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Effect of virtual reality rehabilitation on functional outcomes for return-to-work patients with Parkinson’s disease: an umbrella review of systematic reviews

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Abstract:	BACKGROUND Parkinson’s Disease (PD) is a neurodegenerative disease characterized by loss of substantia nigra neurons with deficiency of dopamine. The main symptoms are tremor, rigidity and bradykinesia. Rehabilitation has an important role in the treatment of this condition and Virtual Reality (VR) is one of the most recent tools. OBJECTIVE The purpose of this umbrella review is to evaluate the effectiveness of virtual reality systems on gait control for return to work in patients with PD. METHODS The electronic search, for reviews and meta-analysis studies that investigated the

	effectiveness of virtual reality on gait control in PD patients, was performed through December 2021 using the following databases: PubMed, Scopus, PEDro, and Google Scholar. Mesh terms used were: Job integration/reintegration OR return-to-work AND Parkinson's disease AND virtual reality OR exergame. No limit on the year of publication of the article was used. RESULTS A total of 14 articles were included in our analysis. The included evidence shows a stride length improvement in patients treated with VR compared to conventional active treatments. No difference was found in walking speed. Also, the included articles show an improvement on various measures of balance, motor function and severity of PD motor symptoms. In addition, the literature shows an improvement in the quality of life and neuropsychiatric symptoms in patients undergoing VR rehabilitation training. CONCLUSIONS The results of our study suggest that VR rehabilitation improves gait performance, particularly stride length, thus being able to provide an improvement in the quality of life and a more effective return to work training in patients with PD.
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Effect of virtual reality rehabilitation on functional outcomes for return-to-work patients with Parkinson's disease: an umbrella review of systematic reviews

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Abstract

BACKGROUND: Parkinson's Disease (PD) is a neurodegenerative disease characterized by loss of substantia nigra neurons with deficiency of dopamine. The main symptoms are tremor, rigidity and bradykinesia. Rehabilitation has an important role in the treatment of this condition and Virtual Reality (VR) is one of the most recent tools .

OBJECTIVE: The purpose of this umbrella review is to evaluate the effectiveness of virtual reality systems on gait control for return to work in patients with PD.

METHODS: The electronic search, for reviews and meta-analysis studies that investigated the effectiveness of virtual reality on gait control in PD patients, was performed through December 2021 using the following databases: PubMed, Scopus, PEDro, and Google Scholar. Mesh terms used were: Job integration/reintegration OR return-to-work AND Parkinson's disease AND virtual reality OR exergame. No limit on the year of publication of the article was used.

RESULTS: A total of 14 articles were included in our analysis. The included evidence shows a stride length improvement in patients treated with VR compared to conventional active treatments. No difference was found in walking speed. Also, the included articles show an improvement on various measures of balance, motor function and severity of PD motor symptoms. In addition, the literature shows an improvement in the quality of life and neuropsychiatric symptoms in patients undergoing VR rehabilitation training.

CONCLUSIONS: The results of our study suggest that VR rehabilitation improves gait performance, particularly stride length, thus being able to provide an improvement in the quality of life and a more effective return to work training in patients with PD.

Keywords

Parkinson's disease; Virtual reality; Rehabilitation; Gait; Return to work

Article type: Review Article

INTRODUCTION

Parkinson's disease (PD) is a progressive neurodegenerative disease of the central nervous system (Samii et al ., 2004). It is characterized by the loss of substantia nigra neurons with significant dopamine deficiency and Lewy body aggregation, inefficient inhibition of the indirect pathway and inadequate activation of the direct one (Balestrino et al., 2020) .

The clinical picture presents with neuro-motor symptoms (bradykinesia, rigidity, tremor, gait disturbances) and non-motor symptoms, including hyposmia, psychiatric symptoms, genitourinary symptoms, gastrointestinal symptoms, and cardiovascular signs (von Campenhausen et al., 2005) .

Neuro-motor symptoms are the most well-known ones, since they significantly affect quality of life, especially the Instrumental Activities of Daily Living (IADL), including the return to work. In fact, work activity is significantly compromised by impaired gait in people with PD and walking performance parameters (temporal and spatial measures) play a crucial role by virtue of their predictive ability for returning to work (Ascherio et al., 2016; Wickremaratchi et al., 2009). The reduction of the ability to coordinate movement in a functional way represents one of the most disabling aspects limiting the patient's functionality in daily life, and not allowing a social re-integration, a complete return to work in PD patients. Rehabilitation strategies, that focus on trying to improve walking efficiency and speed, can improve and make the return to work more effective, also considering the progressive aging of the population (Iosa et al., 2021; Jarvis et al., 2019).

To date, the evaluation scale most used to describe general functional condition is the Movement Disorder Society Unified Parkinson’s Disease Rating Scale (MDS-UPDRS) (Malek et al. 2017) . The therapy, aimed at controlling symptoms and improving the quality of life, consists of a combination of drug therapy (Levo-Dopa, dopamine agonists, MAO B inhibitors, COMT inhibitors) (Armstrong et al., 2020; Gibbins et al., 2017).

Conventional rehabilitation (CR) in PD patients is based on physical therapies application and therapeutic exercise. The aim of the rehabilitation treatment should be to help the patient develop strategies for dealing with different disabilities (Paolucci et al., 2020b) . The main objectives are gait re-education, balance, improvement of postural control, enhancement of aerobic capacity, facilitation of the early movement phase, as well as speech therapy and occupational therapy interventions aimed at acquiring the maximum possible independence in the Activities of Daily Life (ADL) and return to work (Abbruzzese et al., 2015; Keus et al., 2007; Samii et al ., 2004; Paolucci et al., 2020a,b; Petraroli et al., 2021; Petzinger et al., 2013). An innovative neurorehabilitation plan might include exergaming and Virtual Reality (VR), that might be defined as a user-computer interface involving the stimulation and interactions of a subject through multiple sensory channels, based on a synthetic environment in which the subject feels his presence (Tieri et al., 2018). Only recently has it been included as a rehabilitation tool, being able to simulate environments and situations of everyday life that are specific and easily modifiable during the rehabilitation process. VR can also make the patient feel more motivated, increasing the duration and frequency of sessions and their compliance with therapy (Rose et al., 2018; Teo et al., 2016; Voinescu et al., 2021). VR seems to act on neuroplasticity and motor learning, thanks to motor learning strategies (MLS) (Calafiore et al., 2021; Levac et al., 2016) . During VR, which involves both cognitive and motor activity (dual task), the patient receives immediate feedback on his movement and can quickly correct it (Cano Porras et al., 2018; Messier et al., 2007; Mirelman et al., 2011) . Virtual reality is increasingly being used in neurological conditions including Parkinson's disease, although its effects are not yet well demonstrated. Regarding PD, Li et al. (2021), in their systematic review and meta-regression analysis, have suggested a positive impact of VR rehabilitation treatment on balance, quality of life, activities of daily living and depressive symptoms.

Therefore, by the present umbrella review of systematic review, we aimed at evaluating the effects of VR rehabilitation on functional outcomes related to the return to work in patients with PD.

METHODS

Data sources and search strategy

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) was used to guide this review (Moher et al., 2009). The electronic search, for reviews and meta-analysis studies that investigated the effectiveness of virtual reality on gait control in PD patients, was performed from the inception until December 2021 using the following databases: PubMed, Scopus, PEDro, and Google Scholar. Mesh terms used were: Job integration/reintegration OR return-to-work AND Parkinson's disease AND virtual reality OR exergame. No limit on the year of publication of the article was used. Inclusion criteria were: i) systematic reviews; ii) aim of the study was to evaluate the effects of virtual reality on gait of people with PD; iii) studies in full English text. Among the results, oldest reviews, the source-articles of which were already included in newest ones, were excluded, to avoid as much as possible any overlap. To determine the eligibility of each study, the title and abstract were screened. Two independent reviewers searched each database using the same strategy to ensure proper cross-checking of the results. Data including the country, author, affiliated institutions, and enrollment periods were extracted and reviewed to identify and exclude duplicate publications using the same cohort. Any disagreements regarding the acceptance of full-text articles were resolved by discussion until a consensus was reached. The methodological quality of each study was assessed using AMSTAR (assessment of multiple systematic reviews) checklist (Shea et al., 2017) .

P.I.C.O

The P.I.C.O (Population, Intervention, Comparison, Outcome) model was used to adequately formulate the scientific research question and identify the criteria for choosing the studies to be included in the umbrella review.

- Population: people with idiopathic / primary PD, with any degree of severity, of any age and sex;
- Intervention: use of VR systems for gait control and recovery;
- Comparison: VR treatment was compared in studies included with conventional physiotherapy interventions or with no treatment;
- Outcomes: in the included studies, the kinematic variables of gait such as speed and stride length are evaluated.

RESULTS

As a result, 14 articles have been selected, which features are shown in Table 1. The AMSTAR score of each study is reported in Table 2. Table 3 summarizes the characteristics of rehabilitative protocols adopted in included systematic reviews. Table 4 illustrates the features of exercises included in systematic reviews considered. Table 5 reports evaluation methods and scales per review.

Cano Porras et al. (2018) included 97 articles evaluating VR impact on gait and balance in neurologic patients' cohorts in their systematic review, among which 18 studies focused on Parkinson's disease patients. In summary, most studies comparing VR to CR found similar improvements in balance and gait, supporting the use of VR as a rehabilitation strategy combined with CR .

Li et al. (2021), in their systematic review and meta-regression analysis, included 22 randomized controlled trials (836 patients). Authors have suggested a positive impact of VR

rehabilitation treatment on balance, quality of life, activities of daily living and depressive symptoms.

Eight studies suggested that gains might remain or even continue to improve between 2 weeks and 6 months after intervention. One study showed that a combined use of VR and treadmill lead to a more effective reduction of risk of fall compared to a treadmill-only intervention (Mirelman et al., 2016).

A review edited by Wang et al. (2019) considered the impact of VR on balance and gait of PD patients, evaluating twelve studies' results. Regarding gait no significant difference was found in gait velocity and walk distance in Parkinson patients who received virtual reality compared with controls, but significant improvements in stride length was detected in two studies .

In the same year (2019), another review based on sixteen RCTs found out that VR applied to PD patients leads to a significant improvement in step and stride length without effects on gait speed compared to CR. VR rehabilitation training demonstrated also positive effects on quality of life and neuropsychiatric symptoms recorded by Beck Anxiety Inventory (BAI), Beck Depression Inventory (BDI) and Hamilton Depression Rating Scale (HAMD). No significant difference was detected for what concerns global motor function, activities of daily living and cognitive function. This review reports some side effects experienced by patients during VR rehabilitation training, in particular five patient's complaints from mild - to severe dizziness and vomit (Lei et al., 2019).

Triegaardt et al. (2020) recruited twenty-seven studies, ten of which submitted to systematic review and meta-analysis. Studies included in meta-analysis showed a stride length improvement in patients treated with VR compared to the control group, subjected to conventional active treatment. There are no differences in the two treatments in improving walking speed. Compared with CR, VR determines major improvements both on stride length and on gait speed. Also, in other studies included in the review, but not in meta-analysis, major

improvements were detected in the length of the stride and in the speed in patients treated with VR compared to patients treated with conventional treatment. Therefore, we can expect a positive impact of these improvements on social activities.

The systematic review conducted by Freitag et al. (2019) analyzed nineteen studies, which demonstrate that dual-task training with VR induces important improvements in walking speed, in the length stride and in the cadence of the stride in patients treated with Parkinson's Disease. The systematic review and meta-analysis conducted by Lina et al. (2020) examined twelve randomized clinical trials engaging 360 participants. The effectiveness of VR to improve balance was evaluated by the Berg Balance Scale, strengthened motor function as examined by Timed Up and Go Test and enhanced gait ability assessed by the 10-Meter Walk Test Time in patients with Parkinson disease. Results showed how VR was also able to improve individual's ability to perform activities of daily living reported by Barthel Modified Index .

Barry et al. (2014) analyzed seven publications about exergaming and PD, mainly using commercial games like Nintendo Wii. Six studies show there is an improvement on various measures of balance (Berg balance score, single leg stand, functional reach test), motor function (Sit to stand, Time up and go, 10 m walk, timed tapping) and severity of PD motor symptoms (UPDRS II). Two studies highlight those improvements were retained 60 days after the intervention and one of the studies shows also that quality of life can benefit from exergames (with the PDQ-39 for ADL).

Garcia-Agundez et al. (2019) examined sixty-four publications about exergaming and PD, eight of which are RCT and eleven of which are pilot studies. Seventeen studies show improvements in the major outcomes chosen: Timed up and Go, Berg Balance Score, UPDRS scores and MOCA scores. None of the studies showed exergames were worse than traditional rehabilitation therapy. In addition, exergames seem to improve cognitive skills (MOCA scores, attention) in PD patients with MMSE scores > 24 .

Chen et al. (2020) analyzed twelve RCTs about the effect of VR on balance in individuals with PD, six of which used Nintendo Wii Fit system and the other used computerized dancing systems or other. BBS was measured in eight trials, showing a significant increase as a result of VR compared to the active interventions (conventional balance training, in-clinic sensory integration balance training, neurodevelopmental treatment and stationary cycling). Two RCT used the Activities-specific Balance Confidence (ABC) Scale and four RCT used the Timed Up and Go test. Both indicators resulted in no difference between the VR group and the active interventions. DGI and FGA were measured in three trials, in which they show a better improvement in dynamic balance during gait in patients treated with VR with respect to traditional interventions. Only one study reported adverse effects associated with the VR training. When undertaking the exergame, three participants dropped out: one had a non-injurious fall, and two experienced exacerbations of their preexisting lower back pain (cehen et al., 2020).

García-López et al. (2021) included a total of 10 studies in their systematic review whit the aim to evaluate the effectiveness of non-immersive virtual reality in reducing falls and improving balance in patients diagnosed with Parkinson's disease. Balance was analyzed using the Berg Balance Scale, the Activities-specific Balance and Confidence scale, the Tinetti scale, and dynamic posturography performed using the balance master system (NeuroCom International Inc, Clackamas). The risk of falls and balance confidence were analyzed using the Timed Up and Go Test and the Functional Reach Test. They concluded that non-immersive virtual reality could improve balance and reduce the risk and number of falls, being therefore beneficial for people diagnosed with Parkinson's disease.

Santos et al. (2019), realized a systematic review with the aim to analyze RCTs that investigated the effects of Nintendo Wii versus traditional physiotherapy on balance rehabilitation and quality of life of patients with PD. They included five studies concluding

that combined Nintendo Wii and traditional physiotherapy was more effective on balance rehabilitation and quality of life of patients with PD, but the values demonstrated a poor methodological quality and a low level of completeness of the intervention descriptions.

Juras et al. (2019) included 20 studies in their systematic review with the aim to determine the effect of VR on improving balance in different groups of neurological patients (101 stroke, 84 PD and 61 children with cerebral palsy). The authors concluded that the comparison of VR interventions between conventional rehabilitation and no intervention exhibited significantly better results.

Elena et al. (2021), with the to look into the effectiveness of exergaming rehabilitation on the quality of life of people with PD and compare it with conventional physiotherapy, included a total of 14 studies (548 participants) in their systematic review and meta-analysis. Their results showed that exergames as a rehabilitation method can be used to provide alternative interactive intervention with positive results for quality of life in people with PD.

DISCUSSION

The literature reports that VR, as it is designed, is a usable tool for any PD patient without severe impairment of motor or cognitive function with the aim of adequate social reintegration and return to work (Agostini et al., 2021). In patients suffering from PD, the reduction of the ability to coordinate movement in a functional way represents one of the most disabling aspects since it enormously limits the patient's functionality in daily life, not allowing a complete and timely return to work. In this context, psychological factors certainly represent a factor to consider since this impossibility in return-to-work and therefore the loss of autonomy and social self-definition lead the patient to completely abandon his work, as he no longer feels able to do it, and to isolate themselves socially. Our study results suggest that VR rehabilitation training improves gait performance, particularly stride length. One review revealed a

significant improvement of deambulation speed in patients treated with VR with respect to active interventions, using Dynamic Gait Index (DGI) score and Functional Gait Assessment (FGA) score (Chen et al., 2020) . One review suggests VR is comparable to conventional physical therapies that are resource intensive, costly, and sometimes unsustainable. VR might be able to achieve a rehabilitation effect like or even better with an enormous benefit for individuals who do not have enough economic resources (Chen et al., 2020) . One systematic review suggests exergames improve cognitive skills (MOCA scores, attention) in PD patients with MMSE scores > 24 (Garcia-Agundez et al., 2019). Even if our research aimed to focus on gait, some secondary outcomes were detected. VR rehabilitation training leads to statistically significant improvement of balance, cognitive skills, mental health, quality of life, neuropsychiatric symptoms, and activity of daily living performance health (Lei et al., 2019). Among the included studies, there is heterogeneity regarding VR systems and exercises administered to patients. Some studies use systems commonly available on commerce such as: Nintendo Wii, Nintendo Wii Fit and Xbox Kinect 360. Three studies instead utilize immersive systems, semi-immersive systems, or non-immersive systems of VR customized and specially designed for rehabilitation activities, comprising motion perception system, projector screens, audio video systems, treadmill and balance board. Several exercises are proposed in the various studies, such as balancing exercises, loading passages, overcoming obstacles, dual-task exercises, dance, tennis, bowling, boxing, golf, hula-hoop and ski-slalom (Agostini et al., 2021). According to the selected reviews, on average a treatment based on 2-5 times per week, 30-60 minutes duration, pursued to 3-12 weeks seems reasonable. Nevertheless, more studies, involving a large cohort of patients, should follow, to bring more results on VR training effects and to better define the modalities of administrations, in terms of frequency, duration and type of exercise of each VR session. Also follow up should be conducted to outline the effects of VR rehabilitation long term. There is some dishomogeneity between the different scales and

methods of evaluation used in several systematic reviews to evaluate the results obtained, regarding the gait of treated patients. The predominantly used scales and methods of evaluation are: 6 Minutes Walking Test, 10 Meters Walking Test, Timed Up and Go Test and Dynamic Gait Index- Limits of this umbrella review are the inclusion of some poor methodologic quality studies, with small samples and heterogeneity regarding used VR devices and features of rehabilitative sessions. Furthermore, some included reviews may share some articles which could lead to bias. Finally, five of the selected studies did not conduct participant and clinician blinding, which also could lead to bias.

CONCLUSION

Taken together, findings of this umbrella review of systematic reviews showed that VR rehabilitation training seemed to have the same effects as CR training in terms of gait (especially on stride length and balance), providing an improvement in the quality of life and a more effective return to work. Moreover, cognitive skills, quality of life and neuropsychiatric symptoms seem also to improve in patients who undergo VR. Therefore, to provide a stronger evidence-based starting point of VR potential advantages, more multicenter large-sample RCTs of high quality are needed. However, the authors are persuaded that VR should be implemented in clinical practice and become a routine rehabilitation treatment for PD patients whenever possible.

DECLARATION OF INTEREST

Nothing to declare.

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REFERENCES

Abbruzzese, G., Marchese, R., Avanzino, L., & Pelosin, E. (2016). Rehabilitation for Parkinson's disease: Current outlook and future challenges. Parkinsonism and Related Disorders, 22, S60–S64. https://doi.org/10.1016/j.parkreldis.2015.09.005

Agostini, F., Pezzi, L., Paoloni, M., Insabella, R., Attanasi, C., Bernetti, A., Saggini, R., Mangone, M., & Paolucci, T. (2021). Motor Imagery: A Resource in the Fatigue Rehabilitation for Return-to-Work in Multiple Sclerosis Patients-A Mini Systematic Review. Frontiers in neurology, 12, 696276. https://doi.org/10.3389/fneur.2021.696276

Armstrong, M. J., & Okun, M. S. (2020). Diagnosis and Treatment of Parkinson Disease: A Review. JAMA - Journal of the American Medical Association, 323(6), 548–560. https://doi.org/10.1001/jama.2019.22360

Ascherio, A., & Schwarzschild, M. A. (2016). The epidemiology of Parkinson's disease: risk factors and prevention. The Lancet Neurology, 15(12), 1257–1272. https://doi.org/10.1016/S1474-4422(16)30230-7

Balestrino, R., & Schapira, A. H. V. (2020). Parkinson disease. European Journal of Neurology, 27(1), 27–42. https://doi.org/10.1111/ene.14108

Barry, G., Galna, B., & Rochester, L. (2014). The role of exergaming in Parkinson's disease rehabilitation: A systematic review of the evidence. Journal of NeuroEngineering and Rehabilitation, 11(1), 1–10. https://doi.org/10.1186/1743-0003-11-33

Calafiore, D., Invernizzi, M., Ammendolia, A., Marotta, N., Fortunato, F., Paolucci, T., Ferraro, F., Curci, C., Cwirlej-Sozanska, A., & de Sire, A. (2021). Efficacy of Virtual Reality and Exergaming in Improving Balance in Patients With Multiple Sclerosis: A Systematic

Review and Meta-Analysis. Frontiers in neurology, 12, 773459. https://doi.org/10.3389/fneur.2021.773459

Cano Porras, D., Siemonsma, P., Inzelberg, R., Zeilig, G., & Plotnik, M. (2018). Advantages of virtual reality in the rehabilitation of balance and gait: Systematic review. Neurology, 90(22), 1017–1025. https://doi.org/10.1212/WNL.0000000000005603

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

Elena P, Demetris S, Christina M, Marios P. Differences Between Exergaming Rehabilitation and Conventional Physiotherapy on Quality of Life in Parkinson's Disease: A Systematic Review and Meta-Analysis. Front Neurol. 2021 Aug 9;12:683385. doi: 10.3389/fneur.2021.683385.

Freitag, F., Brucki, S. M. D., Barbosa, A. F., Chen, J., De Oliveira Souza, C., Valente, D. F., Chien, H. F., Bedeschi, C., & Voos, M. C. (2019). Is virtual reality beneficial for dual-task gait training in patients with Parkinson's disease?: A systematic review. Dementia e Neuropsychologia, 13(3), 259–267. https://doi.org/10.1590/1980-57642018dn13-030002

Garcia-Agundez, A., Folkerts, A.-K., Konrad, R., Caserman, P., Tregel, T., Goosses, M., Göbel, S., & Kalbe, E. (2019). Recent advances in rehabilitation for Parkinson's Disease with Exergames: A Systematic Review Garcia-Agundez et al. Journal of NeuroEngineering and Rehabilitation. Journal of NeuroEngineering and Rehabilitation, 1–17. http://creativecommons.org/publicdomain/zero/1.0/

García-López H, Obrero-Gaitán E, Castro-Sánchez AM, Lara-Palomo IC, Nieto-Escamez FA, Cortés-Pérez I. Non-Immersive Virtual Reality to Improve Balance and Reduce Risk of Falls in People Diagnosed with Parkinson's Disease: A Systematic Review. Brain Sci. 2021 Oct 28;11(11):1435. doi: 10.3390/brainsci11111435.

Gibbins, N., Awad, R., Harris, S., & Aymat, A. (2017). The diagnosis, clinical findings and treatment options for Parkinson's disease patients attending a tertiary referral voice clinic. Journal of Laryngology and Otology, 131(4), 357–362. https://doi.org/10.1017/S0022215117000159

Iosa, M., Capodaglio, E., Pelà, S., Persechino, B., Morone, G., Antonucci, G., Paolucci, S., & Panigazzi, M. (2021). Artificial Neural Network Analyzing Wearable Device Gait Data for Identifying Patients With Stroke Unable to Return to Work. Frontiers in neurology, 12, 650542. https://doi.org/10.3389/fneur.2021.650542

Jarvis, H. L., Brown, S. J., Price, M., Butterworth, C., Groenevelt, R., Jackson, K., Walker, L., Rees, N., Clayton, A., & Reeves, N. D. (2019). Return to Employment After Stroke in Young Adults: How Important Is the Speed and Energy Cost of Walking?. Stroke, 50(11), 3198–3204. https://doi.org/10.1161/STROKEAHA.119.025614.

Juras G, Brachman A, Michalska J, Kamieniarz A, Pawłowski M, Hadamus A, Białoszewski D, Błaszczyk J, Słomka KJ. Standards of Virtual Reality Application in Balance Training Programs in Clinical Practice: A Systematic Review. Games Health J. 2019 Apr;8(2):101-111. doi: 10.1089/g4h.2018.0034.

Keus, S. H. J., Bloem, B. R., Hendriks, E. J. M., Bredero-Cohen, A. B., & Munneke, M. (2007). Evidence-based analysis of physical therapy in Parkinson's disease with recommendations for practice and research. Movement Disorders, 22(4), 451–460. https://doi.org/10.1002/mds.21244

Lei, C., Sunzi, K., Dai, F., Liu, X., Wang, Y., Zhang, B., He, L., & 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), 1–17. https://doi.org/10.1371/journal.pone.0224819

Levac, D. E., Glegg, S. M. N., Sveistrup, H., Colquhoun, H., Miller, P., Finestone, H., De Paul, V., Harris, J. E., & Velikonja, D. (2016). Promoting therapists' use of motor learning strategies

within virtual reality-based stroke rehabilitation. PLoS ONE, 11(12), 1–16. https://doi.org/10.1371/journal.pone.0168311

Li, R., Zhang, Y., Jiang, Y., Wang, M., Ang, W., & Lau, Y. (2021). Rehabilitation training based on virtual reality for patients with Parkinson's disease in improving balance, quality of life, activities of daily living, and depressive symptoms: A systematic review and meta-regression analysis. Clinical rehabilitation, 35(8), 1089–1102. https://doi.org/10.1177/0269215521995179

Lina, C., Guoen, C., Huidan, W., Yingqing, W., Ying, C., Xiaochun, C., & Qinyong, Y. (2020). The Effect of Virtual Reality on the Ability to Perform Activities of Daily Living, Balance during Gait, and Motor Function in Parkinson Disease Patients: A Systematic Review and Meta-Analysis. American Journal of Physical Medicine and Rehabilitation, 99(10), 917–924. https://doi.org/10.1097/PHM.0000000000001447

Malek, N., Lawton, M. A., Grosset, K. A., Bajaj, N., Barker, R. A., Ben-Shlomo, Y., Burn, D. J., Foltynie, T., Hardy, J., Morris, H. R., Williams, N. M., Wood, N., & Grosset, D. G. (2017). Utility of the new Movement Disorder Society clinical diagnostic criteria for Parkinson's disease applied retrospectively in a large cohort study of recent onset cases. Parkinsonism and Related Disorders, 40, 40–46. https://doi.org/10.1016/j.parkreldis.2017.04.006

Messier, J., Adamovich, S., Jack, D., Hening, W., Sage, J., & Poizner, H. (2007). Visuomotor learning in immersive 3D virtual reality in Parkinson's disease and in aging. Experimental Brain Research, 179(3), 457–474. https://doi.org/10.1007/s00221-006-0802-2

Mirelman, A., Rochester, L., Maidan, I., Del Din, S., Alcock, L., Nieuwhof, F., Rikkert, M. O., Bloem, B. R., Pelosin, E., Avanzino, L., Abbruzzese, G., Dockx, K., Bekkers, E., Giladi, N., Nieuwboer, A., & Hausdorff, J. M. (2016). Addition of a non-immersive virtual reality component to treadmill training to reduce fall risk in older adults (V-TIME): a randomised

controlled trial. The Lancet, 388(10050), 1170–1182. https://doi.org/10.1016/S0140-6736(16)31325-3

Moher, D., Liberati, A., Tetzlaff, J., Altman, D. G., & PRISMA Group (2009). Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. PLoS medicine, 6(7), e1000097. https://doi.org/10.1371/journal.pmed.1000097

Paolucci, T., Sbardella, S., La Russa, C., Agostini, F., Mangone, M., Tramontana, L., Bernetti, A., Paoloni, M., Pezzi, L., Bellomo, R. G., Santilli, V., & Saggini, R. (2020). Evidence of Rehabilitative Impact of Progressive Resistance Training (PRT) Programs in Parkinson Disease: An Umbrella Review. Parkinson's Disease, 2020. https://doi.org/10.1155/2020/9748091

Paolucci, Teresa, Bernetti, A., Sbardella, S., La Russa, C., Murgia, M., Salomè, A., Villani, C., Altieri, M., Santilli, V., Paoloni, M., Agostini, F., & Mangone, M. (2020). Straighten your back! Self-correction posture and postural balance in "non rehabilitative instructed" multiple sclerosis patients. NeuroRehabilitation, 46(3), 333–341. https://doi.org/10.3233/NRE-192987

Petraroli, A., de Sire, A., Pino, I., Moggio, L., Marinaro, C., Demeco, A., & Ammendolia, A. (2021). Effects of rehabilitation on reducing dyskinesias in a Parkinson's disease patient abusing therapy with levodopa-carbidopa intestinal gel: a paradigmatic case report and literature review. Journal of biological regulators and homeostatic agents, 35(4), 10.23812/21-229-L. https://doi.org/10.23812/21-229-L

Petzinger, G., Fisher, B., McEwen, S., Beeler, S., Walsh, J., Jakowec, M. E. N. T. (2013). Cognitive Circuitry in Parkinson's Disease. Lancet Neurol, 12(7), 716–726. https://doi.org/10.1016/S1474-4422(13)70123-6.Exercise-enhanced

Samii, A., Nutt, J. G., & Ransom, B. R. (2004). Parkinson's disease. The Lancet, 363(9423), 1783–1793. https://doi.org/10.1016/S0140-6736(04)16305-8

Santos P., Scaldaferri G., Santos L., Ribeiro N., Neto M., & Melo A. (2019). Effects of the Nintendo Wii training on balance rehabilitation and quality of life of patients with Parkinson's disease: A systematic review and meta-analysis. NeuroRehabilitation. 44(4):569-577. doi: 10.3233/NRE-192700.

Shea, B. J., Reeves, B. C., Wells, G., Thuku, M., Hamel, C., Moran, J., Moher, D., Tugwell, P., Welch, V., Kristjansson, E., & Henry, D. A. (2017). AMSTAR 2: A critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. BMJ (Online), 358, 1–9. https://doi.org/10.1136/bmj.j4008

Teo, W. P., Muthalib, M., Yamin, S., Hendy, A. M., Bramstedt, K., Kotsopoulos, E., Perrey, S., & Ayaz, H. (2016). Does a combination of virtual reality, neuromodulation and neuroimaging provide a comprehensive platform for neurorehabilitation? - A narrative review of the literature. Frontiers in Human Neuroscience, 10(June), 1–15. https://doi.org/10.3389/fnhum.2016.00284

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

Triegaardt, J., Han, T. S., Sada, C., Sharma, S., & Sharma, P. (2020). Correction to: The role of virtual reality on outcomes in rehabilitation of Parkinson’s disease: meta-analysis and systematic review in 1031 participants (Neurological Sciences, (2020), 41, 3, (529-536), 10.1007/s10072-019-04144-3). Neurological Sciences, 41(3), 731–732. https://doi.org/10.1007/s10072-019-04212-8

Voinescu, A., Sui, J., & Stanton Fraser, D. (2021). Virtual Reality in Neurorehabilitation: An Umbrella Review of Meta-Analyses. Journal of clinical medicine, 10(7), 1478. https://doi.org/10.3390/jcm10071478

Von Campenhausen, S., Bornschein, B., Wick, R., Bötzel, K., Sampaio, C., Poewe, W., Oertel, W., Siebert, U., Berger, K., & Dodel, R. (2005). Prevalence and incidence of Parkinson's disease in Europe. European Neuropsychopharmacology, 15(4), 473–490. https://doi.org/10.1016/j.euroneuro.2005.04.007

Wang, B., Shen, M., Wang, Y. X., He, Z. W., Chi, S. Q., & Yang, Z. H. (2019). Effect of virtual reality on balance and gait ability in patients with Parkinson's disease: a systematic review and meta-analysis. Clinical Rehabilitation, 33(7), 1130–1138. https://doi.org/10.1177/0269215519843174

Wickremaratchi, M. M., Perera, D., O'Loghlen, C., Sastry, D., Morgan, E., Jones, A., Edwards, P., Robertson, N. P., Butler, C., Morris, H. R., & Ben-Shlomo, Y. (2009). Prevalence and age of onset of Parkinson's disease in Cardiff: A community based cross sectional study and meta-analysis. Journal of Neurology, Neurosurgery and Psychiatry, 80(7), 805–807. https://doi.org/10.1136/jnnp.2008.162222

Table 1. Features of systematic reviews included.

Author	Study Design	Assessment method of the studies	Results	Limitations	AMSTAR score
Cano Porras et al.	Systematic review (97 studies: 49 RCT or quasi-RCT, 34 cohort studies, 14 case reports)	CONTENT scale; Cochrane Collaboration tool (per RCT e quasi-RCT); Newcastle-Ottawa Scale (per studi di coorte e case reports)	VR has a positive impact on gait and balance, especially when combined with conventional rehabilitation.	Poor methodologic quality of most included studies.	9/11
Li et al.	Systematic review and meta-regression analysis (22 randomized controlled trials)	PEDro score	VR training could be adopted in healthcare institutions as supplementary training for patients with PD.	Small sample size, most included trials were conducted in Asian countries, overall evidence ranged from very low to low, some selected trials did not provide comprehensive intervention descriptions.	8/11
Wang et al.	Systematic review and meta-analysis (12 RCT)	PEDro score	VR determines a significant improvement in stride length compared with CR, no differences in gait velocity and walk distance.	The majority of 12 included studies had small sample size and intervention approaches varied considerably.	10/11
Lei et al.	Systematic review (16 RCT)	Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0	VR rehabilitation improves step and stride length, balance function, quality of life and neuropsychiatric symptoms compared to CR.	Intervention approaches varied considerably among the different studies.	10/11

Triegaardt et al.	Systematic review and meta-analysis (27 studies)	Cochrane Collab. tool	VR compared to active rehabilitation treatment determines a major improvement in the stride length, while compared to traditional rehabilitation treatment allows it to recover better, in addition to the stride length, also the speed of the walk	The review includes a smaller number of studies and participants than those provided for the study of a new technology such as VR. The RV systems used in the various studies included in the review are different from each other. This can affect the results	8/11
Freitag et al.	Systematic review (19 studies)	PEDro score	Dual task training with walk VR induces improvements in length stride, cadence of stride and walking speed	Among the various studies included in the review, evaluation methods, rehabilitation exercises and characteristics of the system of RV used are often different	7/11
Lina et al.	Systematic review and Meta-Analysis (12 RCT)	Cochrane Collab. tool	VR shows to improve balance, strengthen motor function and gait ability	The overall dimension specimen is small and the number of the studies relating to the specific topic is restricted	9/11
Barry et al.	Systematic review (7 studies: 1 RCT, 1 case report, s longitudinal studies, 1 cohort study, 2 other studies)	Personalized evaluation of the quality	Exergaming improves balance, motor function and severity of PD motor symptoms	Heterogeneity of the different exergames; only full articles included	9/11

Garcia-Agundez et al.	Systematic review (64 studies: 8 RCT, 11 pilot studies, 30 technical papers, 15 meta-analysis)	Personalized evaluation of the quality	Exergaming improves balance, and severity of PD motor symptoms	Heterogeneity of the different exergames; only 8 RCT; many studies do not have any control group	7/11
Chen et al.	Systematic review (12 RCT)	PEDro score and Cochrane Handbook for Systematic Reviews of Interventions	VR improves static and dynamic balance in PD patients, more than traditional interventions.	Heterogeneity in the setups and exercise items included and, in the outcomes, measured; little number of trials.	9/11
García-López et al.	Systematic review (10 RCT)	PRISMA and the Cochrane Handbook for Systematic Reviews of Interventions	non-immersive VR can improve balance and reduce the risk and number of falls, being therefore beneficial for people with PD.	Reduced sample size, ranging between 20 and 130 patients.	10/11
Santos et al.	Systematic review and Meta-Analysis (5 RCT)	PRISMA	combined Nintendo Wii and traditional physiotherapy was more effective on balance rehabilitation and quality of life of patients with PD	Studies analyzed with small samples; Heterogeneity of the different exergames; Heterogeneity in the setups and exercise items included and, in the outcomes, measured;	9/11
Juras et al.	Systematic review	PEDro score	Comparison of VR interventions between conventional rehabilitation and no intervention exhibited significantly better results.	Large diversity of implemented VR trainings in the reviewed studies.	8/11

Elena et al.	Systematic Review and Meta-Analysis	PRISMA	Exergames as a rehabilitation method can be used to provide alternative interactive intervention with positive results for quality of life in people with PD	Small number of studies that compared the two different intervention techniques	8/11

VR: Virtual Reality; PD: Parkinson's disease; RCT: Randomized Controlled Trial; CR: Conventional Rehabilitation

Table 2. Methodologic quality of included systematic reviews based on AMSTAR checklist.

Author	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	AMSTAR score
Cano Porras et al.	✓	✓	✓	✓	✓	✓	✓	✓	✗	✗	✓	9/11
Li et al.	✓	✓	✓	✗	✓	✓	✓	✓	✗	✗	✓	8/11
Wang et al.	✓	✓	✓	✗	✓	✓	✓	✓	✓	✓	✓	10/11
Lei et al.	✓	✓	✓	✗	✓	✓	✓	✓	✓	✓	✓	10/11
Triegaardt et al.	✓	✗	✓	✗	✓	✓	✓	✓	✓	✗	✓	8/11
Freitag et al.	✓	✓	✓	✗	✓	✓	✓	✓	✗	✗	✗	7/11
Lina et al.	✓	✓	✓	✗	✓	✓	✓	✓	✓	✓	✗	9/11
Barry et al.	✓	✓	✓	✓	✓	✓	✓	✓	✗	✗	✓	9/11
Garcia-Agundez et al.	✓	✓	✓	✗	✓	✓	✓	✓	✗	✗	✓	7/11
Chen et al.	✓	✓	✓	✗	✓	✓	✓	✓	✓	✗	✓	9/11
García-López et al.	✓	✓	✓	✗	✓	✓	✓	✓	✓	✓	✓	10/11
Santos et al.	✓	✓	✓	✗	✓	✓	✓	✓	✓	✗	✓	9/11
Juras et al.	✓	✓	✓	✗	✓	✓	✓	✓	✗	✗	✓	8/11
Elena et al.	✓	✓	✓	✗	✓	✓	✓	✓	✗	✓	✗	8/11

Question 1 (Q1): Was an 'a priori' design provided?; Q2: Was there duplicate study selection and data extraction?; Q3: Was a comprehensive literature search performed?; Q4: Was the status of publication (i.e. grey literature) used as an inclusion criterion?; Q5: Was a list of studies (included and excluded) provided?; Q6: Were the characteristics of the included studies

provided?; Q7: Was the scientific quality of the included studies assessed and documented?; Q8: Was the scientific quality of the included studies used appropriately in formulating conclusions?; Q9: Were the methods used to combine the findings of studies appropriate?; Q10: Was the likelihood of publication bias assessed?; Q11: Was the conflict of interest included?

Table 3. Features of rehabilitative protocols adopted across all the studies examined in each review.

Author	N° of sessions / week	N° of weeks	Time per VR session (min)	Follow up
Cano Porras et al.	2-5	4-6	20-40	2 weeks - 6 months
Li et al.	2-7	3-12	20-40	-
Wang et al.	2-5	4-12	20-100	1 - 15 months
Lei et al.	2-7	4-12	30-60	-
Triegaardt et al.	-	4-12	-	-
Freitag et al.	2-3	3-12	30-60	1-3 months
Lina et al.	2-5	4-12	30-60	-
Barry et al.	1-3	4-8	30-60	-
Garcia- Agundez et al.	2-5	4-12	15-60	1-2 months
Chen et al.	-	5-12	-	-
García-López et al.	5-12	2-5	30-75	-
Santos et al.	4-12	2-5	30-60	-
Juras et al.	2-4	2-8	20-50	-
Elena et al.	2-5	6-12	40-60	-

VR: Virtual Reality

Table 4. Features of exercises included in systematic reviews considered.

Author	Proposal task
Cano Porras et al.	Obstacle negotiation, exercises challenged control of body lean, strengthening exercises and balance games using Wii
Li et al.	Nintendo Wii™, Microsoft Xbox 360™ Kinect, tablets, and computers.
Wang et al.	VR balance and gait training, Wii Fit VR
Lei et al.	Wii fit VR, Xbox VR, Computerized Balance and gait training system
Triegaardt et al.	Nintendo Wii, Xbox Kinect and other customized virtual reality systems (Neuro VR, Oculus Rift DK2, IREX, OpenGL, SGI Octane)
Freitag et al.	Treadmill training with virtual obstacles, exercises with Wii Fit, balance board and Wii sport (golf or bowling)
Lina et al.	VR balance training, Tele Wii training, Nintendo Wii, Gamepad-based training, Wii Fit exercise, VR plus NDT ad FES, K-box game, Wii-based motor and cognitive training, Wii Fit games
Barry et al.	Nintendo Wii with balance board, walking in place, obstacles, squats, sport like tennis, boxing, bowling and ski slalom
Garcia-Agundez et al.	Nintendo Wii Fit, Xbox kinect and balance board, stretching, muscle strengthening, treadmill + VR, obstacles, sport like table tennis
Chen et al.	Nintendo Wii Fit, training of the balance, dancing, visual feedback training,
García-López et al.	Nintendo Wii Fit, modified Microsoft Kinect connected to a large Screen, a custom-created non-immersive VR system consisting of a 22-inch touch screen and a balance board
Santos et al.	Nintendo Wii Fit
Juras et al.	Nintendo Wii Fit, Xbox kinect and balance board
Elena et al.	Nirvana, Nintendo Wii Fit, Microsoft X-Box Kinect, VR training, VR Unity games, TeleWii, Nintendo Wii, balance board

VR: Virtual Reality; FES: Functional Electrical Stimulation; NDT: NeuroDevelopment Treatment; IREX: Interactive Rehabilitation & Exercise System; DK2: Development Kit 2; OpenGL: Open Graphics Library; SGI Octane: Silicon Graphics Octane.

Table 5. Evaluation methods and scales.

Author and year	Assessment method
Cano Porras et al.	UPDRS III; BBS; 2/6/10 MWT; TUG; DGI.
Li et al.	BBS; PDQ-39; BDI; GDS-15
Wang et al.	BBS; 6MWT; 10MWT; TUG; SLS; UST.
Lei et al.	BBS; TUG; UPDRS; DGI; 6MWT; 10MWT.
Triegaardt et al.	TUG; 6MWT; 10MWT
Freitag et al.	DGI; 6MWT; TUG
Lina et al.	BBS; TUG; 10MWT; MBI
Barry et al.	TUG; 10MWT; DGI; UPDRS
Garcia- Agundez et al.	UPDRS; TUG; 6MWT; 10MWT; Tinetti gait scale
Chen et al.	FGA; TUG; DGI
García-López et al.	BBS; ABC; Tinetti scale; TUG; FRT
Santos et al.	BBS; UPDRS; Fatigue Severity Scale; 6MWT; PDQ-39; TUG
Juras et al.	BBS; TUG; FRT; UPDRS; BOT-2; 2MWT; 10MWT
Elena et al.	PDQ-39; ABC; UPDRS; BBS; TUG; DGI

BBS: Berg Balance Scale; UST: Unipedal Stance Test; SLS: Single Leg Stance test; TUG: Timed Up and Go test; 2MWT/6MWT/10MWT: Two/Six/Ten Minute Walk Test; DGI: Dynamic Gait Index; UPDRS: Unified Parkinson's Disease Rating Scale; FGA: Functional Gait Assessment; ABC: Activities-specific Balance and Confidence scale; FRT: Functional Reach Test; PDQ-39: PDQ-39 Quality of Life Questionnaire; BOT-2: Bruininks–Oseretsky test of Motor Performance 2; BDI: beck depression inventory; GDS-15: 15-item geriatric depression scale

Effect of virtual reality rehabilitation on functional outcomes for return-to-work patients with Parkinson's disease: an umbrella review of systematic reviews

Abstract

BACKGROUND: Parkinson's Disease (PD) is a neurodegenerative disease characterized by loss of substantia nigra neurons with deficiency of dopamine. The main symptoms are tremor, rigidity and bradykinesia. Rehabilitation has an important role in the treatment of this condition and Virtual Reality (VR) is one of the most recent tools .

OBJECTIVE: The purpose of this umbrella review is to evaluate the effectiveness of virtual reality systems on gait control for return to work in patients with PD.

METHODS: The electronic search, for reviews and meta-analysis studies that investigated the effectiveness of virtual reality on gait control in PD patients, was performed through December 2021 using the following databases: PubMed, Scopus, PEDro, and Google Scholar. Mesh terms used were: Job integration/reintegration OR return-to-work AND Parkinson's disease AND virtual reality OR exergame. No limit on the year of publication of the article was used.

RESULTS: A total of 14 articles were included in our analysis. The included evidence shows a stride length improvement in patients treated with VR compared to conventional active treatments. No difference was found in walking speed. Also, the included articles show an improvement on various measures of balance, motor function and severity of PD motor symptoms. In addition, the literature shows an improvement in the quality of life and neuropsychiatric symptoms in patients undergoing VR rehabilitation training.

CONCLUSIONS: The results of our study suggest that VR rehabilitation improves gait performance, particularly stride length, thus being able to provide an improvement in the quality of life and a more effective return to work training in patients with PD.

Keywords

Parkinson’s disease; Virtual reality; Rehabilitation; Gait; Return to work

Article type: Review Article

INTRODUCTION

Parkinson's disease (PD) is a progressive neurodegenerative disease of the central nervous system (Samii et al ., 2004). It is characterized by the loss of substantia nigra neurons with significant dopamine deficiency and Lewy body aggregation, inefficient inhibition of the indirect pathway and inadequate activation of the direct one (Balestrino et al., 2020) .

The clinical picture presents with neuro-motor symptoms (bradykinesia, rigidity, tremor, gait disturbances) and non-motor symptoms, including hyposmia, psychiatric symptoms, genitourinary symptoms, gastrointestinal symptoms, and cardiovascular signs (von Campenhausen et al., 2005) .

Neuro-motor symptoms are the most well-known ones, since they significantly affect quality of life, especially the Instrumental Activities of Daily Living (IADL), including the return to work. In fact, work activity is significantly compromised by impaired gait in people with PD and walking performance parameters (temporal and spatial measures) play a crucial role by virtue of their predictive ability for returning to work (Ascherio et al., 2016; Wickremaratchi et al., 2009). The reduction of the ability to coordinate movement in a functional way represents one of the most disabling aspects limiting the patient's functionality in daily life, and not allowing a social re-integration, a complete return to work in PD patients. Rehabilitation strategies, that focus on trying to improve walking efficiency and speed, can improve and make the return to work more effective, also considering the progressive aging of the population (Iosa et al., 2021; Jarvis et al., 2019).

To date, the evaluation scale most used to describe general functional condition is the Movement Disorder Society Unified Parkinson's Disease Rating Scale (MDS-UPDRS) (Malek et al. 2017) . The therapy, aimed at controlling symptoms and improving the quality of life, consists of a combination of drug therapy (Levo-Dopa, dopamine agonists, MAO B inhibitors, COMT inhibitors) (Armstrong et al., 2020; Gibbins et al., 2017).

Conventional rehabilitation (CR) in PD patients is based on physical therapies application and therapeutic exercise. The aim of the rehabilitation treatment should be to help the patient develop strategies for dealing with different disabilities (Paolucci et al., 2020b) . The main objectives are gait re-education, balance, improvement of postural control, enhancement of aerobic capacity, facilitation of the early movement phase, as well as speech therapy and occupational therapy interventions aimed at acquiring the maximum possible independence in the Activities of Daily Life (ADL) and return to work (Abbruzzese et al., 2015; Keus et al., 2007; Samii et al ., 2004; Paolucci et al., 2020a,b; Petraroli et al., 2021; Petzinger et al., 2013).

An innovative neurorehabilitation plan might include exergaming and Virtual Reality (VR), that might be defined as a user-computer interface involving the stimulation and interactions of a subject through multiple sensory channels, based on a synthetic environment in which the subject feels his presence (Tieri et al., 2018). Only recently has it been included as a rehabilitation tool, being able to simulate environments and situations of everyday life that are specific and easily modifiable during the rehabilitation process. VR can also make the patient feel more motivated, increasing the duration and frequency of sessions and their compliance with therapy (Rose et al., 2018; Teo et al., 2016; Voinescu et al., 2021). VR seems to act on neuroplasticity and motor learning, thanks to motor learning strategies (MLS) (Calafiore et al., 2021; Levac et al., 2016) . During VR, which involves both cognitive and motor activity (dual task), the patient receives immediate feedback on his movement and can quickly correct it (Cano Porras et al., 2018; Messier et al., 2007; Mirelman et al., 2011) . Virtual reality is

increasingly being used in neurological conditions including Parkinson's disease, although its effects are not yet well demonstrated. Regarding PD, Li et al. (2021), in their systematic review and meta-regression analysis, have suggested a positive impact of VR rehabilitation treatment on balance, quality of life, activities of daily living and depressive symptoms.

Therefore, by the present umbrella review of systematic review, we aimed at evaluating the effects of VR rehabilitation on functional outcomes related to the return to work in patients with PD.

METHODS

Data sources and search strategy

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) was used to guide this review (Moher et al., 2009). The electronic search, for reviews and meta-analysis studies that investigated the effectiveness of virtual reality on gait control in PD patients, was performed from the inception until December 2021 using the following databases: PubMed, Scopus, PEDro, and Google Scholar. Mesh terms used were: Job integration/reintegration OR return-to-work AND Parkinson's disease AND virtual reality OR exergame. No limit on the year of publication of the article was used. Inclusion criteria were: i) systematic reviews; ii) aim of the study was to evaluate the effects of virtual reality on gait of people with PD; iii) studies in full English text. Among the results, oldest reviews, the source-articles of which were already included in newest ones, were excluded, to avoid as much as possible any overlap. To determine the eligibility of each study, the title and abstract were screened. Two independent reviewers searched each database using the same strategy to ensure proper cross-checking of the results. Data including the country, author, affiliated institutions, and enrollment periods were extracted and reviewed to identify and exclude duplicate publications using the same cohort. Any disagreements regarding the acceptance of full-text

articles were resolved by discussion until a consensus was reached. The methodological quality of each study was assessed using AMSTAR (assessment of multiple systematic reviews) checklist (Shea et al., 2017) .

P.I.C.O

The P.I.C.O (Population, Intervention, Comparison, Outcome) model was used to adequately formulate the scientific research question and identify the criteria for choosing the studies to be included in the umbrella review.

- Population: people with idiopathic / primary PD, with any degree of severity, of any age and sex;
- Intervention: use of VR systems for gait control and recovery;
- Comparison: VR treatment was compared in studies included with conventional physiotherapy interventions or with no treatment;
- Outcomes: in the included studies, the kinematic variables of gait such as speed and stride length are evaluated.

RESULTS

As a result, 14 articles have been selected, which features are shown in Table 1. The AMSTAR score of each study is reported in Table 2. Table 3 summarizes the characteristics of rehabilitative protocols adopted in included systematic reviews. Table 4 illustrates the features of exercises included in systematic reviews considered. Table 5 reports evaluation methods and scales per review.

Cano Porras et al. (2018) included 97 articles evaluating VR impact on gait and balance in neurologic patients' cohorts in their systematic review, among which 18 studies focused on Parkinson's disease patients. In summary, most studies comparing VR to CR found similar

improvements in balance and gait, supporting the use of VR as a rehabilitation strategy combined with CR .

Li et al. (2021), in their systematic review and meta-regression analysis, included 22 randomized controlled trials (836 patients). Authors have suggested a positive impact of VR rehabilitation treatment on balance, quality of life, activities of daily living and depressive symptoms.

Eight studies suggested that gains might remain or even continue to improve between 2 weeks and 6 months after intervention. One study showed that a combined use of VR and treadmill lead to a more effective reduction of risk of fall compared to a treadmill-only intervention (Mirelman et al., 2016).

A review edited by Wang et al. (2019) considered the impact of VR on balance and gait of PD patients, evaluating twelve studies' results. Regarding gait no significant difference was found in gait velocity and walk distance in Parkinson patients who received virtual reality compared with controls, but significant improvements in stride length was detected in two studies .

In the same year (2019), another review based on sixteen RCTs found out that VR applied to PD patients leads to a significant improvement in step and stride length without effects on gait speed compared to CR. VR rehabilitation training demonstrated also positive effects on quality of life and neuropsychiatric symptoms recorded by Beck Anxiety Inventory (BAI), Beck Depression Inventory (BDI) and Hamilton Depression Rating Scale (HAMD). No significant difference was detected for what concerns global motor function, activities of daily living and cognitive function. This review reports some side effects experienced by patients during VR rehabilitation training, in particular five patient's complaints from mild - to severe dizziness and vomit (Lei et al., 2019).

Triegaardt et al. (2020) recruited twenty-seven studies, ten of which submitted to systematic review and meta-analysis. Studies included in meta-analysis showed a stride length

improvement in patients treated with VR compared to the control group, subjected to conventional active treatment. There are no differences in the two treatments in improving walking speed. Compared with CR, VR determines major improvements both on stride length and on gait speed. Also, in other studies included in the review, but not in meta-analysis, major improvements were detected in the length of the stride and in the speed in patients treated with VR compared to patients treated with conventional treatment. Therefore, we can expect a positive impact of these improvements on social activities.

The systematic review conducted by Freitag et al. (2019) analyzed nineteen studies, which demonstrate that dual-task training with VR induces important improvements in walking speed, in the length stride and in the cadence of the stride in patients treated with Parkinson's Disease. The systematic review and meta-analysis conducted by Lina et al. (2020) examined twelve randomized clinical trials engaging 360 participants. The effectiveness of VR to improve balance was evaluated by the Berg Balance Scale, strengthened motor function as examined by Timed Up and Go Test and enhanced gait ability assessed by the 10-Meter Walk Test Time in patients with Parkinson disease. Results showed how VR was also able to improve individual's ability to perform activities of daily living reported by Barthel Modified Index .

Barry et al. (2014) analyzed seven publications about exergaming and PD, mainly using commercial games like Nintendo Wii. Six studies show there is an improvement on various measures of balance (Berg balance score, single leg stand, functional reach test), motor function (Sit to stand, Time up and go, 10 m walk, timed tapping) and severity of PD motor symptoms (UPDRS II). Two studies highlight those improvements were retained 60 days after the intervention and one of the studies shows also that quality of life can benefit from exergames (with the PDQ-39 for ADL).

Garcia-Agundez et al. (2019) examined sixty-four publications about exergaming and PD, eight of which are RCT and eleven of which are pilot studies. Seventeen studies show

improvements in the major outcomes chosen: Timed up and Go, Berg Balance Score, UPDRS scores and MOCA scores. None of the studies showed exergames were worse than traditional rehabilitation therapy. In addition, exergames seem to improve cognitive skills (MOCA scores, attention) in PD patients with MMSE scores > 24 .

Chen et al. (2020) analyzed twelve RCTs about the effect of VR on balance in individuals with PD, six of which used Nintendo Wii Fit system and the other used computerized dancing systems or other. BBS was measured in eight trials, showing a significant increase as a result of VR compared to the active interventions (conventional balance training, in-clinic sensory integration balance training, neurodevelopmental treatment and stationary cycling). Two RCT used the Activities-specific Balance Confidence (ABC) Scale and four RCT used the Timed Up and Go test. Both indicators resulted in no difference between the VR group and the active interventions. DGI and FGA were measured in three trials, in which they show a better improvement in dynamic balance during gait in patients treated with VR with respect to traditional interventions. Only one study reported adverse effects associated with the VR training. When undertaking the exergame, three participants dropped out: one had a non-injurious fall, and two experienced exacerbations of their preexisting lower back pain (cehen et al., 2020).

García-López et al. (2021) included a total of 10 studies in their systematic review whit the aim to evaluate the effectiveness of non-immersive virtual reality in reducing falls and improving balance in patients diagnosed with Parkinson's disease. Balance was analyzed using the Berg Balance Scale, the Activities-specific Balance and Confidence scale, the Tinetti scale, and dynamic posturography performed using the balance master system (NeuroCom International Inc, Clackamas). The risk of falls and balance confidence were analyzed using the Timed Up and Go Test and the Functional Reach Test. They concluded that non-immersive virtual reality

could improve balance and reduce the risk and number of falls, being therefore beneficial for people diagnosed with Parkinson's disease.

Santos et al. (2019), realized a systematic review with the aim to analyze RCTs that investigated the effects of Nintendo Wii versus traditional physiotherapy on balance rehabilitation and quality of life of patients with PD. They included five studies concluding that combined Nintendo Wii and traditional physiotherapy was more effective on balance rehabilitation and quality of life of patients with PD, but the values demonstrated a poor methodological quality and a low level of completeness of the intervention descriptions.

Juras et al. (2019) included 20 studies in their systematic review with the aim to determine the effect of VR on improving balance in different groups of neurological patients (101 stroke, 84 PD and 61 children with cerebral palsy). The authors concluded that the comparison of VR interventions between conventional rehabilitation and no intervention exhibited significantly better results.

Elena et al. (2021), with the to look into the effectiveness of exergaming rehabilitation on the quality of life of people with PD and compare it with conventional physiotherapy, included a total of 14 studies (548 participants) in their systematic review and meta-analysis. Their results showed that exergames as a rehabilitation method can be used to provide alternative interactive intervention with positive results for quality of life in people with PD.

DISCUSSION

The literature reports that VR, as it is designed, is a usable tool for any PD patient without severe impairment of motor or cognitive function with the aim of adequate social reintegration and return to work (Agostini et al., 2021). In patients suffering from PD, the reduction of the ability to coordinate movement in a functional way represents one of the most disabling aspects since it enormously limits the patient's functionality in daily life, not allowing a complete and

timely return to work. In this context, psychological factors certainly represent a factor to consider since this impossibility in return-to-work and therefore the loss of autonomy and social self-definition lead the patient to completely abandon his work, as he no longer feels able to do it, and to isolate themselves socially. Our study results suggest that VR rehabilitation training improves gait performance, particularly stride length. One review revealed a significant improvement of deambulation speed in patients treated with VR with respect to active interventions, using Dynamic Gait Index (DGI) score and Functional Gait Assessment (FGA) score (Chen et al., 2020) . One review suggests VR is comparable to conventional physical therapies that are resource intensive, costly, and sometimes unsustainable. VR might be able to achieve a rehabilitation effect like or even better with an enormous benefit for individuals who do not have enough economic resources (Chen et al., 2020) . One systematic review suggests exergames improve cognitive skills (MOCA scores, attention) in PD patients with MMSE scores > 24 (Garcia-Agundez et al., 2019). Even if our research aimed to focus on gait, some secondary outcomes were detected. VR rehabilitation training leads to statistically significant improvement of balance, cognitive skills, mental health, quality of life, neuropsychiatric symptoms, and activity of daily living performance health (Lei et al., 2019). Among the included studies, there is heterogeneity regarding VR systems and exercises administered to patients. Some studies use systems commonly available on commerce such as: Nintendo Wii, Nintendo Wii Fit and Xbox Kinect 360. Three studies instead utilize immersive systems, semi-immersive systems, or non-immersive systems of VR customized and specially designed for rehabilitation activities, comprising motion perception system, projector screens, audio video systems, treadmill and balance board. Several exercises are proposed in the various studies, such as balancing exercises, loading passages, overcoming obstacles, dual-task exercises, dance, tennis, bowling, boxing, golf, hula-hoop and ski-slalom (Agostini et al., 2021). According to the selected reviews, on average a treatment based on 2-5 times per week,

30-60 minutes duration, pursued to 3-12 weeks seems reasonable. Nevertheless, more studies, involving a large cohort of patients, should follow, to bring more results on VR training effects and to better define the modalities of administrations, in terms of frequency, duration and type of exercise of each VR session. Also follow up should be conducted to outline the effects of VR rehabilitation long term. There is some dishomogeneity between the different scales and methods of evaluation used in several systematic reviews to evaluate the results obtained, regarding the gait of treated patients. The predominantly used scales and methods of evaluation are: 6 Minutes Walking Test, 10 Meters Walking Test, Timed Up and Go Test and Dynamic Gait Index- Limits of this umbrella review are the inclusion of some poor methodologic quality studies, with small samples and heterogeneity regarding used VR devices and features of rehabilitative sessions. Furthermore, some included reviews may share some articles which could lead to bias. Finally, five of the selected studies did not conduct participant and clinician blinding, which also could lead to bias.

CONCLUSION

Taken together, findings of this umbrella review of systematic reviews showed that VR rehabilitation training seemed to have the same effects as CR training in terms of gait (especially on stride length and balance), providing an improvement in the quality of life and a more effective return to work. Moreover, cognitive skills, quality of life and neuropsychiatric symptoms seem also to improve in patients who undergo VR. Therefore, to provide a stronger evidence-based starting point of VR potential advantages, more multicenter large-sample RCTs of high quality are needed. However, the authors are persuaded that VR should be implemented in clinical practice and become a routine rehabilitation treatment for PD patients whenever possible.

DECLARATION OF INTEREST

Nothing to declare.

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REFERENCES

Abbruzzese, G., Marchese, R., Avanzino, L., & Pelosin, E. (2016). Rehabilitation for Parkinson's disease: Current outlook and future challenges. Parkinsonism and Related Disorders, 22, S60–S64. https://doi.org/10.1016/j.parkreldis.2015.09.005

Agostini, F., Pezzi, L., Paoloni, M., Insabella, R., Attanasi, C., Bernetti, A., Saggini, R., Mangone, M., & Paolucci, T. (2021). Motor Imagery: A Resource in the Fatigue Rehabilitation for Return-to-Work in Multiple Sclerosis Patients-A Mini Systematic Review. Frontiers in neurology, 12, 696276. https://doi.org/10.3389/fneur.2021.696276

Armstrong, M. J., & Okun, M. S. (2020). Diagnosis and Treatment of Parkinson Disease: A Review. JAMA - Journal of the American Medical Association, 323(6), 548–560. https://doi.org/10.1001/jama.2019.22360

Ascherio, A., & Schwarzschild, M. A. (2016). The epidemiology of Parkinson's disease: risk factors and prevention. The Lancet Neurology, 15(12), 1257–1272. https://doi.org/10.1016/S1474-4422(16)30230-7

Balestrino, R., & Schapira, A. H. V. (2020). Parkinson disease. European Journal of Neurology, 27(1), 27–42. https://doi.org/10.1111/ene.14108

Barry, G., Galna, B., & Rochester, L. (2014). The role of exergaming in Parkinson's disease rehabilitation: A systematic review of the evidence. Journal of NeuroEngineering and Rehabilitation, 11(1), 1–10. https://doi.org/10.1186/1743-0003-11-33

Calafiore, D., Invernizzi, M., Ammendolia, A., Marotta, N., Fortunato, F., Paolucci, T., Ferraro, F., Curci, C., Cwirlej-Sozanska, A., & de Sire, A. (2021). Efficacy of Virtual Reality and Exergaming in Improving Balance in Patients With Multiple Sclerosis: A Systematic Review and Meta-Analysis. Frontiers in neurology, 12, 773459. https://doi.org/10.3389/fneur.2021.773459

Cano Porras, D., Siemonsma, P., Inzelberg, R., Zeilig, G., & Plotnik, M. (2018). Advantages of virtual reality in the rehabilitation of balance and gait: Systematic review. Neurology, 90(22), 1017–1025. https://doi.org/10.1212/WNL.0000000000005603

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

Elena P, Demetris S, Christina M, Marios P. Differences Between Exergaming Rehabilitation and Conventional Physiotherapy on Quality of Life in Parkinson's Disease: A Systematic Review and Meta-Analysis. Front Neurol. 2021 Aug 9;12:683385. doi: 10.3389/fneur.2021.683385.

Freitag, F., Brucki, S. M. D., Barbosa, A. F., Chen, J., De Oliveira Souza, C., Valente, D. F., Chien, H. F., Bedeschi, C., & Voos, M. C. (2019). Is virtual reality beneficial for dual-task gait training in patients with Parkinson's disease?: A systematic review. Dementia e Neuropsychologia, 13(3), 259–267. https://doi.org/10.1590/1980-57642018dn13-030002

Garcia-Agundez, A., Folkerts, A.-K., Konrad, R., Caserman, P., Tregel, T., Goosses, M., Göbel, S., & Kalbe, E. (2019). Recent advances in rehabilitation for Parkinson's Disease with Exergames: A Systematic Review Garcia-Agundez et al. Journal of NeuroEngineering and

Rehabilitation. Journal of NeuroEngineering and Rehabilitation, 1–17. http://creativecommons.org/publicdomain/zero/1.0/

García-López H, Obrero-Gaitán E, Castro-Sánchez AM, Lara-Palomo IC, Nieto-Escamez FA, Cortés-Pérez I. Non-Immersive Virtual Reality to Improve Balance and Reduce Risk of Falls in People Diagnosed with Parkinson's Disease: A Systematic Review. Brain Sci. 2021 Oct 28;11(11):1435. doi: 10.3390/brainsci11111435.

Gibbins, N., Awad, R., Harris, S., & Aymat, A. (2017). The diagnosis, clinical findings and treatment options for Parkinson's disease patients attending a tertiary referral voice clinic. Journal of Laryngology and Otology, 131(4), 357–362. https://doi.org/10.1017/S0022215117000159

Iosa, M., Capodaglio, E., Pelà, S., Persechino, B., Morone, G., Antonucci, G., Paolucci, S., & Panigazzi, M. (2021). Artificial Neural Network Analyzing Wearable Device Gait Data for Identifying Patients With Stroke Unable to Return to Work. Frontiers in neurology, 12, 650542. https://doi.org/10.3389/fneur.2021.650542

Jarvis, H. L., Brown, S. J., Price, M., Butterworth, C., Groenevelt, R., Jackson, K., Walker, L., Rees, N., Clayton, A., & Reeves, N. D. (2019). Return to Employment After Stroke in Young Adults: How Important Is the Speed and Energy Cost of Walking?. Stroke, 50(11), 3198–3204. https://doi.org/10.1161/STROKEAHA.119.025614.

Juras G, Brachman A, Michalska J, Kamieniarz A, Pawłowski M, Hadamus A, Białoszewski D, Błaszczyk J, Słomka KJ. Standards of Virtual Reality Application in Balance Training Programs in Clinical Practice: A Systematic Review. Games Health J. 2019 Apr;8(2):101-111. doi: 10.1089/g4h.2018.0034.

Keus, S. H. J., Bloem, B. R., Hendriks, E. J. M., Bredero-Cohen, A. B., & Munneke, M. (2007). Evidence-based analysis of physical therapy in Parkinson's disease with recommendations for

practice and research. Movement Disorders, 22(4), 451–460. https://doi.org/10.1002/mds.21244

Lei, C., Sunzi, K., Dai, F., Liu, X., Wang, Y., Zhang, B., He, L., & 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), 1–17. https://doi.org/10.1371/journal.pone.0224819

Levac, D. E., Glegg, S. M. N., Sveistrup, H., Colquhoun, H., Miller, P., Finestone, H., De Paul, V., Harris, J. E., & Velikonja, D. (2016). Promoting therapists' use of motor learning strategies within virtual reality-based stroke rehabilitation. PLoS ONE, 11(12), 1–16. https://doi.org/10.1371/journal.pone.0168311

Li, R., Zhang, Y., Jiang, Y., Wang, M., Ang, W., & Lau, Y. (2021). Rehabilitation training based on virtual reality for patients with Parkinson's disease in improving balance, quality of life, activities of daily living, and depressive symptoms: A systematic review and meta-regression analysis. Clinical rehabilitation, 35(8), 1089–1102. https://doi.org/10.1177/0269215521995179

Lina, C., Guoen, C., Huidan, W., Yingqing, W., Ying, C., Xiaochun, C., & Qinyong, Y. (2020). The Effect of Virtual Reality on the Ability to Perform Activities of Daily Living, Balance during Gait, and Motor Function in Parkinson Disease Patients: A Systematic Review and Meta-Analysis. American Journal of Physical Medicine and Rehabilitation, 99(10), 917–924. https://doi.org/10.1097/PHM.0000000000001447

Malek, N., Lawton, M. A., Grosset, K. A., Bajaj, N., Barker, R. A., Ben-Shlomo, Y., Burn, D. J., Foltynie, T., Hardy, J., Morris, H. R., Williams, N. M., Wood, N., & Grosset, D. G. (2017). Utility of the new Movement Disorder Society clinical diagnostic criteria for Parkinson's disease applied retrospectively in a large cohort study of recent onset cases. Parkinsonism and Related Disorders, 40, 40–46. https://doi.org/10.1016/j.parkreldis.2017.04.006

Messier, J., Adamovich, S., Jack, D., Hening, W., Sage, J., & Poizner, H. (2007). Visuomotor learning in immersive 3D virtual reality in Parkinson's disease and in aging. Experimental Brain Research, 179(3), 457–474. https://doi.org/10.1007/s00221-006-0802-2

Mirelman, A., Rochester, L., Maidan, I., Del Din, S., Alcock, L., Nieuwhof, F., Rikkert, M. O., Bloem, B. R., Pelosin, E., Avanzino, L., Abbruzzese, G., Dockx, K., Bekkers, E., Giladi, N., Nieuwboer, A., & Hausdorff, J. M. (2016). Addition of a non-immersive virtual reality component to treadmill training to reduce fall risk in older adults (V-TIME): a randomised controlled trial. The Lancet, 388(10050), 1170–1182. https://doi.org/10.1016/S0140-6736(16)31325-3

Moher, D., Liberati, A., Tetzlaff, J., Altman, D. G., & PRISMA Group (2009). Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. PLoS medicine, 6(7), e1000097. https://doi.org/10.1371/journal.pmed.1000097

Paolucci, T., Sbardella, S., La Russa, C., Agostini, F., Mangone, M., Tramontana, L., Bernetti, A., Paoloni, M., Pezzi, L., Bellomo, R. G., Santilli, V., & Saggini, R. (2020). Evidence of Rehabilitative Impact of Progressive Resistance Training (PRT) Programs in Parkinson Disease: An Umbrella Review. Parkinson's Disease, 2020. https://doi.org/10.1155/2020/9748091

Paolucci, Teresa, Bernetti, A., Sbardella, S., La Russa, C., Murgia, M., Salomè, A., Villani, C., Altieri, M., Santilli, V., Paoloni, M., Agostini, F., & Mangone, M. (2020). Straighten your back! Self-correction posture and postural balance in "non rehabilitative instructed" multiple sclerosis patients. NeuroRehabilitation, 46(3), 333–341. https://doi.org/10.3233/NRE-192987

Petraroli, A., de Sire, A., Pino, I., Moggio, L., Marinaro, C., Demeco, A., & Ammendolia, A. (2021). Effects of rehabilitation on reducing dyskinesias in a Parkinson's disease patient abusing therapy with levodopa-carbidopa intestinal gel: a paradigmatic case report and

literature review. Journal of biological regulators and homeostatic agents, 35(4), 10.23812/21-229-L. https://doi.org/10.23812/21-229-L

Petzinger, G., Fisher, B., McEwen, S., Beeler, S., Walsh, J., Jakowec, M. E. N. T. (2013). Cognitive Circuitry in Parkinson's Disease. Lancet Neurol, 12(7), 716–726. https://doi.org/10.1016/S1474-4422(13)70123-6.Exercise-enhanced

Samii, A., Nutt, J. G., & Ransom, B. R. (2004). Parkinson's disease. The Lancet, 363(9423), 1783–1793. https://doi.org/10.1016/S0140-6736(04)16305-8

Santos P., Scaldaferri G., Santos L., Ribeiro N., Neto M., & Melo A. (2019). Effects of the Nintendo Wii training on balance rehabilitation and quality of life of patients with Parkinson's disease: A systematic review and meta-analysis. NeuroRehabilitation. 44(4):569-577. doi: 10.3233/NRE-192700.

Shea, B. J., Reeves, B. C., Wells, G., Thuku, M., Hamel, C., Moran, J., Moher, D., Tugwell, P., Welch, V., Kristjansson, E., & Henry, D. A. (2017). AMSTAR 2: A critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. BMJ (Online), 358, 1–9. https://doi.org/10.1136/bmj.j4008

Teo, W. P., Muthalib, M., Yamin, S., Hendy, A. M., Bramstedt, K., Kotsopoulos, E., Perrey, S., & Ayaz, H. (2016). Does a combination of virtual reality, neuromodulation and neuroimaging provide a comprehensive platform for neurorehabilitation? - A narrative review of the literature. Frontiers in Human Neuroscience, 10(June), 1–15. https://doi.org/10.3389/fnhum.2016.00284

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

Triegaardt, J., Han, T. S., Sada, C., Sharma, S., & Sharma, P. (2020). Correction to: The role of virtual reality on outcomes in rehabilitation of Parkinson's disease: meta-analysis and

systematic review in 1031 participants (Neurological Sciences, (2020), 41, 3, (529-536), 10.1007/s10072-019-04144-3). Neurological Sciences, 41(3), 731–732. https://doi.org/10.1007/s10072-019-04212-8

Voinescu, A., Sui, J., & Stanton Fraser, D. (2021). Virtual Reality in Neurorehabilitation: An Umbrella Review of Meta-Analyses. Journal of clinical medicine, 10(7), 1478. https://doi.org/10.3390/jcm10071478

Von Campenhausen, S., Bornschein, B., Wick, R., Bötzel, K., Sampaio, C., Poewe, W., Oertel, W., Siebert, U., Berger, K., & Dodel, R. (2005). Prevalence and incidence of Parkinson's disease in Europe. European Neuropsychopharmacology, 15(4), 473–490. https://doi.org/10.1016/j.euroneuro.2005.04.007

Wang, B., Shen, M., Wang, Y. X., He, Z. W., Chi, S. Q., & Yang, Z. H. (2019). Effect of virtual reality on balance and gait ability in patients with Parkinson's disease: a systematic review and meta-analysis. Clinical Rehabilitation, 33(7), 1130–1138. https://doi.org/10.1177/0269215519843174

Wickremaratchi, M. M., Perera, D., O'Loghlen, C., Sastry, D., Morgan, E., Jones, A., Edwards, P., Robertson, N. P., Butler, C., Morris, H. R., & Ben-Shlomo, Y. (2009). Prevalence and age of onset of Parkinson's disease in Cardiff: A community based cross sectional study and meta-analysis. Journal of Neurology, Neurosurgery and Psychiatry, 80(7), 805–807. https://doi.org/10.1136/jnnp.2008.162222

Table 1. Features of systematic reviews included.

Author	Study Design	Assessment method of the studies	Results	Limitations	AMSTAR score
Cano Porras et al.	Systematic review (97 studies: 49 RCT or quasi-RCT, 34 cohort studies, 14 case reports)	CONTENT scale; Cochrane Collaboration tool (per RCT e quasi-RCT); Newcastle-Ottawa Scale (per studi di coorte e case reports)	VR has a positive impact on gait and balance, especially when combined with conventional rehabilitation.	Poor methodologic quality of most included studies.	9/11
Li et al.	Systematic review and meta-regression analysis (22 randomized controlled trials)	PEDro score	VR training could be adopted in healthcare institutions as supplementary training for patients with PD.	Small sample size, most included trials were conducted in Asian countries, overall evidence ranged from very low to low, some selected trials did not provide comprehensive intervention descriptions.	8/11
Wang et al.	Systematic review and meta-analysis (12 RCT)	PEDro score	VR determines a significant improvement in stride length compared with CR, no differences in gait velocity and walk distance.	The majority of 12 included studies had small sample size and intervention approaches varied considerably.	10/11
Lei et al.	Systematic review (16 RCT)	Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0	VR rehabilitation improves step and stride length, balance function, quality of life and neuropsychiatric symptoms compared to CR.	Intervention approaches varied considerably among the different studies.	10/11

Triegaardt et al.	Systematic review and meta-analysis (27 studies)	Cochrane Collab. tool	VR compared to active rehabilitation treatment determines a major improvement in the stride length, while compared to traditional rehabilitation treatment allows it to recover better, in addition to the stride length, also the speed of the walk	The review includes a smaller number of studies and participants than those provided for the study of a new technology such as VR. The RV systems used in the various studies included in the review are different from each other. This can affect the results	8/11
Freitag et al.	Systematic review (19 studies)	PEDro score	Dual task training with walk VR induces improvements in length stride, cadence of stride and walking speed	Among the various studies included in the review, evaluation methods, rehabilitation exercises and characteristics of the system of RV used are often different	7/11
Lina et al.	Systematic review and Meta-Analysis (12 RCT)	Cochrane Collab. tool	VR shows to improve balance, strengthen motor function and gait ability	The overall dimension specimen is small and the number of the studies relating to the specific topic is restricted	9/11
Barry et al.	Systematic review (7 studies: 1 RCT, 1 case report, s longitudinal studies, 1 cohort study, 2 other studies)	Personalized evaluation of the quality	Exergaming improves balance, motor function and severity of PD motor symptoms	Heterogeneity of the different exergames; only full articles included	9/11

Garcia-Agundez et al.	Systematic review (64 studies: 8 RCT, 11 pilot studies, 30 technical papers, 15 meta-analysis)	Personalized evaluation of the quality	Exergaming improves balance, and severity of PD motor symptoms	Heterogeneity of the different exergames; only 8 RCT; many studies do not have any control group	7/11
Chen et al.	Systematic review (12 RCT)	PEDro score and Cochrane Handbook for Systematic Reviews of Interventions	VR improves static and dynamic balance in PD patients, more than traditional interventions.	Heterogeneity in the setups and exercise items included and, in the outcomes, measured; little number of trials.	9/11
García-López et al.	Systematic review (10 RCT)	PRISMA and the Cochrane Handbook for Systematic Reviews of Interventions	non-immersive VR can improve balance and reduce the risk and number of falls, being therefore beneficial for people with PD.	Reduced sample size, ranging between 20 and 130 patients.	10/11
Santos et al.	Systematic review and Meta-Analysis (5 RCT)	PRISMA	combined Nintendo Wii and traditional physiotherapy was more effective on balance rehabilitation and quality of life of patients with PD	Studies analyzed with small samples; Heterogeneity of the different exergames; Heterogeneity in the setups and exercise items included and, in the outcomes, measured;	9/11
Juras et al.	Systematic review	PEDro score	Comparison of VR interventions between conventional rehabilitation and no intervention exhibited significantly better results.	Large diversity of implemented VR trainings in the reviewed studies.	8/11

Elena et al.	Systematic Review and Meta-Analysis	PRISMA	Exergames as a rehabilitation method can be used to provide alternative interactive intervention with positive results for quality of life in people with PD	Small number of studies that compared the two different intervention techniques	8/11

VR: Virtual Reality; PD: Parkinson's disease; RCT: Randomized Controlled Trial; CR: Conventional Rehabilitation

Table 2. Methodologic quality of included systematic reviews based on AMSTAR checklist.

Author	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	AMSTAR score
Cano Porras et al.	✓	✓	✓	✓	✓	✓	✓	✓	✗	✗	✓	9/11
Li et al.	✓	✓	✓	✗	✓	✓	✓	✓	✗	✗	✓	8/11
Wang et al.	✓	✓	✓	✗	✓	✓	✓	✓	✓	✓	✓	10/11
Lei et al.	✓	✓	✓	✗	✓	✓	✓	✓	✓	✓	✓	10/11
Triegaardt et al.	✓	✗	✓	✗	✓	✓	✓	✓	✓	✗	✓	8/11
Freitag et al.	✓	✓	✓	✗	✓	✓	✓	✓	✗	✗	✗	7/11
Lina et al.	✓	✓	✓	✗	✓	✓	✓	✓	✓	✓	✗	9/11
Barry et al.	✓	✓	✓	✓	✓	✓	✓	✓	✗	✗	✓	9/11
Garcia-Agundez et al.	✓	✓	✓	✗	✓	✓	✓	✓	✗	✗	✓	7/11
Chen et al.	✓	✓	✓	✗	✓	✓	✓	✓	✓	✗	✓	9/11
García-López et al.	✓	✓	✓	✗	✓	✓	✓	✓	✓	✓	✓	10/11
Santos et al.	✓	✓	✓	✗	✓	✓	✓	✓	✓	✗	✓	9/11
Juras et al.	✓	✓	✓	✗	✓	✓	✓	✓	✗	✗	✓	8/11
Elena et al.	✓	✓	✓	✗	✓	✓	✓	✓	✗	✓	✗	8/11

Question 1 (Q1): Was an 'a priori' design provided?; Q2: Was there duplicate study selection and data extraction?; Q3: Was a comprehensive literature search performed?; Q4: Was the status of publication (i.e. grey literature) used as an inclusion criterion?; Q5: Was a list of studies (included and excluded) provided?; Q6: Were the characteristics of the included studies

provided?; Q7: Was the scientific quality of the included studies assessed and documented?; Q8: Was the scientific quality of the included studies used appropriately in formulating conclusions?; Q9: Were the methods used to combine the findings of studies appropriate?; Q10: Was the likelihood of publication bias assessed?; Q11: Was the conflict of interest included?

Table 3. Features of rehabilitative protocols adopted across all the studies examined in each review.

Author	N° of sessions / week	N° of weeks	Time per VR session (min)	Follow up
Cano Porras et al.	2-5	4-6	20-40	2 weeks - 6 months
Li et al.	2-7	3-12	20-40	-
Wang et al.	2-5	4-12	20-100	1 - 15 months
Lei et al.	2-7	4-12	30-60	-
Triegaardt et al.	-	4-12	-	-
Freitag et al.	2-3	3-12	30-60	1-3 months
Lina et al.	2-5	4-12	30-60	-
Barry et al.	1-3	4-8	30-60	-
Garcia- Agundez et al.	2-5	4-12	15-60	1-2 months
Chen et al.	-	5-12	-	-
García-López et al.	5-12	2-5	30-75	-
Santos et al.	4-12	2-5	30-60	-
Juras et al.	2-4	2-8	20-50	-
Elena et al.	2-5	6-12	40-60	-

VR: Virtual Reality

Table 4. Features of exercises included in systematic reviews considered.

Author	Proposal task
Cano Porras et al.	Obstacle negotiation, exercises challenged control of body lean, strengthening exercises and balance games using Wii
Li et al.	Nintendo Wii™, Microsoft Xbox 360™ Kinect, tablets, and computers.
Wang et al.	VR balance and gait training, Wii Fit VR
Lei et al.	Wii fit VR, Xbox VR, Computerized Balance and gait training system
Triegaardt et al.	Nintendo Wii, Xbox Kinect and other customized virtual reality systems (Neuro VR, Oculus Rift DK2, IREX, OpenGL, SGI Octane)
Freitag et al.	Treadmill training with virtual obstacles, exercises with Wii Fit, balance board and Wii sport (golf or bowling)
Lina et al.	VR balance training, Tele Wii training, Nintendo Wii, Gamepad-based training, Wii Fit exercise, VR plus NDT ad FES, K-box game, Wii-based motor and cognitive training, Wii Fit games
Barry et al.	Nintendo Wii with balance board, walking in place, obstacles, squats, sport like tennis, boxing, bowling and ski slalom
Garcia-Agundez et al.	Nintendo Wii Fit, Xbox kinect and balance board, stretching, muscle strengthening, treadmill + VR, obstacles, sport like table tennis
Chen et al.	Nintendo Wii Fit, training of the balance, dancing, visual feedback training,
García-López et al.	Nintendo Wii Fit, modified Microsoft Kinect connected to a large Screen, a custom-created non-immersive VR system consisting of a 22-inch touch screen and a balance board
Santos et al.	Nintendo Wii Fit
Juras et al.	Nintendo Wii Fit, Xbox kinect and balance board
Elena et al.	Nirvana, Nintendo Wii Fit, Microsoft X-Box Kinect, VR training, VR Unity games, TeleWii, Nintendo Wii, balance board

VR: Virtual Reality; FES: Functional Electrical Stimulation; NDT: NeuroDevelopment Treatment; IREX: Interactive Rehabilitation & Exercise System; DK2: Development Kit 2; OpenGL: Open Graphics Library; SGI Octane: Silicon Graphics Octane.

Table 5. Evaluation methods and scales.

Author and year	Assessment method
Cano Porras et al.	UPDRS III; BBS; 2/6/10 MWT; TUG; DGI.
Li et al.	BBS; PDQ-39; BDI; GDS-15
Wang et al.	BBS; 6MWT; 10MWT; TUG; SLS; UST.
Lei et al.	BBS; TUG; UPDRS; DGI; 6MWT; 10MWT.
Triegaardt et al.	TUG; 6MWT; 10MWT
Freitag et al.	DGI; 6MWT; TUG
Lina et al.	BBS; TUG; 10MWT; MBI
Barry et al.	TUG; 10MWT; DGI; UPDRS
Garcia- Agundez et al.	UPDRS; TUG; 6MWT; 10MWT; Tinetti gait scale
Chen et al.	FGA; TUG; DGI
García-López et al.	BBS; ABC; Tinetti scale; TUG; FRT
Santos et al.	BBS; UPDRS; Fatigue Severity Scale; 6MWT; PDQ-39; TUG
Juras et al.	BBS; TUG; FRT; UPDRS; BOT-2; 2MWT; 10MWT
Elena et al.	PDQ-39; ABC; UPDRS; BBS; TUG; DGI

BBS: Berg Balance Scale; UST: Unipedal Stance Test; SLS: Single Leg Stance test; TUG: Timed Up and Go test; 2MWT/6MWT/10MWT: Two/Six/Ten Minute Walk Test; DGI: Dynamic Gait Index; UPDRS: Unified Parkinson's Disease Rating Scale; FGA: Functional Gait Assessment; ABC: Activities-specific Balance and Confidence scale; FRT: Functional Reach Test; PDQ-39: PDQ-39 Quality of Life Questionnaire; BOT-2: Bruininks–Oseretsky test of Motor Performance 2; BDI: beck depression inventory; GDS-15: 15-item geriatric depression scale

Table 1. Features of systematic reviews included.

Author	Study Design	Assessment method of the studies	Results	Limitations	AMSTAR score
Cano Porras et al.	Systematic review (97 studies: 49 RCT or quasi-RCT, 34 cohort studies, 14 case reports)	CONTENT scale; Cochrane Collaboration tool (per RCT e quasi-RCT); Newcastle-Ottawa Scale (per studi di coorte e case reports)	VR has a positive impact on gait and balance, especially when combined with conventional rehabilitation.	Poor methodologic quality of most included studies.	9/11
Li et al.	Systematic review and meta-regression analysis (22 randomized controlled trials)	PEDro score	VR training could be adopted in healthcare institutions as supplementary training for patients with PD.	Small sample size, most included trials were conducted in Asian countries, overall evidence ranged from very low to low, some selected trials did not provide comprehensive intervention descriptions.	8/11
Wang et al.	Systematic review and meta-analysis (12 RCT)	PEDro score	VR determines a significant improvement in stride length compared with CR, no differences in gait velocity and walk distance.	The majority of 12 included studies had small sample size and intervention approaches varied considerably.	10/11
Lei et al.	Systematic review (16 RCT)	Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0	VR rehabilitation improves step and stride length, balance function, quality of life and neuropsychiatric symptoms compared to CR.	Intervention approaches varied considerably among the different studies.	10/11

Triegaardt et al.	Systematic review and meta-analysis (27 studies)	Cochrane Collab. tool	VR compared to active rehabilitation treatment determines a major improvement in the stride length, while compared to traditional rehabilitation treatment allows it to recover better, in addition to the stride length, also the speed of the walk	The review includes a smaller number of studies and participants than those provided for the study of a new technology such as VR. The RV systems used in the various studies included in the review are different from each other. This can affect the results	8/11
Freitag et al.	Systematic review (19 studies)	PEDro score	Dual task training with walk VR induces improvements in length stride, cadence of stride and walking speed	Among the various studies included in the review, evaluation methods, rehabilitation exercises and characteristics of the system of RV used are often different	7/11
Lina et al.	Systematic review and Meta-Analysis (12 RCT)	Cochrane Collab. tool	VR shows to improve balance, strengthen motor function and gait ability	The overall dimension specimen is small and the number of the studies relating to the specific topic is restricted	9/11
Barry et al.	Systematic review (7 studies: 1 RCT, 1 case report, s longitudinal studies, 1 cohort study, 2 other studies)	Personalized evaluation of the quality	Exergaming improves balance, motor function and severity of PD motor symptoms	Heterogeneity of the different exergames; only full articles included	9/11

Garcia-Agundez et al.	Systematic review (64 studies: 8 RCT, 11 pilot studies, 30 technical papers, 15 meta-analysis)	Personalized evaluation of the quality	Exergaming improves balance, and severity of PD motor symptoms	Heterogeneity of the different exergames; only 8 RCT; many studies do not have any control group	7/11
Chen et al.	Systematic review (12 RCT)	PEDro score and Cochrane Handbook for Systematic Reviews of Interventions	VR improves static and dynamic balance in PD patients, more than traditional interventions.	Heterogeneity in the setups and exercise items included and, in the outcomes, measured; little number of trials.	9/11
García-López et al.	Systematic review (10 RCT)	PRISMA and the Cochrane Handbook for Systematic Reviews of Interventions	non-immersive VR can improve balance and reduce the risk and number of falls, being therefore beneficial for people with PD.	Reduced sample size, ranging between 20 and 130 patients.	10/11
Santos et al.	Systematic review and Meta-Analysis (5 RCT)	PRISMA	combined Nintendo Wii and traditional physiotherapy was more effective on balance rehabilitation and quality of life of patients with PD	Studies analyzed with small samples; Heterogeneity of the different exergames; Heterogeneity in the setups and exercise items included and, in the outcomes, measured;	9/11
Juras et al.	Systematic review	PEDro score	Comparison of VR interventions between conventional rehabilitation and no intervention exhibited significantly better results.	Large diversity of implemented VR trainings in the reviewed studies.	8/11

Elena et al.	Systematic Review and Meta-Analysis	PRISMA	Exergames as a rehabilitation method can be used to provide alternative interactive intervention with positive results for quality of life in people with PD	Small number of studies that compared the two different intervention techniques	8/11

VR: Virtual Reality; PD: Parkinson's disease; RCT: Randomized Controlled Trial; CR: Conventional Rehabilitation

Table 2. Methodologic quality of included systematic reviews based on AMSTAR checklist.

Author	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	AMSTAR score
Cano Porras et al.	✓	✓	✓	✓	✓	✓	✓	✓	✗	✗	✓	9/11
Li et al.	✓	✓	✓	✗	✓	✓	✓	✓	✗	✗	✓	8/11
Wang et al.	✓	✓	✓	✗	✓	✓	✓	✓	✓	✓	✓	10/11
Lei et al.	✓	✓	✓	✗	✓	✓	✓	✓	✓	✓	✓	10/11
Triegaardt et al.	✓	✗	✓	✗	✓	✓	✓	✓	✓	✗	✓	8/11
Freitag et al.	✓	✓	✓	✗	✓	✓	✓	✓	✗	✗	✗	7/11
Lina et al.	✓	✓	✓	✗	✓	✓	✓	✓	✓	✓	✗	9/11
Barry et al.	✓	✓	✓	✓	✓	✓	✓	✓	✗	✗	✓	9/11
Garcia-Agundez et al.	✓	✓	✓	✗	✓	✓	✓	✓	✗	✗	✓	7/11
Chen et al.	✓	✓	✓	✗	✓	✓	✓	✓	✓	✗	✓	9/11
García-López et al.	✓	✓	✓	✗	✓	✓	✓	✓	✓	✓	✓	10/11
Santos et al.	✓	✓	✓	✗	✓	✓	✓	✓	✓	✗	✓	9/11
Juras et al.	✓	✓	✓	✗	✓	✓	✓	✓	✗	✗	✓	8/11
Elena et al.	✓	✓	✓	✗	✓	✓	✓	✓	✗	✓	✗	8/11

Question 1 (Q1): Was an 'a priori' design provided?; Q2: Was there duplicate study selection and data extraction?; Q3: Was a comprehensive literature search performed?; Q4: Was the status of publication

(i.e. grey literature) used as an inclusion criterion?; Q5: Was a list of studies (included and excluded) provided?; Q6: Were the characteristics of the included studies provided?; Q7: Was the scientific quality of the included studies assessed and documented?; Q8: Was the scientific quality of the included studies used appropriately in formulating conclusions?; Q9: Were the methods used to combine the findings of studies appropriate?; Q10: Was the likelihood of publication bias assessed?; Q11: Was the conflict of interest included?

Table 3. Features of rehabilitative protocols adopted across all the studies examined in each review.

Author	N° of sessions / week	N° of weeks	Time per VR session (min)	Follow up
Cano Porras et al.	2-5	4-6	20-40	2 weeks - 6 months
Li et al.	2-7	3-12	20-40	-
Wang et al.	2-5	4-12	20-100	1 - 15 months
Lei et al.	2-7	4-12	30-60	-
Triegaardt et al.	-	4-12	-	-
Freitag et al.	2-3	3-12	30-60	1-3 months
Lina et al.	2-5	4-12	30-60	-
Barry et al.	1-3	4-8	30-60	-
Garcia- Agundez et al.	2-5	4-12	15-60	1-2 months
Chen et al.	-	5-12	-	-
García-López et al.	5-12	2-5	30-75	-
Santos et al.	4-12	2-5	30-60	-
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