Effects of Exercise Therapy on Postural Instability in Parkinson Disease: A Meta-analysis

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Background and Purpose: Exercise therapy is a common intervention for improving postural stability. The purpose of this meta-analysis was to assess the effect of exercise therapy on postural instability in persons with Parkinson disease (PD) based on the available literature, and to evaluate the efficacy across various types of exercise interventions.

Data Sources and Study Selection: In January 2015, electronic databases (PubMed, Scopus, PEDro) and study reference lists were searched for randomized controlled trials with moderate or high methodological quality (PEDro score ≥ 5), investigating the effect of exercise on postural instability in persons with PD.

Data Extraction and Synthesis: Three reviewers extracted data and assessed quality.

Main Outcome and Measure: Postural stability as measured using the Berg Balance Scale, postural sway, Timed Up and Go, or Functional Reach test. Standardized mean differences (SMDs) with 95% confidence intervals (CIs) were calculated.

Results: Twenty-two trials, with a total of 1072 participants, were eligible for inclusion. The pooled estimates of effects showed significantly improved postural instability (SMD, 0.23; 95% CI, 0.10-0.36; $P < 0.001$) after exercise therapy, in comparison with no exercise or sham treatment. Exercise interventions specifically addressing components of balance dysfunction demonstrated the largest efficacy, with moderate to high effect sizes (SMD, 0.43; 95% CI, 0.21-0.66; $P < 0.001$). Little or no beneficial effects were observed for interventions not specifically targeted at postural stability (SMD, 0.20; 95% CI −0.04 to 0.44; $P = 0.11$) or for home-based, multicomponent exercise programs (SMD, 0.02; 95% CI −0.20 to 0.25; $P = 0.86$).

Discussion and Conclusions: Exercise therapies specifically addressing balance dysfunction are an important treatment option for improving postural stability in persons with PD. Future studies should investigate sustainability of the short-term effects and establish the dose-response relationship of balance training in persons with PD.

Video abstract available for additional insights from the authors (see Video, Supplemental Digital Content 1, http://links.lww.com/JNPT/A121).

Key words: *balance, exercise, Parkinson disease, postural control*

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INTRODUCTION

Parkinson disease (PD) is a progressive neurological disorder with a rapidly increasing worldwide prevalence.[1] Parkinson disease is characterized mainly by 4 cardinal motor symptoms: resting tremor, bradykinesia, rigidity, and postural instability (PI).[2] Postural instability describes loss of balance control, therefore often referred to as balance dysfunction.[3,4] It leads to loss of mobility, disability, and reduced quality of life.[5,6] Recent studies have shown that PI begins early after disease onset,[7,8] with around one third of individuals developing PI within the first 2 years after diagnosis.[5]

Postural instability affects balance control in PD mainly in 4 domains: (1) balance during quiet stance, (2) reactive postural adjustments to external perturbations, (3) anticipatory postural adjustments, and (4) dynamic balance.[4] Because of these impairments, people with PD are at a particular risk of falling, with reports ranging from a 2-[9] to 9-fold[10] increased risk compared with healthy older adults. Falls occur in approximately 50% of persons with PD, of which about 30% are injurious.[11,12] Postural instability has been identified as an independent predictor of falls in persons with PD,[13,14] and around one third of falls are caused by an unstable posture.[15]

Current evidence suggests that PI is poorly responsive to general treatment options in persons with PD, such as medication with L-dopa and deep brain stimulation[16]; some domains of balance dysfunction even worsen under pharmacological and surgical treatment.[4] These findings provide an urgent need for other types of treatment, such as exercise therapy. Tomlinson et al[17] demonstrated the beneficial effects of physical therapy interventions (including exercise therapy) on various outcome parameters in participants with PD, including gait, functional mobility, balance, overall disability, and activities of daily living. However, exercise therapy was not the primary focus in this review and the different types of physical interventions were not analyzed on the basis of their specific content. Other recently published meta-analyses focused on specific types of exercise, showing improvements in measures of postural stability in individuals with PD after performing tai chi,[18] dancing,[19] or aerobic exercises.[20] Furthermore, on the basis of their literature review, Canning et al[21] recommend to promote exercise for falls prevention in persons with PD, especially challenging balance exercises in a supervised setting. In a meta-analysis from 2011, Allen et al[22] summarized the effect of exercise therapy on balance-related activities and falls in people with PD. Results showed an improvement of balance-related outcomes after exercising, and there was a trend for highly challenging balance exercises being most effective. These findings were derived from few preliminary studies in this field, particularly lacking evidence for robust practical recommendations regarding the adequate types of exercise interventions, the optimal level of postural challenge in exercises, and the required dosage (number and duration of sessions) of training. Aggregated research activities in the last years provide a more sophisticated body of literature today.

Therefore, the primary aim of this meta-analysis was to strengthen current evidence and to quantify the effectiveness of exercise therapy on PI in participants with PD. A secondary objective was to evaluate whether specific exercise interventions show superior effects, to identify the optimal mode of exercise therapy for improving postural stability in people with PD.

METHODS

Search Strategy

We conducted a systematic literature search including articles published until the end of January 2015 in the following databases: PubMed (Medline), Scopus, and PEDro (Physiotherapy Evidence Database). The search strategy was developed on the basis of the PICO framework (Population, Intervention, Comparison, Outcome) and was applied to each database with minor adaptations.[23] An exploratory search with different combinations of key words was conducted in PubMed to identify the most precise search terms according to the research question. The final search is based on the following strategy: "Parkinson disease" or Parkinson, combined with (and) "exercise therapy" or exercise, combined with (and) balance. For PubMed searches, the following terms were included as MeSH terms: Parkinson disease, exercise therapy, and exercise. In addition, we hand searched reference lists to identify further relevant articles.

Selection Criteria

Three reviewers (S.K., S.S., and S.D.) independently screened identified studies, and inclusion was decided on the basis of consensus, reached by discussion among reviewers. For inclusion, studies had to be randomized controlled trials (RCTs), published in English or German language, and evaluating the effect of exercise therapy on PI in people with PD. Eligible studies had to compare any type of exercise therapy (eg, balance, aerobic, and resistance exercise) against either no intervention or sham exercise (stretching exercises, usual care with no specific exercise therapy, education, or interventions where authors stated that it was intended to be sham treatment). With regard to the secondary aim of this meta-analysis, trials were also accepted if they compared balance exercises against other types of exercise. To avoid heterogeneity and to assure high quality of data, eligible PI measures were defined before analysis. On the basis of a review of relevant literature, we decided about eligibility and priority of PI assessments according to (a) their frequency of usage, and (b) the test quality (reliability and validity).[24–27] The ranking was as follows: (1) Berg Balance Scale (BBS),[24] (2) postural sway in quiet stance (center of pressure sway area, Sensory Organization Test conditions 1 and 2),[25] (3) the Timed Up and Go (TUG) test,[26] and (4) the Functional Reach (FR) test.[27] Studies were only included in the meta-analysis if they used one of these 4 PI measures. If studies used more than one PI measure, the one with the highest priority was included in the analysis.

Studies were excluded from analysis if the intervention did not primarily focus on performing exercises (eg, whole body vibration without performing exercises), if exercise interventions (experimental or control) were not adequate for meta-analytic comparisons, if data for statistical analysis were missing, or if methodological quality of studies was poor (PEDro score < 5).

Quality Assessment

Assessment of methodological quality of all eligible studies was performed with the PEDro scale.[28,29] The scale contains 11 items to assess risk of bias, with 1 criterion (item 1) addressing external validity. This criterion is not included in calculation of the total score and therefore a maximum of 10 points could be reached. A point was allocated to a criterion (yes) if it was clearly satisfied; otherwise, the item was rated as not fulfilled (no). In case of missing information in the publication, authors were contacted via e-mail (sending one reminder). Two reviewers (S.K. and S.S.) independently examined quality rating. Disagreements in ratings were discussed until consensus was found.

Data Extraction and Statistical Analysis

The main characteristics of each included study were extracted, including information about the sample (initial sample size, age, PD status, and dropout rate), intervention (experimental and control), and PI outcomes (assessment and follow-up). Only data assessed immediately after intervention period were extracted; data from longer follow-up periods were not taken into account because of the large variety of intervals. For studies with more than 2 intervention arms, data from several groups were combined if intervention groups were adequate for comparison.[30] Authors were contacted via e-mail (sending one reminder) if descriptive information or data for statistical analysis were missing.

To investigate the overall effect of exercise therapy on PI in participants with PD, the primary analysis compared exercise (including various types of exercise) versus no exercise or sham treatment. To compare the effect of various exercise interventions with each other, different secondary analyses were performed. As a first step, subgroup analyses of the primary comparison were conducted. Subgroups were built according to the interventions' level of postural challenge for persons with PD. The rationale for this was based on a previously published framework for balance dysfunction in persons with PD. Accordingly, exercises including (a) balance during quiet stance, (b) reactive postural adjustments to external perturbation, (c) anticipatory postural adjustments in preparation for voluntary movements, and (d) dynamic balance during movements were intended to be most challenging for PI in this population.[4]

Four subgroups were defined for analysis:

1. Balance-specific exercise: Interventions focusing on all 4 domains (a-d) of balance dysfunction in PD (conventional balance exercise),
2. Exercise with balance components: Interventions incorporating exercises that challenge the participant's balance (tai chi and dancing),
3. Exercise with no specific balance component: Exercises not primarily targeting at PI (aerobic, strength, walking, cycling, and yoga),
4. Home-based multicomponent exercise programs: A combination of different types of exercises (eg, flexibility, endurance, strength, and balance), which were performed in a home-based setting.

Another exploratory subgroup analysis of the primary comparison was performed specifically for aerobic training (exercise primarily containing components to improve cardiorespiratory fitness, eg, walking or cycling exercise), on the basis of a framework suggesting that aerobic exercise enhances neuroplasticity and thereby motor performance in persons with PD.[31] Our secondary analyses also included a separate statistical analysis evaluating the effect of balance training (including balance-specific exercise or exercise with balance component) when directly compared with other exercise programs.

The Cochrane Collaboration's software Review Manager (RevMan, version 5.3, Copenhagen) was used for the meta-analysis. All outcome variables used for analysis were continuous data and entered as mean values with standard deviation. Standardized mean differences (SMD = Hedge' adjusted g, defined as difference between the posttest means of treatment and control group divided by the pooled standard deviation) with 95% confidence intervals (CIs) were calculated to combine data of outcomes with different units. For scales indicating improvement by decrease (TUG, center of pressure sway area), mean values were adjusted by multiplication with -1.[30] When data from multiple studies were available, they were pooled using a random-effects model. Heterogeneity was assessed by using I^2 and χ^2 statistics and 95% CI. To detect reporting bias for the primary comparison, the relationship between the effect estimates of the interventions and the standard error of these effect estimates was analyzed with a funnel plot.[32]

In addition, random-effects meta-regression was performed to investigate the influence of different types of exercises on PI. Specifically, we compared the effect of exercises containing balance components (subgroups 1 and 2) to exercises with no specific balance component (subgroups 3). A metaregression analysis was performed with SPSS (version 23, IBM Corp, Armonk) using the MetaReg macro (version 2005.05.23) published by Lipsey and Wilson.[33,34]

RESULTS

Study Characteristics

The selection process (Figure 1) revealed 22 RCTs[35–56] being eligible for the meta-analysis. All included trials were published between 2003 and January 2015. A summary of the main characteristics is presented in Table 1. Sample size ranged from 10 to 195 participants, and mean age varied between 58 years and 73 years. The majority of participants were in mild to moderate disease stages (Hoehn & Yahr [H&Y] 1-3).[57,58] Only 6 studies[36,38,43,44,49,54] also included severely disabled participants (H&Y $\geq$ 4) and 5 articles[35,48,50,51,53] did not report H&Y stage or only mean scores. In addition, the Unified Parkinson's Disease Rating Scale motor subscale was assessed in 15 trials[35,37–40,42,43,45–47,49,51,53,55,56] ranging from 15 to 31. A large variability exists in the exercise interventions of the included studies. In general, these interventions included either a specific form of exercise (eg, balance, tai chi, and dancing) or a combination of various exercise components (typically strength, flexibility, aerobic, and balance). Nearly all of the participants exercised 2 to 3 times per week for 40 to 60 minutes per session. The duration of the intervention period varied widely among the RCTs from 4 weeks up to 2 years, but the majority of exercise therapies were conducted between 10 and 24 weeks. Ten of the included studies reported follow-up periods, which were all short term and ranged from 1 to 6 months.[36,38,43,44,48–51,54,56] Except 2 trials,[37,45] reported dropout rates were below 20% for short-term follow-up. Among the eligible balance assessments, the BBS and TUG were most frequently reported.

Methodological Quality

The majority of studies showed a moderate risk of bias (PEDro score 5-6), and 8 out of the 22 included trials[35,36,44,49,50,52,53,56] presented high methodological quality (PEDro score $\geq$ 7) (Table 2). Because only RCTs were accepted as being eligible, all trials fulfilled the criteria of randomization but only very few reported concealed allocation procedures for group assignment.[35,36,44,50,55] Study groups were comparable at baseline in all trials, and point estimates as well as measures of variability were presented. None of the trials reported blinding of participants or care providers, but except for 4 trials[38,42,44,48] all assessors were blinded. The majority of articles demonstrated an adequate follow-up, but only half of the 22 trials[35,36,38–40,43,44,48–50,52–54,56] conducted their analyses on the basis of intention-to-treat principles.

Effects of Exercise Therapy

For the primary comparison (exercise vs no exercise/sham exercise), 18 RCTs[35–46,49–53,56] with a total sample size of 957 participants were included (Figure 2). The pooled effect estimates revealed a small significant positive effect of exercise therapy on PI (SMD, 0.23; 95% CI, 0.10-0.36; $P < 0.001$). There was no heterogeneity in the estimates of the effect of exercise therapy on PI in PD ($P = 0.71$; $I^2 = 0\%$).

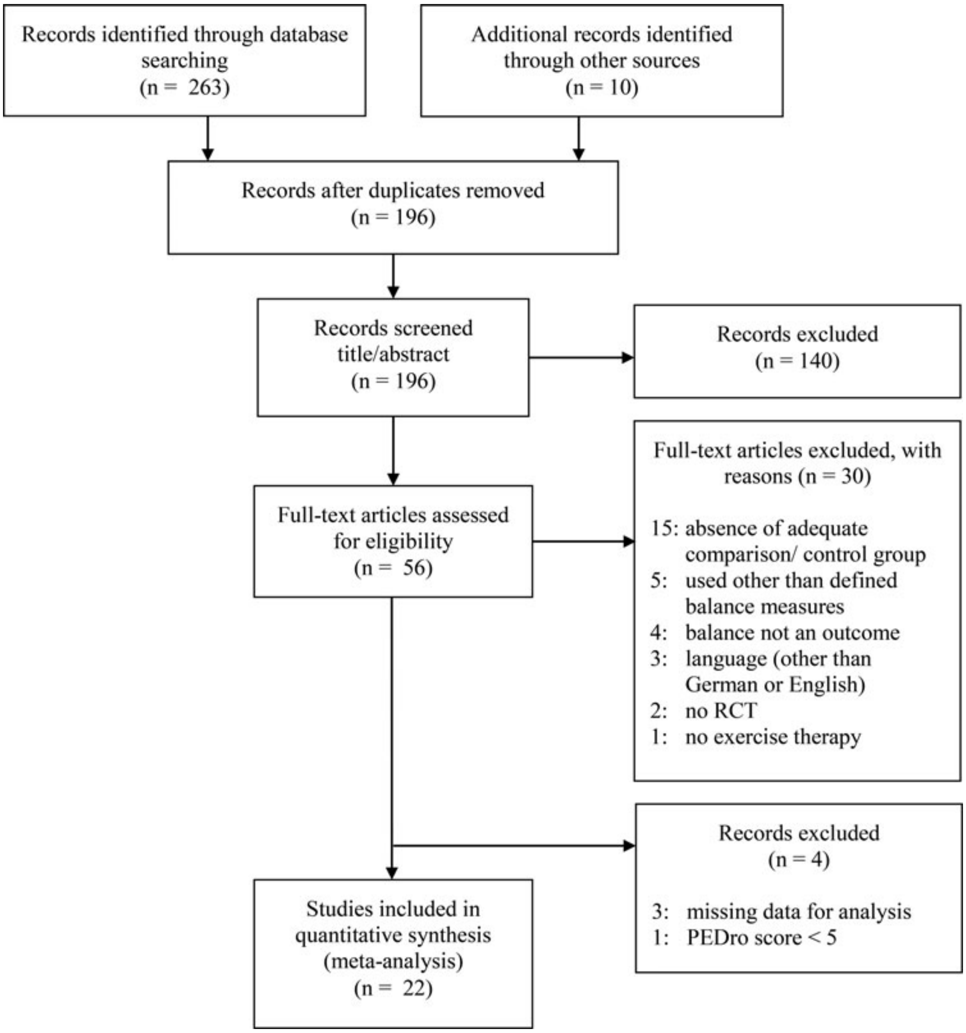

Figure 1. PRISMA flow diagram showing the selection process.

Results of subgroup analyses on the basis of specific types of exercise are presented in Figure 2. Two trials[38,56] (n = 62) investigated balance-specific training programs, showing a nonsignificant moderate effect on PI outcomes (SMD, 0.43; 95% CI, −0.10 to 0.96; $P = 0.11$). A subgroup analysis of 6 studies[39,41,43,45,46,49] (n = 310) incorporating exercises with balance components showed a significant moderate effect on PI (SMD, 0.43; 95% CI, 0.21-0.66; $P < .001$). Data from 7 trials[37,40,42,50–53] (n = 283) were available for subgroup analysis of exercise with no specific balance component. The pooled estimate of effect sizes revealed a nonsignificant small effect on PI (SMD, 0.20; 95% CI, −0.04 to 0.44; $P = 0.11$). However, meta-regression revealed that the difference between the effects of these subgroups was not statistically significant ($P = 0.253$). The pooled SMD of home-based multicomponent exercise programs[35,36,44] (n = 302) showed no beneficial effect on PI in participants with PD (SMD, 0.02; 95% CI, −0.20 to 0.25; $P = 0.86$). No statistical heterogeneity was present in any of the subgroup analyses (balance-specific exercise: $P = 0.42$, $I^2 = 0\%$; exercise with balance component: $P = 0.79$, $I^2 = 0\%$; exercise with no specific balance component: $P = 0.80$, $I^2 = 0\%$; home-based multicomponent exercise programs: $P = 0.89$, $I^2 = 0\%$). The funnel plot (Figure 3) showed that smaller studies had a tendency to produce larger effect sizes, indicating some reporting bias in this comparison.

Four trials[37,51–53] (n = 172) investigated the effect of aerobic training compared with no exercise or sham treatment (Figure 4). Pooled effect estimates indicated no beneficial effects of aerobic training on PI in participants with PD (SMD, 0.09, 95% CI, −0.22 to 0.40, $P = 0.57$). No statistical heterogeneity was observed in this comparison ($P = 0.93$, $I^2 = 0\%$).

Four studies[47,48,54,55] directly compared balance training interventions with other forms of exercise therapy (all multicomponent) (Figure 4). Pooled data (n = 115) revealed a large significant effect on PI in favor of balance training (SMD, 1.31; 95% CI, 0.37 to 2.24; $P = 0.006$). Tests for heterogeneity suggested a substantial variability among estimates of effects ($P = 0.007$; $I^2 = 75\%$) in this comparison.

Table 1. Characteristics of Included Studies

Author	Initial Sample Size	Mean Age, y	PD Status: H&Y (Range) UPDRS Motor (Mean)	Intervention Groups	Intervention Period, wk	Intervention Dosage	Follow-Up, mo	Dropout Rate	Eligible Balance Assessments
Allen et al[35]	48	67	– 30	1. Multicomponent exercise program (home-based) 2. Usual care (no exercise)	24	72 sessions 3 sessions/wk 40-60 min/session	–	3	CoP sway area
Ashburn et al[36]	142	72	2-4 –	1. Multicomponent exercise program (home-based) 2. Usual care (no exercise)	6	42 sessions 7 sessions/wk 60 min/session	6	9	BBS[a], TUG, FR
Cakit et al[37]	54	72	2-3 18	1. Treadmill training 2. No exercise control	8	– – 30 min/session	–	21	BBS
Capecci et al[38]	20	69	2-4 23	1. Balance exercise 2. Balance exercise 3. No exercise control	4	12 sessions 3 sessions/wk 40 min/session	1	0	BBS[a], TUG
Choi et al[39]	22	63	1-2 20	1. Tai chi 2. No exercise control	12	36 sessions 3 sessions/wk 60 min/session	–	2	TUG
Colgrove and Sharma[40]	13	68	1-2 18	1. Yoga 2. No exercise control	12	24 sessions 2 sessions/wk 60 min/session	–	0	BBS[a], CoP sway area
Duncan and Earhart[41]	10	68	2-3 –	1. Dancing 2. No exercise control	104	208 sessions 2 sessions/wk 60 min/session	–	0	TUG
Gao et al[43]	76	69	1 to $\geq$3 31	1. Tai chi 2. No exercise control	12	36 sessions 3 sessions/wk 60 min/session	6	0	BBS[a], TUG
Ganesan et al[42]	60	58	2-2.5 31	1. Treadmill training 2. Gait training 3. No exercise control	4	16 sessions 4 sessions/wk 30 min/session	–	0	BBS
Goodwin et al[44]	150	71	1-4 –	1. Multicomponent exercise program (home-based) 2. Usual care (no exercise)	10	30 sessions 3 sessions/wk 60 min/session	2.5	26	BBS[a], TUG
Hackney et al[47]	19	71	2-3 29	1. Dancing 2. Multicomponent exercise program	10-13	20 sessions 2 sessions/wk 60 min/session	–	0	BBS[a], TUG
Hackney and Earhart[45]	33	64	1.5-3 25	1. Tai chi 2. No exercise control	10-13	20 sessions 2 sessions/wk 60 min/session	–	7	BBS[a], TUG
Hackney and Earhart[46]	58	67	1-3 27	1. Dancing 2. Dancing 3. No exercise control	13	26 sessions 2 sessions/wk 60 min/session	–	10	BBS[a], TUG
Hirsch et al[48]	15	73	1.9 (mean) –	1. Multicomponent exercise program 2. Balance exercise	10	30 sessions 3 sessions/wk 30-45 min/session	1	0	SOT
Li et al[49]	195	69	1-4 15	1. Tai chi 2. Strength exercise 3. Sham exercise (stretching)	24	48 sessions 2 sessions/wk 60 min/session	3	0	TUG[a], FR

(*continues*)

Table 1. Characteristics of Included Studies (*Continued*)

Author	Initial Sample Size	Mean Age, y	PD Status: H&Y (Range) UPDRS Motor (Mean)	Intervention Groups	Intervention Period, wk	Intervention Dosage	Follow-Up, mo	Dropout Rate	Eligible Balance Assessments
Paul et al[50]	40	66	2.0 (mean) –	1. Strength exercise 2. Sham exercise (home-based)	12	24 sessions 2 sessions/wk 45 min/session	3	2	TUG
Qutubuddinet al[51]	23	68	– 16	1. Cycling exercise 2. Usual care (no exercise)	8	16 sessions 2 sessions/wk 30 min/session	4	0	BBS
Reuter et al[52]	90	62	2-3 –	1. Nordic walking 2. Walking 3. Sham exercise (stretching)	24	72 sessions 3 sessions/wk 70 min/session	–	0	BBS
Sage and Almeida[53]	53	66	– 22	1. Aerobic exercise 2. Multicomponent exercise program 3. No exercise control	10-12	30-36 sessions 3 sessions/wk 40-60 min/session	–	7	TUG
Smania et al[54]	64	68	3-4 –	1. Balance exercises 2. Multicomponent exercise program	7	21 sessions 3 sessions/wk 50 min/session	1	7	BBS
Volpe et al[55]	24	63	2-3 24	1. Dancing 2. Multicomponent exercise program	24	24 sessions 1 session/wk 90 min/session	–	0	BBS[a], TUG
Yen et al[56]	42	71	2-3 16	1. Balance exercise 2. Balance exercise 3. No exercise control	6	12 sessions 2 sessions/wk 30 min/session	1	0	SOT

Abbreviations: BBS, Berg Balance Scale; CoP, center of pressure; FR, Functional Reach; H&Y, Hoehn and Yahr; PD, Parkinson disease; TUG, Timed Up and Go; SOT, Sensory Organization Test; UPDRS, Unified Parkinson's Disease Rating Scale.

[a]Outcome used for statistical analysis according to priority ranking.

DISCUSSION

The aim of this meta-analysis was to strengthen current evidence regarding the effectiveness of exercise therapy on PI in participants with PD and to evaluate whether specific exercise interventions show superior effects. Our findings demonstrate that exercise therapy is an effective treatment option to improve postural stability in persons with PD, and provide first guiding principles for the optimal mode of exercise therapy in this field. Our findings suggest that exercises containing a balance component were most beneficial in improving postural stability in individuals with PD. The minimal and optimal amount of postural challenge during exercise currently remains unclear. Exercises not specifically targeting at balance dysfunction and programs conducted in a home-based setting seem to have no beneficial effect on PI.

Our primary analysis revealed a small positive effect of short-term exercise therapy on PI. These results support preliminary findings from another meta-analysis[22]; however, the larger amount of underlying data (22 trials; n = 1072) and the high consistency in the included data (low statistical heterogeneity) allow more robust conclusions from the present study. Allen et al[22] reported a significant improvement (SMD, 0.33; 95% CI, 0.11-0.55; $P = 0.003$) of balance-related activities in participants with PD in favor of exercise, but their meta-analysis was based on 15 trials (n = 747) and a moderate level of statistical heterogeneity ($P = 0.013$; $I^2 = 47\%$) in the estimates. Furthermore, subgroup analyses revealed statistical significance only for turning time and gait-related outcomes (mainly gait velocity), but not for PI measures such as BBS, TUG, or FR. In another meta-analysis, Tomlinson et al[59] evaluated the effect of physical therapy compared with no intervention/placebo in people with PD and reported significant superior effects of physiotherapy on PI for TUG (9 RCTs; n = 639), BBS (5 RCTs; n = 385) and FR (4 RCTs; n = 193). Tomlinson et al[17] also investigated whether the various types of physical therapy show different treatment effects on PI in participants with PD, but no intervention presented superior results. However, they did not focus on the level of postural challenge included in the various physical therapy interventions.

A key feature of the present meta-analysis was the investigation of the most effective types of exercise therapy for improving postural stability in persons with PD. Our subgroup analyses demonstrated the most beneficial effects for exercises incorporating balance components, such as dancing or tai chi. Recently, published meta-analyses specifically investigating the effectiveness of tai chi[18] and dancing[19] on balance in participants with PD presented similar positive results in favor of these types of exercise therapy. Our findings are also in line with results from Allen et al[22] who classified tai chi and dancing as "highly challenging" balance exercise and concluded that these interventions are most beneficial for balance-related activities in participants with PD. However, results from meta-regression revealed that effect estimates of exercise containing balance components (subgroups 1 and 2) and exercise with no specific balance component (subgroups 3) were not significantly different. Thus, there still remains some uncertainty regarding the optimal dosage of postural challenge during exercise. Trials comparing exercise interventions incorporating different amounts of balance components are needed to establish dose-response relationships in this particular target group. A consequent application of the framework suggested by Schoneburg et al[4] might provide a methodological basis for a structured motor rehabilitation aiming to improve postural stability in PD.

Results from this meta-analysis revealed no evidence for multicomponent exercise programs being beneficial for PI in individuals with PD. The pooled SMD (subgroup 4, Figure 2) suggests that multicomponent exercise programs are not effective in improving postural stability when performed in a home-based setting. These results support current evidence from Canning et al,[21] who conclude that there is only little evidence to promote home-based (minimally supervised) multicomponent exercise programs for the prevention of falls in persons with PD. Furthermore, our secondary analysis (Figure 3) showed that even if multicomponent exercise programs are performed in a supervised setting, they are less beneficial compared with balance training (balance-specific exercise and exercise with balance components). Thus, our findings suggest that multicomponent exercise programs, conducted at home or in a supervised setting, seem to have a reduced potential to improve postural stability in this specific population. Some caution needs to be taken because these findings are based on a small existing body of evidence and the underlying studies included participants with PD who were at risk of falling or had a history of falls. Nevertheless, our results support the advantage of taking task specificity into account as a key physical training principle in motor rehabilitation for people with PD.[60−62]

In a secondary analysis, we investigated the effect of aerobic exercise on PI in participants with PD. We based the rationale for this analysis on a previously published model by Petzinger et al,[63] suggesting that regular aerobic exercise combined with goal-based motor training enhances neural plasticity via improvements in overall brain health and strengthening of neural circuitry. There was no evidence that aerobic training alone is effective in improving PI, compared with no exercise or sham treatment. Our findings are in contrast to a recent meta-analysis, which reported a large significant effect (SMD, 2.02; 95% CI, 0.45-3.59; $P = 0.01$) of aerobic exercise on PI in participants with PD.[20] However, Shu et al[20] included exercise interventions that incorporated not only aerobic but also balance components (eg, tai chi and dancing), whereas we only included exercises not specifically targeting at postural stability (eg, stationary bicycling,[51] elliptical cross-trainer,[53] aerobic walking training[37,52]). These findings support the idea that aerobic exercise alone is not sufficient in improving motor performance, but in combination with goal-based training (eg, gait or balance training) might be particularly beneficial for motor skill acquisition.[63] Whether this holds true, particularly for PI, needs to be confirmed in future investigations.

The main study characteristics varied substantially among the 22 RCTs included in this meta-analysis. This specifically involves the types of exercise applied, duration of interventions, and exercise dosage (number of exercise sessions per week, duration of exercise session), as well as sample characteristics. Regarding the types of exercise therapies, we tried to overcome the present heterogeneity by building subgroups

Table 2. Quality Assessment (PEDro) of Included Studies

Author	Randomization	Concealed Allocation	Baseline Comparability	Patients Blinded	Care Provider Blinded	Assessor Blinded	Adequate Follow-Up	Intention-to-Treat	Between-Group Comparisons	Point Estimates and Variability	Score
Allen et al[35]	√	√	√	×	×	√	√	√	√	√	8
Ashburn et al[36]	√	√	√	×	×	√	√	√	√	√	8
Cakit et al[37]	√	×	√	×	×	√	×	×	√	√	5
Capecci et al[38]	√	×	√	×	×	×	√	√	√	√	6
Choi et al[39]	√	×	√	×	×	√	√	×	√	√	6
Colgrove and Sharma[40]	√	×	√	×	×	√	√	√	×	√	6
Duncan and Earhart[41]	√	×	√	×	×	√	×	×	√	√	5
Ganesan et al[42]	√	×	√	×	×	×	×	√	√	√	5
Gao et al[43]	√	×	√	×	×	√	√	×	√	√	6
Goodwin et al[44]	√	√	√	×	×	×	√	√	√	√	7
Hackney et al[47]	√	×	√	×	×	√	×	×	√	√	5
Hackney and Earhart[45]	√	×	√	×	×	√	×	×	√	√	5
Hackney and Earhart[46]	√	×	√	×	×	√	×	×	√	√	5
Hirsch et al[48]	√	×	√	×	×	×	√	×	√	√	5
Li et al[49]	√	×	√	×	×	√	√	√	√	√	7
Paul et al[50]	√	√	√	×	×	√	√	√	√	√	8
Qutubuddin et al[51]	√	×	√	×	×	√	×	×	√	√	5
Reuter et al[52]	√	×	√	×	×	√	√	√	√	√	7
Sage and Almeida[53]	√	×	√	×	×	√	√	√	√	√	7
Smania et al[54]	√	×	√	×	×	√	√	×	√	√	6
Volpe et al[55]	√	√	√	×	×	√	×	×	√	√	6
Yen et al[56]	√	×	√	×	×	√	√	√	√	√	7

Abbreviations: √, criteria fulfilled; ×, criteria not fulfilled.

Study or Subgroup	Experimental (exercise) Mean	SD	Total	Control (no exercise) Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
1.1.1 Balance-specific exercise								
Balance (Capecci 2014)	51.23	4.01	13	50.71	4.15	7	2.0%	0.12 [-0.80, 1.04]
Balance (Yen 2011)	91.2	2.1	14	89.3	3.6	28	3.9%	0.58 [-0.07, 1.24]
Subtotal (95% CI)			**27**			**35**	**5.9%**	**0.43 [-0.10, 0.96]**
Heterogeneity: Tau² = 0.00; Chi² = 0.64, df = 1 (P = 0.42); I² = 0%								
Test for overall effect: Z = 1.58 (P = 0.11)								
1.1.2 Exercise with balance component								
Dancing (Duncan 2014)	-10.51	2.35	5	-12	2.27	5	1.0%	0.58 [-0.70, 1.86]
Dancing (Hackney 2009)	52.05	4.12	31	47	10.31	17	4.5%	0.72 [0.11, 1.33]
Tai Chi (Choi 2013)	-7.03	0.9	11	-9.32	4.16	9	2.0%	0.77 [-0.15, 1.69]
Tai Chi (Gao 2014)	50.19	8.34	37	46.36	9.16	39	8.1%	0.43 [-0.02, 0.89]
Tai Chi (Hackney 2008)	51.38	3.5	13	51.07	4.11	13	2.9%	0.08 [-0.69, 0.85]
Tai Chi (Li 2012)	-7.55	2.69	65	-8.67	3.45	65	14.0%	0.36 [0.01, 0.71]
Subtotal (95% CI)			**162**			**148**	**32.6%**	**0.43 [0.21, 0.66]**
Heterogeneity: Tau² = 0.00; Chi² = 2.38, df = 5 (P = 0.79); I² = 0%								
Test for overall effect: Z = 3.75 (P = 0.0002)								
1.1.3 Exercise with no specific balance component								
Aerobic (Sage 2009)	-7.9	2.5	13	-8.2	2.1	15	3.1%	0.13 [-0.62, 0.87]
Cycling (Qutubuddin 2013)	46.8	11.3	13	46.7	8.2	10	2.5%	0.01 [-0.81, 0.83]
Strength (Paul 2014)	-8.3	2.4	19	-8.6	4.3	19	4.2%	0.08 [-0.55, 0.72]
Walking (Cakit 2007)	44.09	7.11	21	41.4	10.65	10	2.9%	0.31 [-0.44, 1.07]
Walking (Ganesan 2013)	51.5	4.88	40	48.9	2.8	20	5.6%	0.60 [0.05, 1.14]
Walking (Reuter 2011)	51.45	1.84	60	51.4	1.86	30	8.8%	0.03 [-0.41, 0.47]
Yoga (Colgrove 2012)	54.13	2.48	8	53.2	3.03	5	1.3%	0.32 [-0.81, 1.45]
Subtotal (95% CI)			**174**			**109**	**28.4%**	**0.20 [-0.04, 0.44]**
Heterogeneity: Tau² = 0.00; Chi² = 3.10, df = 6 (P = 0.80); I² = 0%								
Test for overall effect: Z = 1.61 (P = 0.11)								
1.1.4 Home-based multicomponent exercise programs								
Allen 2010	-121.7	93.4	21	-127.5	51	24	4.9%	0.08 [-0.51, 0.66]
Ashburn 2007	45.8	9.2	67	45.2	9.9	66	14.6%	0.06 [-0.28, 0.40]
Goodwin 2011	44.7	11.4	61	45.2	11.2	63	13.6%	-0.04 [-0.40, 0.31]
Subtotal (95% CI)			**149**			**153**	**33.1%**	**0.02 [-0.20, 0.25]**
Heterogeneity: Tau² = 0.00; Chi² = 0.22, df = 2 (P = 0.89); I² = 0%								
Test for overall effect: Z = 0.18 (P = 0.86)								
Total (95% CI)			**512**			**445**	**100.0%**	**0.23 [0.10, 0.36]**
Heterogeneity: Tau² = 0.00; Chi² = 13.35, df = 17 (P = 0.71); I² = 0%								
Test for overall effect: Z = 3.49 (P = 0.0005)								
Test for subgroup differences: Chi² = 7.00, df = 3 (P = 0.07), I² = 57.2%								

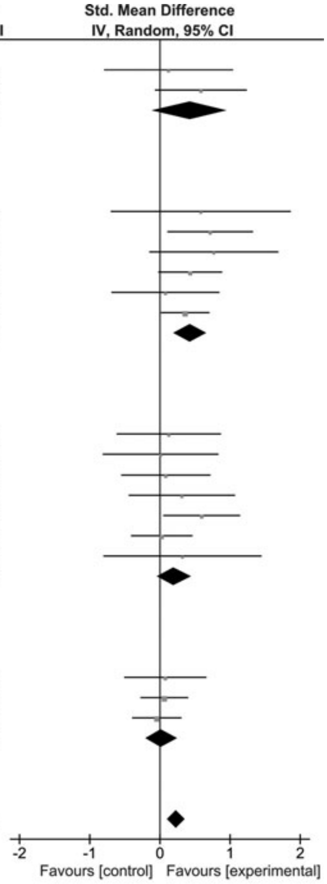

Figure 2. Forest plot showing the effect of exercise therapy on postural instability compared with no exercise/sham treatment (with subgroup analyses).

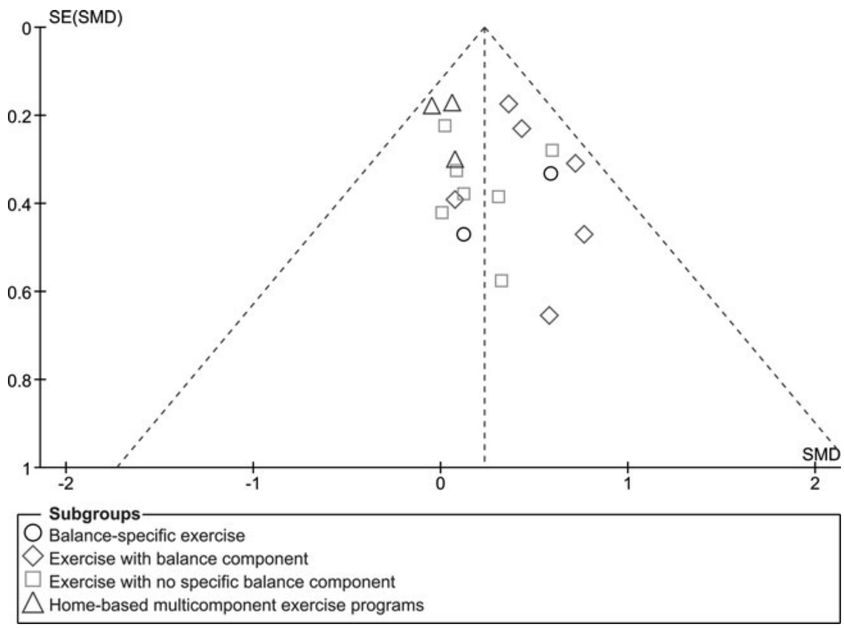

Figure 3. Funnel plot of SMD and SE (SMD) for primary comparison. SE, standard error; SMD, standardized mean difference.

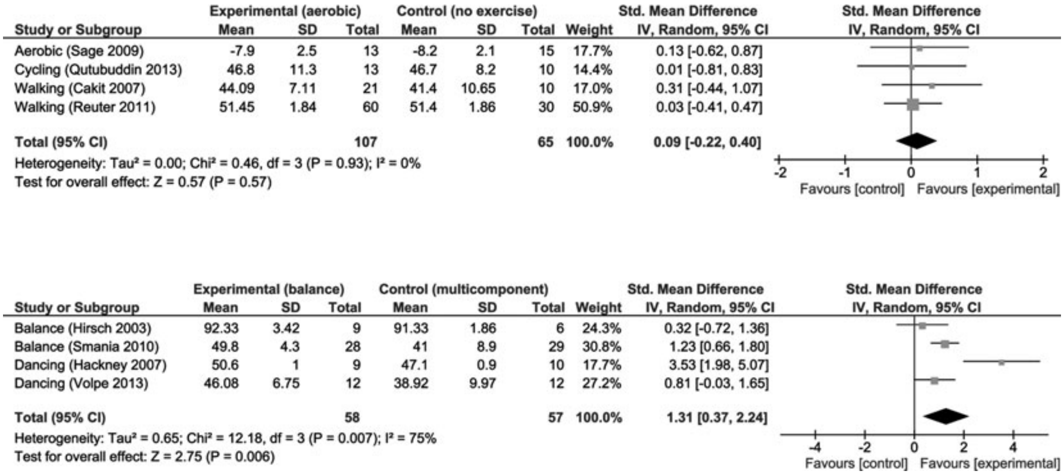

Figure 4. Forest plots showing the effect of aerobic exercise on postural instability compared with no exercise/sham treatment and the effect of balance training (balance-specific exercise or exercise with balance component) on postural instability compared with multicomponent exercise programs.

on the basis of the intervention level of postural challenge for persons with PD. The absence of heterogeneity in our subgroup analyses supports this categorization, which was based on a Parkinson-specific framework of balance dysfunction.[4] In comparison, Allen et al[22] classified balance exercise on the basis of findings from falls prevention in older adults (criteria: movement of center of mass, narrowing of the base of support, minimizing upper limb support).[64] These different approaches should be taken into consideration when comparing the results of both studies, as they might lead to differences in interpretation.

The overall duration of interventions also varied widely among the 22 included trials (4 weeks to 2 years), but the majority of participants exercised 12 weeks or less. Therefore, the conclusions from this meta-analysis mainly represent short-term effects of exercise therapy. It remains unclear whether longer intervention periods would lead to comparable or even larger improvements. Studies in this meta-analysis also varied substantially in the intervention dosage, ranging from 1 to 7 sessions per week and from 30- to 90-minute training per session. Thus, it is difficult to provide robust recommendations for exercise prescription on the basis of this meta-analysis. It is noteworthy, though, that most of the trials conducted exercises for 40 to 60 minutes on 2 to 3 days a week, which seems to be an effective dose to improve postural stability in individuals with PD. According to the H&Y scale, only a few trials ($n = 6$) included participants with PD whose disease was in more advanced stages (H&Y ≥ 4), whereas the majority of studies included participants with PD who were mildly to moderately affected (H&Y 1-3). Thus, the present findings mainly apply for persons in earlier stages of PD, and it remains unclear whether people in advanced stages of PD might show different responses to exercise.

There are limitations to this meta-analysis that should be considered when interpreting the results. To counteract heterogeneity, eligible studies were required to use one of the predetermined PI measures (BBS, postural sway, TUG, FR test). Therefore, we might have omitted trials that also used other appropriate instruments, such as Mini-Balance Evaluation Systems Test (mini-BESTest)[65] or Functional Gait Assessment.[66] However, literature screening showed that studies using such newer or less widespread PI measures also included traditional tools such as the BBS or TUG, and therefore were also likely to be included in this meta-analysis. Furthermore, anti-Parkinson medication might have affected the results because 1 trial tested their participants during off-state of medication and 6 studies did not control for medication intake. The results of this meta-analysis should be interpreted with caution as they are mainly based on short-term exercise interventions and mainly represent effects in mildly to moderately affected persons with PD.

CONCLUSIONS

Exercise therapy is effective in improving postural stability in individuals with PD, particularly when exercises incorporate components of balance dysfunction. In contrast, interventions that are not specifically targeted at PI, as well as multicomponent exercise programs, seem to have a reduced potential to improve postural stability. Therefore, we highly recommend to integrate balance exercises in motor rehabilitation targeting at improvement of PI in individuals with PD, and to tailor these exercise interventions specifically to the different domains of balance dysfunction in persons with PD. These conclusions are mainly drawn from data of short-duration trials; thus, the long-term effects of exercise on PI remain unclear. An important future step is to evaluate the minimal and the optimal amount and intensity of balance exercises necessary to achieve optimal effects on PI. In addition, future trials should include participants with PD in different disease stages and with varying levels of balance impairment to investigate the potential of exercise therapy on PI throughout the course of the disease. Furthermore, there is an urgent need for long-term follow-up studies that ascertain the sustainability of the beneficial short-term effects of exercise therapy, and their potential to reduce falls in persons with PD.

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