L., Peskar, M., Pišot, R., & Marusic, U. (2023).** Environmental enrichment through virtual reality as multisensory stimulation to mitigate the negative effects of prolonged bed rest. *Frontiers in Aging Neuroscience*, *15*. <https://doi.org/10.3389/fnagi.2023.1169683>.
- Tieri, G., Morone, G., Paolucci, S., & Iosa, M. (2018).** Virtual reality in cognitive and motor rehabilitation: Facts, fiction and fallacies. *Expert Review of Medical Devices*, *15*(2), 107–117. <https://doi.org/10.1080/17434440.2018.1425613>.
- Tollár, J., Nagy, F., & Hortobágyi, T. (2019).** Vastly Different Exercise Programs Similarly Improve Parkinsonian Symptoms: A Randomized Clinical Trial. *Gerontology*, *65*(2), 120–127. <https://doi.org/10.1159/000493127>.
- van den Heuvel, M. R., van Wegen, E. E., de Goede, C. J., Burgers-Bots, I. A., Beek, P. J., Daffertshofer, A., & Kwakkel, G. (2013).** The effects of augmented visual feedback during balance training in Parkinson's disease: Study design of a randomized clinical trial. *BMC neurology*, *13*(137), 1–9. <https://doi.org/10.1186/1471-2377-13-137>.
- Yang, W.-C., Wang, H.-K., Wu, R.-M., Lo, C.-S., & Lin, K.-H. (2016).** Home-based virtual reality balance training and conventional balance training in Parkinson's disease: A randomized controlled trial. *Journal of the Formosan Medical Association = Taiwan Yi Zhi*, *115*(9), 734–743. <https://doi.org/10.1016/j.jfma.2015.07.012>.
- Yen, C.-Y., Lin, K.-H., Hu, M.-H., Wu, R.-M., Lu, T.-W., & Lin, C.-H. (2011).** Effects of virtual reality-augmented balance training on sensory organization and attentional demand for postural control in people with Parkinson disease: A randomized controlled trial. *Physical Therapy*, *91*(6), 862–874. <https://doi.org/10.2522/ptj.20100050>.
- Yong Joo, L., Yin, T., Xu, D., Thia, E., Fen, C., Kuah, C., & Kong, K.-H. (2010).** A feasibility study using interactive commercial off-the-shelf computer gaming in upper limb rehabilitation in patients after stroke. *Journal of Rehabilitation Medicine: Official Journal of the UEMS European Board of Physical and Rehabilitation Medicine*, *42*(5), 437–441. <https://doi.org/10.2340/16501977-0528>.