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SYSTEMATIC REVIEW
THE ITALIAN CONSENSUS CONFERENCE CICERONE

Effects of robot-assisted gait training on postural instability in Parkinson's disease: a systematic review

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ABSTRACT

INTRODUCTION: Postural instability is a cardinal feature of Parkinson's disease, together with rest tremor, rigidity and bradykinesia. It is a highly disabling symptom that becomes increasingly common with disease progression and represents a major source of reduced quality of life in patients with Parkinson's disease. Rehabilitation aims to enable patients with Parkinson's disease to maintain their maximum level of mobility, activity and independence. To date, a wide range of rehabilitation approaches has been employed to treat postural instability in Parkinson's disease, including robotic training. Our main aim was to conduct a systematic review of current literature about the effects of robot-assisted gait training on postural instability in patients with Parkinson's disease.

EVIDENCE ACQUISITION: A systematic search using the following MeSH terms "Parkinson disease," "postural balance," "robotics," "rehabilitation" AND string "robotics [mh]" OR "robot-assisted" OR "electromechanical" AND "rehabilitation [mh]" OR "training" AND "postural balance [mh]" was conducted on PubMed, Cochrane Library and Pedro electronic databases. Full text articles in English published up to December 2020 were included. Data about patient characteristics, robotic devices, treatment procedures and outcome measures were considered. Every included article got checked for quality. Level of evidence was defined for all studies.

EVIDENCE SYNTHESIS: Three authors independently extracted and verified data. In total, 18 articles (2 systematic reviews, 9 randomized controlled trials, 4 uncontrolled studies and 3 case series/case reports) were included. Both end-effector and exoskeleton devices were investigated as to robot-assisted gait training modalities. No clear relationship between treatment parameters and clinical conditions was observed. We found a high level of evidence about the effects of robot-assisted gait training on balance and freezing of gait in patients with Parkinson's disease.

CONCLUSIONS: This systematic review provides to the reader a complete overview of current literature and levels of evidence about the effects of robot-assisted gait training on postural instability issues (static and dynamic balance, freezing of gait, falls, confidence in activities of daily living and gait parameters related to balance skills) in patients with Parkinson's disease.

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KEY WORDS: Parkinson disease; Postural balance; Robotics; Rehabilitation.

Introduction

Parkinson's disease (PD) is a common neurodegenerative disorder due to the loss of dopaminergic neurons in the substantia nigra pars compacta, which alters the function of basal ganglia (and in particular of the putamen) that is involved in control of upright stance, movement performance, motor learning and motor control.[1] Postural instability is a cardinal feature of PD, together with rest tremor, rigidity and bradykinesia.[2] It represents a highly disabling symptom that becomes increasingly common with disease progression and is a main source for reduction of quality of life in patients with PD.[2, 3] The pathogenesis of postural instability in PD involves impaired postural reflexes, pathological postures, increased postural sway, compensatory attentional strategies and disordered sensory systems.[1, 4] This may result in changes about the strategies of postural control during standing tasks, unexpected destabilizing perturbations and voluntary movements, such as walking.[1, 4, 5]

Rehabilitation is an adjuvant treatment to pharmacological and surgical procedures for PD in order to maximize functional ability, level of mobility and independence, also minimizing secondary complications.[2, 6] To date, a number of rehabilitative approaches has been proposed to treat the disabling features of PD, including physiotherapy (*i.e.* stretching procedures, muscle strengthening, therapeutic exercises), occupational therapy, treadmill training and advanced technologies.[6-11] Unfortunately, it remains unclear which intervention is the most effective.[12, 13]

In the last decades, there was a growing diffusion of robotic devices in rehabilitation facilities. The main aim of robots is to assist the training of patients with neurological disabilities. As to patients with PD, robotic training has been proposed to treat the impairments involving walking and the upper limbs.[14-18] Based on the evidences about the beneficial effect on balance skills of rehabilitation procedures aimed at improving gait (such as treadmill),[19] robot-assisted gait training has been proposed as a treatment approach for postural instability in PD.[20] This was also because robotic machines for walking training may improve the safety profile of treatment in patients with balance impairment by means of exoskeleton or end-effector devices with harness for supporting body weight and controlling body sway.

Despite the amount of evidence about the use of robot-assisted gait training for treating patients with PD suffering from postural instability to date there is scant consensus on these procedures according to the wide range of protocols proposed in literature. This paper presents the results of a systematic review of current studies about the effects of robot-assisted gait training on postural instability in patients with PD, which was conducted by the working group on balance of the Italian Consensus Conference on "Rehabilitation assisted by robotic and electromechanical devices for persons with disability of neurological origin" (CICERONE), promoted by the Italian Society of Physical and Rehabilitative Medicine and the Italian Society of Neurological Rehabilitation.

Evidence acquisition

This systematic review was conducted according to the PRISMA statement.[21]

A systematic search using the following MeSH terms "Parkinson disease," "postural balance," "robotics," "rehabilitation" AND string "robotics [mh]" OR "robot-assisted" OR "electromechanical" AND "rehabilitation [mh]" OR "training" AND "postural balance [mh]" was conducted on PubMed, Cochrane Library and Pedro electronic databases.

Selection criteria

Full text articles in English published up to December 2020 were included according to the following criteria, which considered participants (adults with PD), type of intervention (robot-assisted gait training for treating postural instability), comparators (no treatment; conventional exercises; overground walking training; treadmill training) and outcomes (balance control and related skills).

Study selection and data extraction

Three independent reviewers selected the studies according to the criteria listed above. Any disagreement was resolved by a discussion between them. After the inclusion of a study, data about patient characteristics, robotic devices, treatment procedures and outcome measures were extracted and verified.

Quality assessment

Study quality was assessed by means of the Pedro Scale, which assigns a score ranging from 0 to 10.[22] A Pedro Score of 9-10 was considered excellent, a score of 6-8 was considered good, a score of 4-5 was considered fair, a score lower than 4 was considered poor.[23] The methodological assessment of systematic reviews was done according to the Measurement Tool to Assess Systematic Reviews (AMSTAR)-2.[22]

Level of evidence

The level of evidence was defined for all studies by means of the framework for quantitative research on intervention studies (Oxford Center for Evidence-Based Medicine) as follows: level 1a – systematic review of randomized controlled trials; level 1b – individual randomized controlled trials; level 2a – systematic review of non-randomized controlled trials; level 2b – individual cohort studies; level 3a – systematic review of case-control study; level 3b – individual case control studies; level 4 – case series, poor quality cohort and case-control studies; and level 5 – expert opinion.

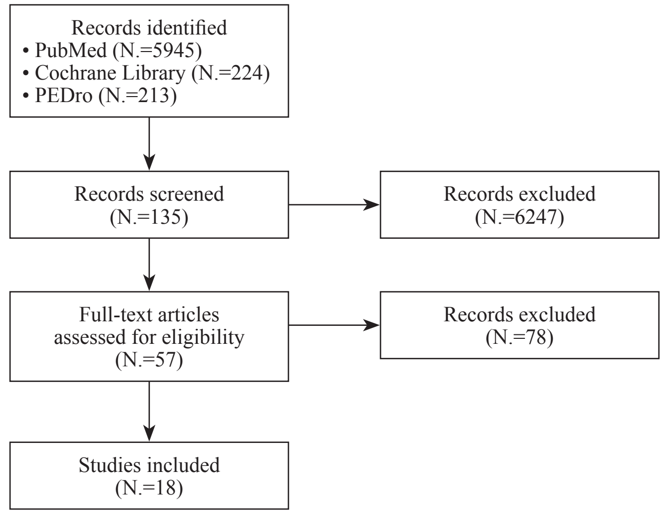

Figure 1.—Flow chart on the selection process of studies.

Evidence synthesis

In total, 18 articles (2 systematic reviews, 9 randomized controlled trials, 4 uncontrolled studies and 3 case series/case reports) were included (Figure 1). Supplementary Digital Material 1: Supplementary Table I reports detailed information about them.

Both end-effector and exoskeleton devices were investigated as to robot-assisted gait training modalities. Considering only the studies reporting original data, exoskeleton devices (Lokomat, Hocoma, Volketswil, Switzerland; Robotic Gait Trainer – RGT Rehastim, Berlin, Gernany; Walkbot_S, P&S Mechanics, Seoul, South Korea) were used in 9 studies,[24-32] while end-effector devices (GangTrainer GT1, Reha-Stim, Berlin, Germany; G-EO System Evolution, Reha Technology, Olten, Switzerland) were used in 7 studies.[17, 18, 20, 33-36]

The duration of robotic training (both with exoskeleton and end-effector devices) was mainly between 4 and 5 weeks. Only one study proposed a 2-week treatment protocol as well as one trial applied a 3-week training protocol.[25, 30] As to the treatment protocols considered in this review, they consisted of a number of sessions ranging from 10 to 20 with a frequency that could be two, three or five times a week. The duration of each treatment session was between 20 and 45 minutes. Most of the studies used the body-weight support integrated in the robotic device.[17, 18, 20, 24-31, 33-36] When used, the body-weight support was progressively reduced during the single treatment session and/or along the treatment cycle according to the growing confidence with the robotic device.

Some studies used robot-assisted gait training as part of a broader and more articulate training protocol, which last from 1 to 3 hours per session.[31, 33, 35] Treatments were inpatients in two cases.[29, 31]

A physiotherapy protocol performed overground was provided as control treatment in five randomized controlled trials.[17, 18, 20, 31, 34] Five randomized controlled trials proposed treadmill training as comparative treatment.[18, 26, 33, 35, 36]

Most of the studies enrolled subject's suffering from both early-moderate (Hoehn and Yahr <3) and advanced (Hoehn and Yahr ≥3) stage of Parkinson's disease.[17, 27, 28, 30-33, 35, 36] Carda *et al*. enrolled only people with early stage of disease, while Picelli *et al*. studied the effect of robotic training on subjects with postural instability.[18, 20, 26, 34]

With regard to the treatment outcomes, both specific scales for the assessment of balance and more global scales (including issues related to postural control in experimental and real-life conditions) were used. The most used outcome measure specific for assessing balance skills was the Berg Balance Scale.[14, 18, 20, 30, 32, 34] In five studies, the impact of training on freezing of gait was studied.[24, 25, 28, 30, 36] Analysis of gait parameters related to balance skills (*e.g.* stride length, coefficient of variation of stride time, cadence, single support and double support duration) was done in some studies.[17, 18, 24, 25, 28, 29, 33, 35]

All enrolled trials showed robotic training induced improvements of outcomes measures, both specific for postural instability (*i.e.* BBS or Tinetti scores) and more generic gait-related measures.[2, 14, 18, 30, 32, 34, 35] Randomized controlled trials showed a possibly better effect of robotic training with respect to over-ground physiotherapy not specific for balance and gait problems.[17, 18, 20, 31, 34] Conversely, robot-assisted gait training seems not superior to treadmill training, (probably except for balance and freezing of gait).[18, 26, 33-36]

The assessment of outcomes was performed at the end of the treatment in six trials,[24, 25, 30, 33, 35, 36] after the 1st[17, 20, 28, 29, 32] and 3rd[18, 27, 31, 34] month after the end of the training in five studies. Carda *et al*. assessed outcomes at the 6-month follow-up.[26] The quality of the RCTs ranged from a score of 6 to 8 on the Pedro scale; concealed allocation, patient's or physiotherapist's blindness and an adequate follow-up were the most often omitted study features.[20, 26, 27, 32, 34, 35]

Discussion

This systematic review was carried out by the working group on balance of the Italian Consensus Conference on "Rehabilitation assisted by robotic and electromechanical devices for persons with disability of neurological origin" (CICERONE), promoted by the Italian Society of Physical and Rehabilitative Medicine and the Italian Society of Neurological Rehabilitation. It deals with the effects of robot-assisted gait training on postural instability in patients with PD.

Consistent with the type of training investigated, balance skills were not considered as primary outcome by the majority of studies included in this systematic review. On the same line, some studies reported indirectly the effects on postural control of robot-assisted gait training by investigating some gait parameters related to balance skills. Thus, it is not surprising that this review included both patients with PD suffering from postural instability (Hoehn and Yahr Score ≥3) as well as those without balance impairment.

Considering the studies included in this review, it seems to be no correspondence between the type of device (exoskeleton or end-effector), the protocols used (in terms of total duration of the treatment cycle, frequency of treatment sessions and their duration), the treatment parameters (*i.e.* gait speed and percentage of body-weight support) and the PD severity (expressed in terms of Hoehn and Yahr Score) of patients treated with robot-assisted gait training. Despite these limitations, the current literature shows that robot-assisted gait training may effectively lead to significant improvements of postural control and gait parameters related to balance skills after treatment and at the follow-up evaluations (up to one month after the end of treatment) when compared to the baseline assessment or to unspecific conventional training procedures at low intensity.[17, 20, 24, 25, 27-31, 37, 38] On the other hand, there is a high level of evidence supporting the non-superiority of robot-assisted gait training with respect to conventional balance training and equal intensity treadmill training for improving postural instability and gait parameters associated with balance control in patients with PD.[26, 33, 34] Only three studies reported better improvements of postural instability due to robot-assisted gait training in comparison with treadmill training.[18, 34, 36] A study by Picelli *et al.* considered a sample of patients suffering from PD with postural instability (Hoehn and Yahr 3) treated by means of robot-assisted gait training *vs*. equal intensity treadmill training (Supplementary Table I).[18] The authors found the Berg Balance Scale to achieve greater improvements after robot-assisted gait training than after equal intensity treadmill training. However, these findings had been overcome by the same research group in a later study on the same type of population, which found no significant difference between robot-assisted gait training and conventional training specific for balance.[34] Another study by Galli *et al.* reported significantly greater improvements in some gait parameters related to balance control (*i.e.* gait speed, step length and cadence) due to robot-assisted gait training compared to intensive treadmill training (Supplementary Table I).[35] However, this study has some limitations regarding balance issues. Indeed, the Authors included both patients with PD suffering from postural instability and those without balance impairment (Hoehn and Yahr Score of the sample ranged from 1.5 to 4). Furthermore, the intensity of treadmill training was not defined. A further study by Capecci *et al.* included patients suffering from PD with Hoehn and Yahr Score ≥ 2.[36] The Authors found that robot-assisted gait training was more effective than equal intensity treadmill training on freezing of gait, especially in individuals with greater walking disability (Supplementary Table I).[36]

As to the findings of this systematic review, we would like to discuss, from a clinical rehabilitation practice point of view, about the non-superiority of robot-assisted gait training to conventional training (equal intensity treadmill training and balance exercises) for treating postural instability in patients with PD. At first sight, our observations might be read as a demonstration of not usefulness (further supported by the cost of robotic devices). However, another way for interpreting our results is to consider robot-assisted gait training not inferior to conventional training for postural instability in PD. On this line, robotic devices may support some labor-intensive aspects of physical therapy allowing therapists to focus on functional rehabilitation during individual training and supervise (more than one) patients simultaneously during robotic training sessions. This is further important in patients with postural instability considering the high level of safety given by (exoskeleton or end-effector) robot devices for gait training. In addition, it would be beneficial in clinical settings to promote a cost-effective use of human resources and standardization of rehabilitation programs. Our view agrees with this way of thinking, in particular as to the treatment of specific symptoms, such as freezing of gait. In addition, it would be beneficial in clinical settings to promote a cost-effective use of human resources and standardization of rehabilitation programs.

As to the reasons for the effect of robot-assisted gait training on patients with postural instability due to PD, a possible mechanisms of action may be the facilitation of neuromuscular regulation produced by repetitive locomotor training.[19] Indeed, robot-assisted gait training provides several repetitions of gait-like movements that may have a positive influence on the central pattern generators at the spinal level with a consequent reduction of muscle cocontraction and improvement of contraction/inhibition patterns within lower limbs muscles (in patients with PD a disruption of proprioceptive reflexes together with a co-activation of ankle dorsiflexors and plantar flexors has been proposed to explain gait and balance disturbances).[19] On the same line, robot-assisted gait training may exert a proprioceptive cueing effect by providing an external rhythm that could compensate for the defective internal rhythm of the basal ganglia (rhythmic cues have been found to improve gait and balance skills in patients with PD).[39] In addition, the intensive lower-body muscles training together with the cardiovascular fitness given by robot-assisted gait training has to be considered.[40]

Limitations of the study

This systematic review was conducted according to the methodological indications given by the Promoter Committee and the Scientific Technical Committee of the Italian Consensus Conference on "Rehabilitation assisted by robotic and electromechanical devices for persons with disability of neurological origin" (CICERONE). Its main limitation is the absence of meta-analysis. Another limitation may be represented by the inclusion of all studies (not only randomized controlled trials). This was because a great part of evidence about the effects of robot-assisted gait training for treating postural instability in patients with PD comes from uncontrolled trials and case series/single cases. Thus, we decided to provide a complete overview of the literature.

Conclusions

This systematic review provides to the reader a complete overview of current literature and levels of evidence about the effects of robot-assisted gait training on postural instability issues (static and dynamic balance, freezing of gait, falls, confidence in activities of daily living and gait parameters related to balance skills) in patients with PD. Future studies are needed to overcome the limits of current literature reported in this review.

References

1. Kalia LV, Lang AE. Parkinson's disease. Lancet 2015;386:896–912.

2. Viseux FJ, Delval A, Defebvre L, Simoneau M. Postural instability in Parkinson's disease: review and bottom-up rehabilitative approaches. Neurophysiol Clin 2020;50:479–87.

3. Barone P, Erro R, Picillo M. Quality of life and nonmotor symptoms in Parkinson's disease. Int Rev Neurobiol 2017;133:499–516.

4. Bohnen NI, Cham R. Postural control, gait, and dopamine functions in parkinsonian movement disorders. Clin Geriatr Med 2006;22:797–812, vi.

5. Picelli A, Camin M, Tinazzi M, Vangelista A, Cosentino A, Fiaschi A, *et al.* Three-dimensional motion analysis of the effects of auditory cueing on gait pattern in patients with Parkinson's disease: a preliminary investigation. Neurol Sci 2010;31:423–30.

6. Abbruzzese G, Marchese R, Avanzino L, Pelosin E. Rehabilitation for Parkinson's disease: current outlook and future challenges. Parkinsonism Relat Disord 2016;22(Suppl 1):S60–4.

7. Xu X, Fu Z, Le W. Exercise and Parkinson's disease. Int Rev Neurobiol 2019;147:45–74.

8. Lei C, Sunzi K, Dai F, Liu X, Wang Y, Zhang B, *et al.* Effects of virtual reality rehabilitation training on gait and balance in patients with Parkinson's disease: A systematic review. PLoS One 2019;14:e0224819.

9. Santos P, Scaldaferri G, Santos L, Ribeiro N, Neto M, Melo A. 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 2019;44:569–77.

10. Radder DL, Sturkenboom IH, van Nimwegen M, Keus SH, Bloem BR, de Vries NM. Physical therapy and occupational therapy in Parkinson's disease. Int J Neurosci 2017;127:930–43.

11. Alves Da Rocha P, McClelland J, Morris ME. Complementary physical therapies for movement disorders in Parkinson's disease: a systematic review. Eur J Phys Rehabil Med 2015;51:693–704.

12. Tomlinson CL, Patel S, Meek C, Herd CP, Clarke CE, Stowe R, *et al.*

Physiotherapy versus placebo or no intervention in Parkinson's disease. Cochrane Database Syst Rev 2013;9:CD002817.

13. Tomlinson CL, Herd CP, Clarke CE, Meek C, Patel S, Stowe R, *et al.* Physiotherapy for Parkinson's disease: a comparison of techniques. Cochrane Database Syst Rev 2014;7:CD002815.

14. Alwardat M, Etoom M, Al Dajah S, Schirinzi T, Di Lazzaro G, Sinibaldi Salimei P, *et al.* Effectiveness of robot-assisted gait training on motor impairments in people with Parkinson's disease: a systematic review and meta-analysis. Int J Rehabil Res 2018;41:287–96.

15. Alwardat M, Etoom M. Effectiveness of robot-assisted gait training on freezing of gait in people with Parkinson disease: evidence from a literature review. J Exerc Rehabil 2019;15:187–92.

16. Picelli A, Tamburin S, Passuello M, Waldner A, Smania N. Robot-assisted arm training in patients with Parkinson's disease: a pilot study. J Neuroeng Rehabil 2014;11:28.

17. Picelli A, Melotti C, Origano F, Waldner A, Fiaschi A, Santilli V, *et al.* Robot-assisted gait training in patients with Parkinson disease: a randomized controlled trial. Neurorehabil Neural Repair 2012;26:353–61.

18. Picelli A, Melotti C, Origano F, Neri R, Waldner A, Smania N. Robot-assisted gait training versus equal intensity treadmill training in patients with mild to moderate Parkinson's disease: a randomized controlled trial. Parkinsonism Relat Disord 2013;19:605–10.

19. Toole T, Maitland CG, Warren E, Hubmann MF, Panton L. The effects of loading and unloading treadmill walking on balance, gait, fall risk, and daily function in Parkinsonism. NeuroRehabilitation 2005;20:307–22.

20. Picelli A, Melotti C, Origano F, Waldner A, Gimigliano R, Smania N. Does robotic gait training improve balance in Parkinson's disease? A randomized controlled trial. Parkinsonism Relat Disord 2012;18:990–3.

21. Moher D, Liberati A, Tetzlaff J, Altman DG. PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. PLoS Med 2009;6:1000097.

22. de Morton NA. The PEDro scale is a valid measure of the methodological quality of clinical trials: a demographic study. Aust J Physiother 2009;55:129–33.

23. Hariohm K, Prakash V, Saravankumar J. Quantity and quality of randomized controlled trials published by Indian physiotherapists. Perspect Clin Res 2015;6:91–7.

24. Lo AC, Chang VC, Gianfrancesco MA, Friedman JH, Patterson TS, Benedicto DF. Reduction of freezing of gait in Parkinson's disease by repetitive robot-assisted treadmill training: a pilot study. J Neuroeng Rehabil 2010;7:51.

25. Ustinova K, Chernikova L, Bilimenko A, Telenkov A, Epstein N. Effect of robotic locomotor training in an individual with Parkinson's disease: a case report. Disabil Rehabil Assist Technol 2011;6:77–85.

26. Carda S, Invernizzi M, Baricich A, Comi C, Croquelois A, Cisari C. Robotic gait training is not superior to conventional treadmill training in parkinson disease: a single-blind randomized controlled trial. Neurorehabil Neural Repair 2012;26:1027–34.

27. Paker N, Bugdayci D, Goksenoglu G, Sen A, Kesiktas N. Effects of robotic treadmill training on functional mobility, walking capacity, motor symptoms and quality of life in ambulatory patients with Parkinson's disease: a preliminary prospective longitudinal study. NeuroRehabilitation 2013;33:323–8.

28. Barbe MT, Cepuran F, Amarell M, Schoenau E, Timmermann L. Long-term effect of robot-assisted treadmill walking reduces freezing of gait in Parkinson's disease patients: a pilot study. J Neurol 2013;260:296–8.

29. Nardo A, Anasetti F, Servello D, Porta M. Quantitative gait analysis in patients with Parkinson treated with deep brain stimulation: the effects of a robotic gait training. NeuroRehabilitation 2014;35:779–88.

30. Pilleri M, Weis L, Zabeo L, Koutsikos K, Biundo R, Facchini S, *et al.* Overground robot assisted gait trainer for the treatment of drug-resistant freezing of gait in Parkinson disease. J Neurol Sci 2015;355:75–8.

31. Furnari A, Calabrò RS, De Cola MC, Bartolo M, Castelli A, Mapelli A, *et al.* Robotic-assisted gait training in Parkinson's disease: a three-month follow-up randomized clinical trial. Int J Neurosci 2017;127:996–1004.

32. Yun SJ, Lee HH, Lee WH, Lee SH, Oh BM, Seo HG. Effect of robot-assisted gait training on gait automaticity in Parkinson disease: A prospective, open-label, single-arm, pilot study. Medicine (Baltimore) 2021;100:e24348.

33. Sale P, De Pandis MF, Le Pera D, Sova I, Cimolin V, Ancillao A, *et al.* Robot-assisted walking training for individuals with Parkinson's disease: a pilot randomized controlled trial. BMC Neurol 2013;13:50.

34. Picelli A, Melotti C, Origano F, Neri R, Verzè E, Gandolfi M, *et al.* Robot-assisted gait training is not superior to balance training for improving postural instability in patients with mild to moderate Parkinson's disease: a single-blind randomized controlled trial. Clin Rehabil 2015;29:339–47.

35. Galli M, Cimolin V, De Pandis MF, Le Pera D, Sova I, Albertini G, *et al.* Robot-assisted gait training versus treadmill training in patients with Parkinson's disease: a kinematic evaluation with gait profile score. Funct Neurol 2016;31:163–70.

36. Capecci M, Pournajaf S, Galafate D, Sale P, Le Pera D, Goffredo M, *et al.* Clinical effects of robot-assisted gait training and treadmill training for Parkinson's disease. A randomized controlled trial. Ann Phys Rehabil Med 2019;62:303–12.

37. Lu C, Lu T, Ge L, Yang N, Yan P, Yang K. Use of AMSTAR-2 in the methodological assessment of systematic reviews: protocol for a methodological study. Ann Transl Med 2020;8:652.

38. Oxford Centre for Evidence-Based Medicine 2011 Levels of Evidence. CEBM; [Internet]. Available from: https://www.cebm.net/wp-content/uploads/2014/06/CEBM-Levels-of-Evidence-2.1.pdf [cited 2021, Feb 27].

39. Nieuwboer A, Kwakkel G, Rochester L, Jones D, van Wegen E, Willems AM, *et al.* Cueing training in the home improves gait-related mobility in Parkinson's disease: the RESCUE trial. J Neurol Neurosurg Psychiatry 2007;78:134–40.

40. Toole T, Park S, Hirsch MA, Lehman DA, Maitland CG. The multicomponent nature of equilibrium in persons with parkinsonism: a regression approach. J Neural Transm (Vienna) 1996;103:561–80.

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