

Physiotherapy for freezing of gait in Parkinson's disease: a systematic review and meta-analysis

Kyle J. Miller, David Suárez-Iglesias, Manuel Seijo-Martínez, Carlos Ayán

Introduction. Freezing of gait (FOG) is one of the most severe symptoms associated with Parkinson's disease (PD). Physiotherapy treatment could be an effective strategy for treating FOG, but no systematic review has been carried out in this regard.

Aim. To identify the characteristics, methodological quality, and main outcomes of the studies that have analyzed the effects of physiotherapy interventions in FOG up to date, by performing a systematic review and a meta-analysis.

Patients and methods. Four electronic databases were searched in order to find randomized controlled trials that provided information regarding the effects of any kind of physiotherapy treatment on FOG. The methodological quality of the included investigations was assessed by means of the PEDro scale.

Results. Twelve studies were identified for inclusion into the qualitative analysis, with four randomized controlled trials included in the final meta-analysis. The quality of the trials was generally good. Those physiotherapy modalities including cues were more effective for treating FOG than traditional physiotherapy approaches. The meta-analysis indicated that physiotherapy interventions had a significantly greater impact on FOG than control comparisons.

Conclusions. Physiotherapy treatment, especially those modalities including visual and auditory cueing, should be prescribed to PD patients with FOG. Future studies including PD patients with cognitive impairment and FOG objective measurement tools are needed to complete the existing scientific evidence.

Key words. Cueing. Exercise. Freezing of gait. Parkinson's disease. Physiotherapy. Systematic review.

Introduction

Freezing of gait (FOG) is a disabling episodic motor phenomenon of Parkinson's disease (PD) that affects gait, movement and speech, and can be present in up to 80% of patients [1]. Usually described as a brief episodic absence or marked reduction in forward progression of the feet despite the intention to walk [2], FOG remains a challenging PD symptom with a complex pathophysiology and a poorly understood onset [3].

Treatment of FOG is perceived by clinicians as very challenging, as the existing evidence regarding the efficacy of actual pharmacological and surgical treatment approaches are inconclusive [4]. Given the limited options for successful treatment, non-pharmacological alternatives such as physiotherapy interventions have been considered in the rehabilitation of FOG [5].

Physiotherapy treatment for PD is aimed at optimizing patient independence and is based on transfers, posture, upper limb function, balance, gait, physical capacity and (in)activity employing cueing strategies, cognitive movement strategies and exercise [6]. Scientific evidence has shown that physio-

therapy interventions can be effective for improving several PD symptoms through different movement rehabilitation approaches such as dancing, water exercises or robotic gait training [7] or virtual reality [8]. As a consequence of the increasing scientific evidence on the effects of physiotherapy interventions on PD, clinicians are more inclined to suggest it as a rehabilitation option for their patients [6].

However, before recommending physiotherapy interventions for the treatment of FOG in PD, health and rehabilitation professionals should be able to identify the methodological quality and main outcomes reported by the existing research that has focused on this issue. This goal can be achieved by conducting a systematic review and meta-analysis that synthesizes and summarizes the scientific evidence concerning the efficacy of physiotherapy treatment on FOG. However, to the very best of the authors' knowledge, no study of this kind has been carried out so far.

In the light of all this, the purpose of this study was to perform a systematic review and meta-analysis aimed at identifying the characteristics, methodological quality, and main outcomes of the stud-

School of Health and Life Sciences; Federation University; Ballarat, Victoria, Australia (K.J. Miller). VALFIS Research Group; Institute of Biomedicine, IBIOMED; Faculty of Physical Activity and Sports Sciences; Department of Physical Education and Sport; University of León; León, Spain (D. Suárez-Iglesias). Department of Neurology; Complejo Hospitalario Pontevedra-Salnés; Pontevedra, Spain (M. Seijo-Martínez). Well-Move Research Group; Faculty of Education and Sport Science; Department of Special Didactics; University of Vigo; Vigo, Pontevedra, Spain (C. Ayán).

Corresponding author:

Dr. David Suárez-Iglesias. Facultad de Ciencias de la Actividad Física y del Deporte. Universidad de León. Campus de Vegazana, s/n. E-24071 León (Spain).

E-mail:

dsuai@unileon.es

Accepted:

10.12.19.

How to cite this paper:

Miller KJ, Suárez-Iglesias D, Seijo-Martínez M, Ayán C. Physiotherapy for freezing of gait in Parkinson's disease: a systematic review and meta-analysis. *Rev Neurol* 2020; 70: 161-70. doi: 10.33588/rn.7005.2019417.

Versión española disponible en www.neurologia.com

© 2020 Revista de Neurología

ies that have analyzed the effects of physiotherapy interventions in FOG up to date.

Patients and methods

This systematic review was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [9]. The selected search strategy and methods of analysis were registered in the PROSPERO database (ref: CRD42018086543).

Search strategy

Four electronic databases (Medline/PubMed, PEDro, SPORTDiscus, and Scopus) were searched systematically from their inception until April 2019. The following search terms, Boolean operators, and combinations were used: '*physical therapy*' OR '*exercise*' OR '*rehabilitation*' AND '*freezing of gait*'. It should be noted that after a general screening using first the term '*physiotherapy*', and then the term '*physical therapy*', it was decided the subsequent use of the term '*physical therapy*' for the purpose of this review due to a larger number of results produced in the databases.

Eligibility criteria

Randomized controlled trials (RCTs) that provided information regarding the effects of any kind of physiotherapy treatment on FOG were considered eligible. For the purpose of this review, standard physiotherapy, physical exercise, treadmill training, cueing, dance and martial arts, were considered as physiotherapy interventions, following previous procedures in this regard [6].

Investigations were excluded if: a) physiotherapy treatment was performed in combination with other treatment options; b) the study included non-freezing PD patients, unless separate data were available for the freezing subgroup; and c) the research was not written in English or Spanish.

Study selection

Two authors screened the titles and abstracts of the identified studies for eligibility. After independently reviewing the selected studies for inclusion, these were compared by both authors to reach an agreement. Once the agreement had been reached, a full-text copy of every potentially relevant study was obtained. If it was unclear whether the study met

the selection criteria, advice was sought from a third author and a consensus was reached.

Data extraction

Information on the participants' characteristics, physiotherapy treatment program, adverse events, attrition, and outcomes were extracted from the original reports by one researcher and checked by a second investigator. Missing data were obtained from the study authors, whenever possible.

Quality assessment

The methodological quality of the selected RCTs was directly retrieved from the Physiotherapy Evidence Database (PEDro). The quality appraisal of those RCTs not rated in PEDro was performed by two authors independently with discrepancies in ratings arbitrated by a third author.

The suggested cut-off points to categorize studies by quality were excellent (9-10), good (6-8), fair (4-5), and poor (≤ 3) [10].

Data synthesis

Data were analyzed using Stata software v. 15.1 [11]. Studies were only included in the meta-analysis if they included both a physiotherapy treatment group and control group without any physiotherapy treatment component. The meta-analysis was performed provided that the same outcomes had been assessed in at least two RCTs in a comparable way, and pre and post data were presented for the control and physiotherapy treatment groups [12]. A fixed effect model and a random-effects model were used to calculate pooled effect sizes estimates. Standardized mean differences (SMD) and 95% confidence intervals (95% CIs) were used to assess the difference in change between the physiotherapy intervention and control group using baseline and post-treatment sample sizes, means \pm standard deviations for FOG scores.

Heterogeneity in the model was assessed using the I^2 statistic and corresponding p -value. The SMD was significant when the 95% CIs excluded zero and interpreted according to Cohen [13], whereby the effect was considered small (0.2), medium (0.5) or large (0.8). Positive effect size estimates were indicative of the physiotherapy treatment group having a greater post-treatment effect on FOG scores, whereas negative values favour the control group. The significance level was $p < 0.05$ for all analyses.

Results

Search strategy

The initial literature search yielded a total of 83 eligible records after duplicates were removed ($n = 64$). Titles and abstracts were screened independently by two authors and 38 relevant full-text articles were assessed for inclusion criteria. Twelve studies were identified for inclusion into the qualitative analysis, with five RCTs identified for inclusion into the meta-analysis. Sufficient effect size data was not available for one RCT [14], so it was consequently excluded from the meta-analysis. The remaining four RCTs were included in the final meta-analysis [15-18] (Fig. 1).

Studies characteristics

All studies included PD patients with a mean age of 68.88 years (range: 61.6-81.4 years). Five of the studies were RCTs comparing a physiotherapy intervention to a control group [14-18], and seven studies were randomized trials comparing two physiotherapy interventions without a control group [19-25]. A full description of study characteristics can be found in table I.

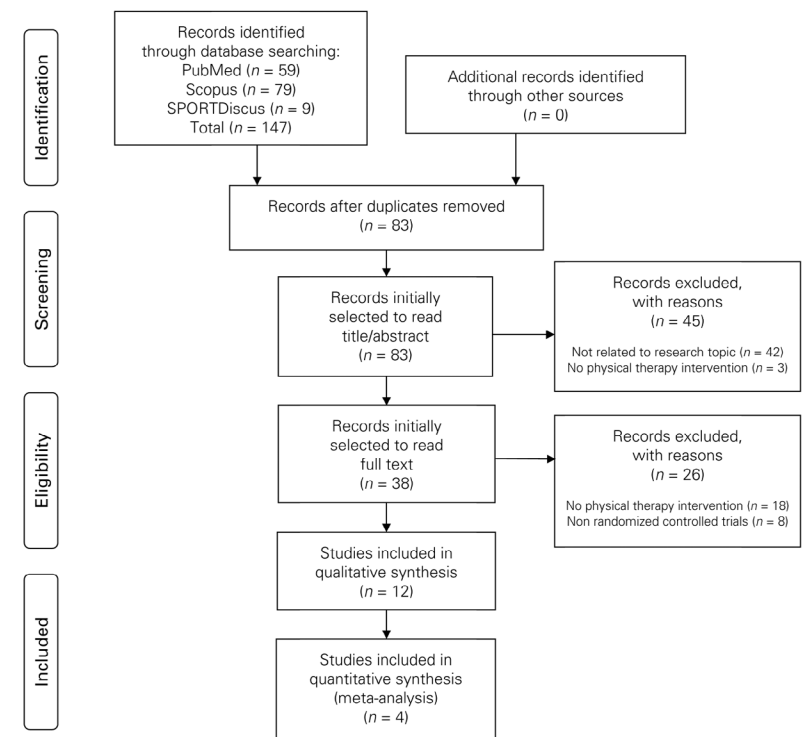
Absence of cognitive impairment was established as an inclusion criterion in nine studies [14,15,18-20,22-25]. The three remaining studies did not report any information on cognitive functioning [16, 17,21]. The length of interventions lasted between two weeks and 12 months, with sessions lasting 20-90 minutes each. No adverse events were reported in any studies and the attrition rate was 10.81% across all studies. Six studies reported adherence rates ranging from 70-100%, with an average adherence rate of 86.18%.

Five intervention conditions included strengthening exercises incorporating flexibility and/or balance [15,18,19,21,23], four included dancing [16,21, 22,24], two included aquatic exercise [14,25], two included walking exercises [19,20], two included physiotherapy [17,24], and one included general rehabilitation [20].

Results of individual studies

The effects of the proposed interventions on FOG were assessed by means of the Freezing of Gait Questionnaire (FOG-Q) in all analyzed studies. For the studies that reported intragroup (pre-post) differences, significant post-treatment improvements in FOG scores were observed for both walking in-

Figure 1. Flow chart of the review process. Flow diagram depicting the subsequent stages of searching for relevant reports, abstract screening the reports for potential candidates, and assessing the full-texts of those reports to select the studies that comply with the pre-defined inclusion criteria. The reasons for exclusion are stated.



terventions [19,20] and the general rehabilitation intervention [20]. Significant improvements were observed for two out of four dancing interventions [22,24] and only one out of five strengthening interventions [18]. No intragroup differences were observed for physiotherapy interventions [24].

Intergroup differences were also found in randomized trials comparing two physiotherapy interventions without a control group. Curved walking was significantly more effective than general exercises [19]. Treadmill walking with general rehabilitation was significantly more effective than general rehabilitation alone [20]. Irish set dancing was significantly more effective than standard physiotherapy [24]. Obstacle aquatic therapy was significantly more effective than general aquatic therapy [25]. Conversely, lower limb muscle strength exercises and static and dynamic postural control tasks were not significantly different [23]. Argentine tango and mixed-genre therapeutic dance were also not significantly different, although only the mixed-genre

Table 1. Characteristics of the studies included in the systematic review.

	Participants	Intervention and control groups	Responsive outcomes	FOG scores	FOG differences
Zhu et al [25]	IG (1): $n = 23$ (67 ± 5 years) IG (2): $n = 23$ (65 ± 6 years) Inclusion criteria: idiopathic PD; Hoehn and Yahr stages II-III; stable medication for over 2 weeks; ability to walk independently; ability to stand at least 20 min unassisted; no physical therapy conducted over the past 6 months MMSE: minimum score >24	Length: 6 weeks IG (1): 30 min of aquatic therapy five times per week IG (2): 30 min of obstacle aquatic therapy five times per week	Recruitment: 90.2% (46 out of 51) Attrition rate: IG (1): 0.0% (23 to 23) IG (2): 0.0% (23 to 23) Adherence rate: IG (1): NR IG (2): NR Adverse events: none	Pre-test: IG (1): 11.7 ± 3.6 IG (2): 12.3 ± 3.9 Post-test: IG (1): 8.7 ± 3.3 IG (2): 6.2 ± 2.1	Intergroup difference: Post IG (1) vs. Post IG (2) ^e Intragroup differences: Pre IG (1) vs. Post IG (1) (NR) Pre IG (2) vs. Post IG (2) (NR)
Cheng et al [19]	IG (1): $n = 12$ (65.8 ± 11.5 years) IG (2): $n = 12$ (67.3 ± 6.4 years) Inclusion criteria: idiopathic PD; Hoehn and Yahr stages I-III; stable medication; history of other serious medical conditions MMSE: NR (IG = 27.7 ± 1.3 ; CG = 28.1 ± 1.1)	Length: 4-6 weeks IG (1): 30 min of curved walking training for 12 sessions IG (2): 30 min of general exercises for 12 sessions	Recruitment: 75% (24 out of 32) Attrition rate: IG (1): 0% (12 to 12) IG (2): 0% (12 to 12) Adherence rate: IG (1): 100% IG (2): 100% Adverse events: muscle soreness ($n = 2$)	Pre-test: IG (1): 11.8 ± 4.7 IG (2): 10.6 ± 5.6 Post-test: IG (1): 7.8 ± 4 IG (2): 10.3 ± 5.9	Intergroup difference: Post IG (1) ^c vs. Post IG (2) Intragroup differences: Pre IG (1) vs. Post IG (1) ^d Pre IG (2) vs. Post IG (2) (NS)
Rocha et al [22]	IG (1): $n = 10$ (70.2 ± 5.5 years) IG (2): $n = 11$ (72.9 ± 5.5 years) Inclusion criteria: idiopathic PD; Hoehn and Yahr stages I-IV; ability to stand for at least 2 min; ability to walk independently for more than 3 m MMSE: minimum score >24 (IG = 29.3 ± 1.0 ; CG = 29.2 ± 0.8)	Length: 8 weeks IG (1): 60 min of in-person Argentine tango once per week, as well as 40 min of self-managed home dance program once per week IG (2): 60 min of in-person mixed-genre therapeutic dance once per week, as well as 40 min of self-managed home dance program once per week	Recruitment: 50% (21 out of 42) Attrition rate: IG (1): 20% (10 to 8) IG (2): 9.1% (11 to 10) Adherence rate: IG (1): 70% IG (2): 78.4% Adverse events: none	Pre-test: IG (1): 9.5 ± 6.7 IG (2): 7.8 ± 6.4 Post-test: IG (1): 6.9 ± 6.7 IG (2): 5.3 ± 4.9	Intergroup difference: Post IG (1) vs. Post IG (2) (NS) Intragroup differences: Pre IG (1) vs. Post IG (1) (NS) Pre IG (2) vs. Post IG (2) ^c
Volpe et al [24]	IG (1): $n = 12$ (61.6 ± 4.5 years) IG (2): $n = 12$ (65.0 ± 5.3 years) Inclusion criteria: mild to moderate Idiopathic PD; Hoehn and Yahr stage less than III MMSE: score range = 24-29 (IG = 26.5 ± 1.4 ; CG = 26.3 ± 1.8)	Length: 6 months IG (1): 90 min of Irish set dancing once a week IG (2): 90 min of standard physiotherapy exercises once a week	Recruitment: NR Attrition rate: IG (1): 0% (12 to 12) IG (2): 0% (12 to 12) Adherence rate: IG (1): 90.9% IG (2): 87.8% Adverse events: non-injurious falls ($n = 1$)	Pre-test: IG (1): 11.4 ± 2.8 IG (2): 10.8 ± 3.4 Post-test: IG (1): 4.9 ± 2.1 IG (2): 10.2 ± 4.5	Intergroup difference: Post IG (1) ^e vs. Post IG (2) Intragroup differences: Pre IG (1) vs. Post IG (1) ^d Pre IG (2) vs. Post IG (2) (NS)
Schlenstedt et al [23]	IG (1): $n = 12$ (78.3 ± 5.8 years) IG (2): $n = 8$ (81.4 ± 7.3 years) Inclusion criteria: idiopathic PD; stable medication; no participation in previous exercise treatment MMSE: NR (IG = 27.4 ± 3.7 ; CG = 26.2 ± 4.0)	Length: 7 weeks IG (1): 60 min of lower limb muscle strength exercises twice per week IG (2): 60 min of static and dynamic postural control tasks twice per week	Recruitment: NR Attrition rate: IG (1): 0% (12 to 12) IG (2): 0% (8 to 8) Adherence rate: IG (1): NR IG (2): NR Adverse events: NR	Pre-test: IG (1): 6.6 ± 7.2 IG (2): 5.9 ± 4.4 Post-test: IG (1): 6.9 ± 9.1 IG (2): 8.7 ± 5.1	Intergroup difference: Post IG (1) vs. Post IG (2) (NS) Intragroup differences: Pre IG (1) vs. Post IG (1) (NS) Pre IG (2) vs. Post IG (2) (NS)
Hackney et al [21]	IG (1): $n = 9$ (72.6 ± 2.2 years) IG (2): $n = 10$ (69.6 ± 2.1 years) Inclusion criteria: idiopathic PD; stable medication MMSE: NR	Length: 13 weeks IG (1): 1 h of progressive tango dance lessons for 20 sessions IG (2): 1 h of structured strength/flexibility exercise classes for 20 sessions	Recruitment: NR Attrition rate: IG(1): 0.0% (9 to 9) IG(2): 0.0% (10 to 10) Adherence rate: IG(1): 100% IG(2): 100% Adverse events: NR	Pre-test: IG (1): 8.4 ± 0.6 IG (2): 7.9 ± 0.5 Post-test: IG (1): 7.4 ± 0.6 IG (2): 6.5 ± 0.5	Intergroup difference: Post IG (1) vs. Post IG (2) (NR) Intragroup differences: Pre IG (1) vs. Post IG (1) (NS) Pre IG (2) vs. Post IG (2) (NS)

Table I. Characteristics of the studies included in the systematic review (cont.).

	Participants	Responsive outcomes	Resultados sensibles	FOG scores	FOG differences
Frazzitta et al [20]	IG (1): $n = 20$ (71 ± 8 years) IG (2): $n = 20$ (71 ± 7 years) Inclusion criteria: idiopathic PD; Hoehn and Yahr stage III; stable medication; ability to walk without any physical assistance; FOG at the time of peak medication effect MMSE: minimum score > 26	Length: 4 weeks IG (1): 20 min of treadmill training associated with auditory and visual cues every day IG (2): 20 min of rehabilitation including auditory and visual cues every day	Recruitment: NR Attrition rate: IG (1): 0% (20 to 20) IG (2): 0% (20 to 20) Adherence rate: IG (1): NR IG (2): NR Adverse events: NR	Pre-test: IG (1): 11.6 ± 3 IG (2): 11.4 ± 2.4 Post-test: IG (1): 6.5 ± 1.9 IG (2): 7.7 ± 1.8	Intergroup difference: Post IG (1) ^d vs. Post IG (2) Intragroup differences: Pre IG (1) vs. Post IG (1) ^e Pre IG (2) vs. Post IG (2) ^e
Allen et al [15] ^a	IG: $n = 24$ (66 ± 10 years) CG: $n = 24$ (68 ± 7 years) Inclusion criteria: idiopathic PD; stable medication for over 2 weeks; ability to walk independently; aged 30-80; fallen or at risk of falling MMSE: minimum score > 24 (IG = 29 ± 1 ; CG = 29 ± 1)	Length: 6 months IG: 40-60 min of progressive lower limb strengthening and balance exercises three times per week CG: usual care	Recruitment: 54.4% (48 out of 92) Attrition rate: IG: 12.5% (24 to 21) CG: 0% (24 to 24) IG adherence rate: 70% Adverse events: none	Pre-test: IG: 6.8 ± 5.1 CG: 8.3 ± 5.8 Post-test: IG: 5.5 ± 5.9 CG: 9.4 ± 6.2	Intergroup difference: Post IG ^c vs. Post CG Intragroup differences: Pre IG vs. Post IG (NR) Pre CG vs. Post CG (NR)
Duncan et al [16] ^a	IG: $n = 32$ (63.3 ± 1.9 years) CG: $n = 30$ (69.0 ± 1.5 years) Inclusion criteria: PD; Hoehn and Yahr stages I-IV; history of other serious medical conditions MMSE: NR	Length: 12 months IG: 1 h of community-based Argentine tango classes twice per week CG: usual care	Recruitment: 50.4% (62 out of 123) Attrition rate: IG: 50% (32 to 16) CG: 36.7% (30 to 19) IG adherence rate: 78.5% Adverse events: NR	Pre-test: IG: 6.1 ± 5.1 CG: 4.6 ± 4.6 Post-test: IG: 5.7 ± 5 CG: 6.5 ± 6	Intergroup difference: Post IG ^d vs. Post CG Intragroup differences: Pre IG vs. Post IG (NR) Pre CG vs. Post CG (NR)
Fietzek et al [17] ^a	IG: $n = 14$ (69.8 ± 6.5 years) CG: $n = 9$ (64.2 ± 5.9 years) Inclusion criteria: PD; Hoehn and Yahr stages I-IV; a gait disorder with freezing; ability to walk independently outside the house MMSE: NR	Length: 2 weeks IG: 30 min of repetitive physiotherapy exercises with cueing and movement strategies three times per week CG: delayed treatment	Recruitment: 43.4% (23 out of 53) Attrition rate: IG: 0% (14 to 14) CG: 22.2% (9 to 7) IG adherence rate: NR Adverse events: NR	Pre-test: IG: 13.5 ± 3.7 CG: 15.6 ± 2.4 Post-test: IG: 11.7 ± 3.6 CG: 15 ± 2.3	Intergroup difference: Post IG ^d vs. Post CG Intragroup differences: Pre IG vs. Post IG (NR) Pre CG vs. Post CG (NR)
Carroll et al [14]	IG: $n = 11$ (69.5 years) CG: $n = 10$ (74 years) Inclusion criteria: idiopathic PD; Hoehn and Yahr stages I-III; stable medication over 3 months; ability to walk 10 m three times without assistance MMSE: minimum score > 24	Length: 6 weeks IG: 45 min of aquatic exercise therapy twice per week CG: usual care	Recruitment: 42% (21 out of 50) Attrition rate: IG: 9.1% (11 to 10) CG: 20% (10 to 8) IG adherence rate: NR Adverse events: none	Pre-test: IG: 5.5 (3.75-8.25) ^b CG: 5.0 (2.25-13) ^b Post-test: IG: 3.5 (1-9) ^b CG: 6.5 (3.5-12.75) ^b	Intergroup difference: Post IG vs. Post CG (NS) Intragroup differences: Pre IG vs. Post IG (NR) Pre CG vs. Post CG (NR)
Santos et al [18] ^a	IG: $n = 11$ (73.1 ± 9.8 years) CG: $n = 11$ (78.1 ± 5.2 years) Inclusion criteria: idiopathic PD; Hoehn and Yahr stages I-III; stable medication; ability to stand on two feet for at least 2 min; ability to walk at least 10 m without assistance; no neurological disease MMSE: mean score > 24	Length: 6 weeks IG: 23 min of balance training using a slackline twice per week CG: control group	Recruitment: NR Attrition rate: IG: 9.1% (11 to 10) CG: 9.1% (11 to 10) IG adherence rate: NR Adverse events: NR	Pre-test: IG: 3.9 ± 3.6 CG: 4.4 ± 6.2 Post-test: IG: 2.9 ± 3.7 CG: 4.8 ± 6.5	Intergroup difference: Post IG vs. Post CG (NR) Intragroup differences: Pre IG vs. Post IG ^c Pre CG vs. Post CG (NS)

Statistics are reported as means \pm standard deviations unless otherwise specified. CG: control group; FOG: freezing of gait; IG: intervention group; MMSE: Mini-Mental State Examination; NR: not reported; NS: non-significant; PD: Parkinson's disease. ^a Studies included in the meta-analysis; ^b Values are reported as median (interquartile range); ^c $p < 0.05$; ^d $p < 0.01$; ^e $p < 0.001$.

Table II. Quality assessment (PEDro scale).

	1 ^b	2	3	4	5	6	7	8	9	10	11	Total
Allen et al [15] ^a	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	8/10
Duncan et al [16] ^a	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	8/10
Zhu et al [25]	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	8/10
Fietzek et al [17] ^a	Yes	Yes	Yes	Yes	No	No	Yes	Yes	No	Yes	Yes	7/10
Carroll et al [14]	Yes	Yes	Yes	Yes	No	No	No	Yes	Yes	Yes	Yes	7/10
Cheng et al [19]	Yes	Yes	Yes	Yes	No	No	Yes	Yes	No	Yes	Yes	7/10
Rocha et al [22]	Yes	Yes	No	Yes	No	No	Yes	Yes	Yes	Yes	Yes	7/10
Volpe et al [24]	Yes	Yes	Yes	Yes	No	No	Yes	No	No	Yes	Yes	6/10
Schlenstedt et al [23]	Yes	Yes	No	Yes	No	No	Yes	Yes	No	Yes	Yes	6/10
Hackney et al [21]	Yes	Yes	No	Yes	No	No	Yes	No	No	Yes	Yes	5/10
Frazzitta et al [20]	Yes	Yes	No	Yes	No	No	No	Yes	No	Yes	Yes	5/10
Santos et al [18] ^a	Yes	Yes	No	No	No	No	No	Yes	No	Yes	Yes	4/10

^a Studies included in the meta-analysis; ^b Not included in total score.

therapeutic dance showed a significant difference from baseline [21].

For the five RCTs comparing a physiotherapy intervention to a control group, significant intergroup differences were found in three studies, including interventions using strengthening exercises [15], dancing [16], and physiotherapy [17]. This indicates that these intervention groups reported significantly greater improvements in FOG-Q scores than their control counterparts. Another study [18] did not report statistics for intergroup differences, however trends indicated that FOG-Q scores improved in the balance training group and worsened in the control group. The final study used aquatic exercise therapy [14] and did not find a significant difference between intervention and control groups.

Quality assessment

The methodological quality of the included studies can be found in table II. The obtained average score was 6.5 out of 10, with 75% of the studies reporting good to excellent quality ($\geq 6/10$). For the four RCTs included in the meta-analysis, three [15-17] were higher quality ($\geq 7/10$) and one [18] was fair quality (4/10).

Results of the meta-analysis

Data from a total of 138 (71 intervention and 67 control) participants across four RCTs were included in the meta-analysis. Egger's regression test [26] indicated the absence of publication bias (bias: -0.60 ; $p = 0.171$). No heterogeneity was observed in the model ($I^2 = 0.0\%$; $p = 0.992$). A forest plot reporting the SMD and 95% CI for each effect size can be found in figure 2. Pooled effect size estimates showed a significant difference in FOG-Q scores, with a pooled SMD = 0.38 (95% CI = $0.04-0.72$). This indicated that physiotherapy interventions had a significantly greater improvement on FOG-Q scores than control comparisons.

Discussion

In the field of evidence-based medicine, it is considered that the highest level of scientific evidence on an issue is achieved through systematic reviews based on the inclusion and detailed analysis of published RCTs [27]. Therefore, in this report, we examined and critically reviewed the scientific evidence regarding the effectiveness of the current physio-

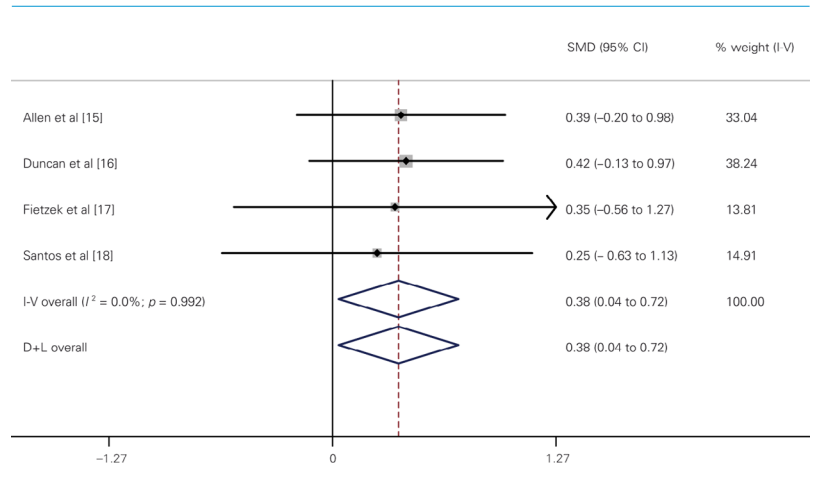
therapy interventions available for treating FOG, by analyzing the methodological quality and main outcomes of the RCTs published up to date. Judging from the number of reports located and considering their methodological quality, it seems that the information provided in the present review could be of interest for the prescription of physiotherapy interventions as part of the FOG treatment process.

An important finding was that, in general, traditional physiotherapy treatment modalities do not seem to be effective for the treatment of FOG. The analyzed studies showed that general exercises, standard physiotherapy, strengthening training, aquatic, and postural control activities do not result in significant changes on the FOG-Q score. On the contrary, using strategies such as adding visual or auditory cues to standard physiotherapy treatment modalities (i.e. treadmill walking), as well as using new therapy approaches that challenge the patient's mobility (i.e. curved walking, obstacle course, slack-line), lead to significant improvements on self-reported FOG.

Visual cues appear to act mainly on FOG motor blocks and the ability to maintain an effective scaling of motor amplitude which are crucial in gait initiation; auditory cues act upon the FOG motor rhythm generation, helping to maintain and reduce asymmetry during turning [28]. The complexity of FOG, the interaction and participation of executive, visuospatial and other cognitive functions reinforces the idea that tailored cueing adapted for individual needs may yield the best results in stabilizing gait in those who experience FOG [2].

People with PD face many barriers to exercise, such as lack motivation, fatigue, and low expectations, among others [29,30]. In this regard, dancing has been proposed as an interesting physiotherapy treatment alternative, since it is a motivating activity that has been shown to have beneficial effects on several PD symptoms [31]. Indeed, dance has potential as a recreational activity for treating FOG since it promotes visual and auditory stimuli [32]. However, the results of this review only partially support the idea of prescribing dancing as a rehabilitation therapy for people with FOG, since the beneficial effects of dancing programs are not universal. It should be noted that the two investigations that did not observe significant changes on the FOG-Q scores included interventions that only lasted a few weeks. On the contrary, the remaining two studies had a much longer intervention and found that dancing did have beneficial effects on FOG. These findings appear to imply that when proposing dancing as rehabilitation strategy for

Figure 2. Forest plot of individual and pooled effect size estimates. 95% CI: 95% confidence interval; SMD: standardized mean differences.



FOG, long-lasting interventions could have greater effects.

In an evidence-based approach to the evaluation of effectiveness, meta-analysis of RCTs generates the highest level of evidence. According to the results of the meta-analysis carried out in this research, physiotherapy interventions had a significantly greater improvement on FOG-Q scores than control comparisons. This is an important revelation, since lack of informational support provided by neurologists as well as lack of referral to physiotherapy services has been identified as important factors that discourage PD patients from taking part in exercise programs [33]. Therefore, these results can be considered by neurologists and rehabilitation professionals to encourage people with FOG to take part in physiotherapy treatment programs.

In spite of the apparently beneficial effects of some of the physiotherapy interventions reviewed here, there are two factors that should be taken into account when interpreting the results of the present review. First, despite the existence of objective measurement tools, FOG was assessed in all the studies by means of a questionnaire. However, it has been suggested that further clinimetric work is required to determine the responsiveness and validity against objective measures of this assessment tool [34]. Moreover, since a unique methodological tool that encompasses the entire complexity of FOG is lacking, a combined examination has been suggested as the best approach for assessing FOG severity [35]. None of the authors followed these suggestions.

Second, it should be noted that diverse cognitive functions and mental/affective states appear to play a role in both the pathogenesis and precipitation of FOG episodes [36]. Since PD patients with lower cognitive functioning, especially executive functioning, may not be able to compensate for the attention directed towards cueing of stimuli [28], rehabilitation strategies should be adjusted in accordance with the cognitive profile of the patient. This demonstrates that PD patients with cognitive impairment represent an important target population for testing the efficacy of physiotherapy interventions on FOG. Despite this, most of the studies with positive effects on FOG included a sample that was made up of people without cognitive impairment. Therefore, evidence in support of the benefits of physiotherapy interventions on FOG in PD patients with cognitive impairment is still needed.

In closing, the findings of this review indicate that physiotherapy interventions, particularly those modalities that include visual or auditory cues, can lead to significant improvements on FOG. Nevertheless, the fact that the most of the participants included in the reviewed studies were free from cognitive impairment, as well as the lack of objective measurement tools for assessing the effects of physiotherapy treatment on FOG, constitute two important aspects that need to be considered to accurately interpret the data shown here. It should also be noted that blinding of participants and researchers was not possible in physiotherapy interventions, which reduced the overall quality of the included studies and may have increased the risk of performance bias. Finally, there are certain methodological limitations inherent to the review design, such as language restriction, possible publication bias, or not having reviewed grey literature, that should also be acknowledged.

Future studies including PD patients with cognitive impairment and FOG objective measurement tools are needed to complete the existing scientific evidence.

References

- Hely MA, Reid WGJ, Adena MA, Halliday GM, Morris JGL. The Sydney multicenter study of Parkinson's disease: the inevitability of dementia at 20 years. *Mov Disord* 2008; 23: 837-44.
- Ginis P, Nackaerts E, Nieuwboer A, Heremans E. Cueing for people with Parkinson's disease with freezing of gait: a narrative review of the state-of-the-art and novel perspectives. *Ann Phys Rehabil Med* 2018; 61: 407-13.
- Ehgoetz Martens KA, Lukasik EL, Georgiades MJ, Gilat M, Hall JM, Walton CC, et al. Predicting the onset of freezing of gait: a longitudinal study. *Mov Disord* 2018; 33: 128-35.
- Nonnekes J, Snijders AH, Nutt JG, Deuschl G, Giladi N, Bloem BR. Freezing of gait: a practical approach to management. *Lancet Neurol* 2015; 14: 768-78.
- Gilat M, Lúgia Silva de Lima A, Bloem BR, Shine JM, Nonnekes J, Lewis SJG. Freezing of gait: promising avenues for future treatment. *Parkinsonism Relat Disord* 2018; 52: 7-16.
- 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; 6: CD002815.
- 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.
- Morales-Gómez S, Elizagaray-García I, Yepes-Rojas O, De la Puente-Ranea L, Gil-Martínez A. Efectividad de los programas de inmersión virtual en los pacientes con enfermedad de Parkinson. Revisión sistemática. *Rev Neurol* 2018; 66: 69-80.
- Moher D, Shamseer L, Clarke M, Ghersi D, Liberati A, Petticrew M, et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Syst Rev* 2015; 4: 1.
- Foley NC, Teasell RW, Bhogal SK, Speechley MR. Stroke rehabilitation evidence-based review: methodology. *Top Stroke Rehabil* 2003; 10: 1-7.
- Stata Statistical Software: release 15. College Station, TX: Stata Corp. LLC; 2017.
- Valentine JC, Pigott TD, Rothstein HR. How many studies do you need?: a primer on statistical power for meta-analysis. *J Educ Behav Stat* 2010; 35: 215-47.
- Cohen J. *Statistical power analysis for the behavioral sciences*. 2 ed. Hillsdale, NJ: Lawrence Erlbaum Associates; 1988.
- Carroll LM, Volpe D, Morris ME, Saunders J, Clifford AM. Aquatic exercise therapy for people with Parkinson disease: a randomized controlled trial. *Arch Phys Med Rehabil* 2017; 98: 631-8.
- Allen NE, Canning CG, Sherrington C, Lord SR, Latt MD, Close JCT, et al. The effects of an exercise program on fall risk factors in people with Parkinson's disease: a randomized controlled trial. *Mov Disord* 2010; 25: 1217-25.
- Duncan RP, Earhart GM. Randomized controlled trial of community-based dancing to modify disease progression in Parkinson disease. *Neurorehabil Neural Repair* 2012; 26: 132-43.
- Fietzek UM, Schroeteler FE, Ziegler K, Zwosta J, Ceballos-Baumann AO. Randomized cross-over trial to investigate the efficacy of a two-week physiotherapy programme with repetitive exercises of cueing to reduce the severity of freezing of gait in patients with Parkinson's disease. *Clin Rehabil* 2014; 28: 902-11.
- Santos L, Fernández-Río J, Winge K, Barragán-Pérez B, Rodríguez-Pérez V, González-Díez V, et al. Effects of supervised slackline training on postural instability, freezing of gait, and falls efficacy in people with Parkinson's disease. *Disabil Rehabil* 2017; 39: 1573-80.
- Cheng FY, Yang YR, Wu YR, Cheng SJ, Wang RY. Effects of curved-walking training on curved-walking performance and freezing of gait in individuals with Parkinson's disease: a randomized controlled trial. *Parkinsonism Relat Disord* 2017; 43: 20-6.
- Frazzitta G, Maestri R, Uccellini D, Bertotti G, Abelli P. Rehabilitation treatment of gait in patients with Parkinson's disease with freezing: a comparison between two physical therapy protocols using visual and auditory cues with or without treadmill training. *Mov Disord* 2009; 24: 1139-43.
- Hackney ME, Kantorovich S, Levin R, Earhart GM. Effects of tango on functional mobility in Parkinson's disease: a preliminary study. *J Neurol Phys Ther* 2007; 31: 173-9.
- Rocha P, Aguiar L, McClelland JA, Morris ME. Dance therapy for Parkinson's disease: a randomised feasibility trial. *Int J Ther Rehabil* 2018; 25: 64-72.
- Schlenstedt C, Paschen S, Seuthe J, Raethjen J, Berg D, Maetzler W, et al. Moderate frequency resistance and balance training do not improve freezing of gait in Parkinson's disease: a pilot study. *Front Neurol* 2018; 9: 1084.
- Volpe D, Signorini M, Marchetto A, Lynch T, Morris ME. A comparison of Irish set dancing and exercises for people

- with Parkinson's disease: a phase II feasibility study. *BMC Geriatr* 2013; 13: 54.
25. Zhu Z, Yin M, Cui L, Zhang Y, Hou W, Li Y, et al. Aquatic obstacle training improves freezing of gait in Parkinson's disease patients: a randomized controlled trial. *Clin Rehabil* 2018; 32: 29-36.
 26. Egger M, Smith GD, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. *BMJ* 1997; 315: 629-34.
 27. Burns PB, Rohrich RJ, Chung KC. The levels of evidence and their role in evidence-based medicine. *Plast Reconstr Surg* 2011; 128: 305-10.
 28. Nieuwboer A. Cueing for freezing of gait in patients with Parkinson's disease: a rehabilitation perspective. *Mov Disord* 2008; 23 (Suppl 2): S475-81.
 29. Ellis T, Boudreau JK, DeAngelis TR, Brown LE, Cavanaugh JT, Earhart GM, et al. Barriers to exercise in people with Parkinson disease. *Phys Ther* 2013; 93: 628-36.
 30. Afshari M, Yang A, Bega D. Motivators and barriers to exercise in Parkinson's disease. *J Parkinsons Dis* 2017; 7: 703-11.
 31. Bognar S, DeFaria AM, O'Dwyer C, Pankiw E, Simic Bogler J, Teixeira S, et al. More than just dancing: experiences of people with Parkinson's disease in a therapeutic dance program. *Disabil Rehabil* 2017; 39: 1073-8.
 32. Dos Santos Delabary M, Komeroski IG, Monteiro EP, Costa RR, Haas AN. Effects of dance practice on functional mobility, motor symptoms and quality of life in people with Parkinson's disease: a systematic review with meta-analysis. *Aging Clin Exp Res* 2018; 30: 727-35.
 33. Khalil H, Nazzal M, Al-Sheyab N. Parkinson's disease in Jordan: barriers and motivators to exercise. *Physiother Theory Pract* 2016; 32: 509-19.
 34. Nieuwboer A, Rochester L, Herman T, Vandenberghe W, Emil GE, Thomaes T, et al. Reliability of the new freezing of gait questionnaire: agreement between patients with Parkinson's disease and their carers. *Gait Posture* 2009; 30: 459-63.
 35. Barthel C, Mallia E, Debù B, Bloem BR, Ferraye MU. The practicalities of assessing freezing of gait. *J Parkinsons Dis* 2016; 6: 667-74.
 36. Cancela JM, Nascimento CM, Varela S, Seijo-Martínez M, Lorenzo-López L, Millán-Calenti JC, et al. Influencia del deterioro cognitivo en la congelación de la marcha en pacientes con enfermedad de Parkinson sin demencia. *Rev Neurol* 2018; 66: 289-96.

Fisioterapia para la congelación de la marcha en la enfermedad de Parkinson: revisión sistemática y metaanálisis

Introducción. La congelación de la marcha (CDM) es uno de los síntomas más graves asociados con la enfermedad de Parkinson (EP). El tratamiento fisioterapéutico podría ser una estrategia efectiva para su tratamiento, pero no se ha realizado ninguna revisión sistemática al respecto.

Objetivo. Identificar las características, la calidad metodológica y los principales resultados de los estudios que han analizado los efectos de las intervenciones fisioterapéuticas en CDM hasta la fecha, mediante la realización de una revisión sistemática y un metaanálisis.

Pacientes y métodos. Se realizaron búsquedas en cuatro bases de datos electrónicas para encontrar ensayos controlados aleatorizados que proporcionaran información con respecto a los efectos de cualquier tipo de tratamiento fisioterapéutico sobre la CDM. La calidad metodológica de las investigaciones se evaluó mediante la escala PEDro.

Resultados. Se identificaron 12 estudios para su inclusión en el análisis cualitativo y cuatro ensayos controlados aleatorizados se incluyeron en el metaanálisis final. La calidad de los ensayos fue generalmente buena. Las modalidades de fisioterapia que incluían señales fueron más efectivas para tratar la CDM que los enfoques de fisioterapia tradicionales. El metaanálisis indicó que las intervenciones fisioterapéuticas tuvieron un impacto significativamente mayor sobre la CDM que las comparaciones de control.

Conclusiones. El tratamiento fisioterapéutico, especialmente las modalidades que incluyen señales visuales y auditivas, debe prescribirse a los pacientes con EP con CDM. Se necesitan estudios futuros que incluyan pacientes con EP con deterioro cognitivo y herramientas de medición objetiva de la CDM para completar la evidencia científica existente.

Palabras clave. Congelación de la marcha. Ejercicio. Enfermedad de Parkinson. Fisioterapia. Revisión sistemática. Señalización.