Systematic review on strength training in Parkinson’s disease: an unsolved question

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Abstract: The purpose of this study was to investigate the effectiveness of strength training, performed against a different resistance from body weight, in improving motor and nonmotor symptoms in patients with Parkinson’s disease (PD). The following electronic databases were searched: PubMed, Physiotherapy Evidence Database, Cochrane Central Register of Controlled Trials, Scopus, and Web of Science. The review was conducted and reported in accordance with the PRISMA statement. Thirteen high-quality randomized controlled trials were included. Strength training performed against external resistance is well tolerated and appears to be a suitable physical activity to improve both physical parameters and quality of life parameters of PD subjects. However, although the study intervention included strength training, only a few selected studies assessed the improvement of muscle strength. Despite the encouraging results, it is difficult to establish a correlation between strength training and the improvements made. Our review highlights the lack of common intent in terms of study design and the presence of different primary and secondary outcomes. Accordingly, further studies are needed to support the beneficial effects of different types of strength training in PD subjects and to underline the superiority of strength training in PD patients with respect to other training.

Keywords: Parkinson's disease, strength training, muscle strength

Introduction

Parkinson’s disease (PD) is an age-related neurodegenerative disorder characterized by specific motor symptoms such as tremor, slowed movement, rigid muscles, impaired posture, and balance.1,2 An increased body of evidence highlights also the presence of nonmotor symptoms like hyposmia, sleep disorders, and gastrointestinal dysfunctions. These symptoms accompany the onset and progression of the pathology, often preceding cardinal motor features of PD.2–4

PD is characterized by the selective loss of dopaminergic neurons of the substantia nigra pars compacta, the main region affected by this pathology. The histopathological hallmark of PD is the development of cytoplasmic inclusions known as Lewy bodies (LB) and Lewy neurites (LN). The latter are insoluble proteinaceous aggregate formed primarily within the body and processes of brain cell neurons, but they are also present in the spinal cord and peripheral nervous system.2 LB and LN are mainly composed of alpha-synuclein, an endogenous protein that plays a crucial role in PD. Toxic alpha-synuclein oligomers may impact cells in a number of ways, including the disruption of membranes, mitochondrial depolarization, cytoskeleton changes, impairment of protein clearance pathways, and enhanced oxidative stress. The loss of functions of native alpha-synuclein and the gain of toxic functions following the misfolding or oligomerization process play a pivotal role in the pathogenesis of PD.5,6
Although the etiology of PD remains obscure, multifactorial theories have been postulated concerning both environmental and genetic factors. The current therapeutic approaches to PD include levodopa (the most potent drug for controlling PD symptoms), dopamine agonists, catechol-O-methyltransferase inhibitors, and non-dopaminergic agents. Nevertheless, these drugs only slow down the disease progression and are often associated with comorbid problems. In order to improve the quality of life of PD patients, physical activity is considered to be one of the most important non-pharmacological strategies. There is a strong consensus that physical exercise can improve the management of symptoms, delay disease progression, and improve the physiological and structural function of the human brain. However, a great deal of additional research must be carried out to clarify the effects of physical exercise on brain neuroplasticity. Despite the fact that physical activity improves quality of life and functional independence of PD patients, it cannot reverse PD symptoms.

A lot of recent reviews describe the effect of aerobic exercise in improving motor and nonmotor symptoms in PD patients. Less attention has been focused on specific muscle training against an external resistance (resistance/strength training). For this reason, the purpose of this study was to conduct a systematic review of published literature concerning the effects of resistance training, performed against a resistance different from the body weight, in PD patients. The primary outcome of this review was to assess the effectiveness of resistance training on muscle strength improvement. The secondary outcome was to shed light on the effects of resistance training in improving physical performance and quality of life of PD patients.

Materials and methods

The review was conducted and reported in accordance with the PRISMA statement (www.prisma-statement.org).

Databases and search strategy

The following electronic databases were searched: PubMed, Physiotherapy Evidence Database (PEDro), Cochrane Central Register of Controlled Trials, Scopus, and Web of Science.

The keywords used were “Parkinson disease and physical exercise”, “Parkinson disease and physical therapy”, “Parkinson disease and training”, “Parkinson disease and strength physical exercise”, “Parkinson disease and strength physical therapy”, “Parkinson disease and strength training”, “Parkinson disease and eccentric training”, “Parkinson disease and resistance physical exercise”, “Parkinson disease and resistance physical therapy”, “Parkinson disease and resistance training”, “Parkinson disease and aquatic training” and “Parkinson disease and aquatic exercise”.

A manual search of reference lists of selected papers and reviews on the topics was performed to identify additional relevant articles. To identify gray literature, a search was conducted in Google and Google Scholar using the aforementioned keywords. The electronic databases were investigated until February 2016.

Selection criteria for studies

Strength training was defined as an intervention in which participants exercised a muscle or group of muscles against an external resistance. For this study, we considered as external resistance cycle ergometer, weight machine, elastic band, punching bag, and water. In further analysis, we included articles in which the effect of strength training in subjects affected by PD was evaluated and the articles that matched the following inclusion criteria based on PICO (Patient, Intervention, Comparison, Outcome) principles:

- randomized controlled trials related to both sexes;
- stages 1–3 on the Hoehn and Yahr scale;
- study design comparing the effects of strength training versus different exercise protocol;
- study outcomes: muscle strength, physical performance, quality of life;
- training/assessment of subjects during the “on” medication period;
- articles written in English.

Exclusion criteria were as follows:

- observational studies;
- studies with healthy or non-exercise controls;
- studies employing supplementary intervention therapies in addition to strength training;
- studies with tailored exercise programs to meet individual capacity.

Two authors (IR and BB) independently screened the articles by title and abstract against the selection criteria. Articles that were unclear from their title or abstract were reviewed against the selection criteria through the full text. Any discrepancies between authors were resolved through discussion. The second step was to screen all full-text articles that passed the first step.

Conference and symposium abstracts were assessed but deemed unsuitable due to the limited body of data related to the study design and the intervention program.

Data extraction and analysis

Two authors (IR and BB) independently extracted data from the 13 studies that met the inclusion criteria. In agreement
with PICO principles, the data included the following: disease population and disease status, the study design and number of participants, strength training (duration, frequency, intensity of strength training, and specific exercises employed), outcomes, participant retention and dropouts, and adverse effects associated with strength training. Any discrepancies between reviewers were resolved through discussion with the third author (CC).

Assessment of risk of bias
The methodological quality of selected articles was assessed using the PEDro scale checklist. For the purposes of this review, studies were included if they achieved a score ≥6 (high-quality study). If the articles’ score was not reported in the PEDro database, two researchers (IR and BB) assessed the score independently. The researchers were blinded to each other’s quality assessment, and in the event of disagreement, a third opinion was sought (CC).

Results
Overview of the inclusion process and methodological quality assessment
The reviewing process is presented in Figure 1; duplicate articles, review articles, conference proceedings, book chapters, and articles written in languages other than in English were excluded from the initial records retrieved from different databases. From a total of 511 selected articles, 449 did not meet the inclusion criteria as previously reported in materials and methods section. Of the remaining 62 items, 49 were excluded after quality assessment. A total of 13 articles were included in this review.26–38 Two articles showed shared data, so we combined them and considered them as a single item.35,36 The PEDro scale score of the articles is reported in Table 1. All the studies included had a PEDro scale score of 6 or higher, indicating low risk of bias. Eligibility criteria were not used to calculate the PEDro scale score because they influenced external validity but not the internal or statistical validity of the trial.

Details of the included articles
The details of the reviewed articles are reported in Table 2. The range of disease severity assessed by the Hoehn and Yahr scale is 1.5–3; the lowest mean age considered is 58.6±5.6 years old28 and the maximum is 75.7±7.2 years old,32 and the number of subjects per study ranged from 22 to 60. The lowest intervention per week considered is reported in the study of Mateos-Toset et al, in which they highlighted the effects of a brief exercise session of hand exercise 26–38.
training with therapeutic putty. The longest intervention is reported in the study of Carvalho et al., in which they assessed the effects of 2 years of progressive resistance training. As regards the length of the training session, the shortest was the single 15-minute hand exercise reported by Mateos-Toset et al and the longest was the double 30-minute session of specific training plus one additional 60-minute session of common exercises, reported by Arcolin et al. Most of the reviewed articles assessed the post-treatment effects, and only three reported the long-term effects.

Three out of the twelve studies included, considered as external resistance cycle ergometer, three weight machines, and two studies considered both weight machines and cuff weights. One study analyzed elastic bands and cuff weights, punching bag, water, or therapeutic putty, respectively, as external resistance. In all the studies reviewed, strength training was compared with the PD active control group. The latter performed traditional physiotherapy, treadmill training, and balance training. The focus of training was to maintain and/or improve functional ability of PD patients and improve their quality of life. However, which intervention was the most effective is still being debated.

The details of strength training included in the selected articles are reported in Table 3. Most of the studies involved the training of the lower body with cycle ergometer, water, weight machines, elastic bands, and cuff weights, or both weight machines and cuff weights. Two studies involved training of both upper and lower limbs with weights/resistance machines. One study focused on manual dexterity and strength. Regarding the intervention program with weight machines, the initial intensity settled at a different percentage of one repetition maximum (1RM), ranging from 40% to 70%–80% of 1RM for lower limbs and from 30%–40% to 70%–80% of 1RM for upper limbs. Also increase within the training program varied between the studies.

Primary outcome: muscle strength

Out of the twelve studies that performed strength training, only six involved specific tests to verify the improvement of PD subjects’ muscle strength (Tables 2 and 3). In particular, three studies assessed the muscle isometric contraction, one of which also assessed the maximal voluntary contraction and the rate of force development. One study considered peak muscle power, one-hand grip, and pinch strength, and the other performed physical tests and no instrumental evaluation. In this review, we have considered only the effects tested at the peak of the medication cycle. As reported in Table 2, a statistically significant improvement was reported between the strength training group and the control group in two studies that used weight machines. Moreover, a statistically significant improvement in manual dexterity was reported after a single-hand exercise session with therapeutic putty. On the contrary, Carvalho et al reported a statistical improvement within both the strength- and treadmill-training groups but no statistically significant improvement was highlighted between the groups and with respect to the physiotherapy group. Dibble et al also reported a statistically significant improvement within the groups but not between the strength training group and the control group. The study reported by Schlenstedt et al showed an improvement in muscle strength both in the strength training group and control group, but the data are not statistically significant.

Due to the heterogeneity of data reported in the selected studies, it was not possible to perform a meta-analysis to highlight the effect of resistance training in improving PD muscle strength from baseline to post-intervention.

Secondary outcomes: physical parameters

The studies reviewed have analyzed a variety of outcomes to assess the effects of training in people with PD, including both physical parameters and quality of life parameters, as reported in Table 2. For the secondary outcomes, we also considered the effects tested at the peak of the medication cycle.
Seven studies assessed balance using both self-reported scales and specific physical tests. Mini-Balance Evaluation System Test,26 Berg Balance Scale,27,37,38 Activities-Specific Balance Confidence Scale (ABC),27,35,37 FAB Scale,32 and the Latency of Compensatory Postural Response to External Perturbation Test16 were administered. Regardless of intervention type, most of the articles reviewed reported an improvement in balance in agreement with the literature data.19,41,42 However, a statistically significant improvement highlighted by the ABC test was reported in the study of Combs et al in the group that carried out traditional exercises compared to the box training group.27 Shen and Mak also reported a statistically significant improvement in terms of balance/limit of stability in repetitive step group training with respect to the strength training group, although there was no statistically significant improvement between groups.35,36 It is worth noting that Volpe et al pointed out a statistically significant improvement in the hydrotherapy group with respect to physiotherapy.37

Gait parameters were evaluated in six studies,26,27,31,32,34–36 three of which reported an improvement but no statistically significant difference between groups.27,34–36 Only one study analyzed aerobic performance with the 2-minute step test and reported a statistically significant improvement in strength- and treadmill-training groups with respect to traditional physiotherapy exercises.38 The same study reported improvement in former two trainings with regard to electroencephalographic activity, while only treadmill training determined a moderate effect in PD subjects’ flexibility.38

Only one study assessed the effect of strength training with respect to freezing of gait events using Freezing of Gait Questionnaire, but no group difference was highlighted.31

Four studies reported the effect of training on the number of falls31,34–37 Only Volpe et al pointed out an improvement in PD subjects who underwent hydrotherapy.37

Most of the studies selected reported an improvement in Unified Parkinson’s Disease Rating Scale, part III (UPDRS-III), but no statistically significant difference between groups.

Regarding the effects of training on physical performance, different tests were administered to PD subjects. The most frequent test was the Timed Up and Go Test.26,27,31,33,37,38 Other widely used tests were the 6-Minute Walk Test26,27,29 and the 10-Meter Walk Test.31,38 Most of the studies reported an improvement in physical performance but only one study evidenced an improvement in PD subjects who underwent strength training.30

Secondary outcome: quality of life parameters
Six of the twelve selected studies assessed the quality of life of PD subjects, with the administration of different questionnaires: UPDRS-II,37,38 Parkinson’s Disease Questionnaire,28,29,32,37 Parkinson’s Disease Quality of Life Scale,27 and Beck Depression Inventory.32 Two studies29,32 reported no change in outcome, while four studies reported improvement in quality of life.27,28,37,38 In particular, two studies highlighted a statistically significant improvement in the strength training group with respect to the control group.28,37

Strengths and limits of this review
The strengths of this review are the selective eligibility criteria and high methodological quality of the articles included. However, we could not answer the question of whether strength training improves motor symptoms and quality of life of PD patients, as we were not able to perform a meta-analysis because data included studies with different designs and different primary and secondary outcomes.

What are the findings?
- Strength training performed against a resistance different from body weight is well tolerated in subjects with mild to moderate PD.
- Strength training improves both physical parameters and quality of life parameters of PD patients.
- To support the beneficial effects of strength training, clinical trials that include specific muscle strength evaluation are required.

Conclusion
Our purpose was to investigate the effect of different types of strength training performed against an external resistance (cycle ergometer, weight machine, elastic band, punching bag, and water) on the improvement of different symptoms of PD patients. In most of the studies selected, the results were positive and strength training appears to be a suitable physical activity to improve both physical parameters and quality of life parameters of PD subjects. Importantly, strength training did not determine a decline in most of the outcomes considered with respect to the other training. Nevertheless, the effect of strength training on balance is uncertain because, on the basis of the items included, data are conflicting. There is also limited evidence of improvements on freezing events. Moreover, the effect on the number of falls is not clear and one study reported no training effect on the majority of outcomes examined.32 These evidences are
### Table 2 Details of intervention type and outcomes of the articles reviewed

<table>
<thead>
<tr>
<th>Study</th>
<th>Intervention type</th>
<th>Number of subjects</th>
<th>Intervention details (weeks)</th>
<th>Follow-up</th>
<th>Physical parameters</th>
<th>Strength</th>
<th>Balance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arcolin et al²⁰</td>
<td>Treadmill</td>
<td>13</td>
<td>3</td>
<td>Post-treatment</td>
<td>↑*</td>
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<tr>
<td></td>
<td>Cycle ergometer</td>
<td>16</td>
<td>9</td>
<td>Post-treatment</td>
<td>↑*</td>
<td></td>
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<tr>
<td>Carvalho et al²⁸</td>
<td>PKT</td>
<td>9</td>
<td>12</td>
<td>Post-treatment</td>
<td>↑*</td>
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<tr>
<td></td>
<td>Treadmill</td>
<td>5</td>
<td>12</td>
<td>Post-treatment</td>
<td>↑*</td>
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<tr>
<td></td>
<td>ST (weight machines)</td>
<td>8</td>
<td>12</td>
<td>Post-treatment</td>
<td>↑*</td>
<td></td>
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</tr>
<tr>
<td>Combs et al²⁷</td>
<td>Traditional exercise</td>
<td>14 (3)</td>
<td>12</td>
<td>Post-treatment</td>
<td>↑*</td>
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<tr>
<td></td>
<td>Box</td>
<td>17 (6)</td>
<td>2–3</td>
<td>Post-treatment</td>
<td>↑*</td>
<td></td>
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<tr>
<td>Corcos et al²⁰</td>
<td>mFC</td>
<td>24</td>
<td>104</td>
<td>Post-treatment</td>
<td>↑*</td>
<td></td>
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<tr>
<td></td>
<td>PREP (weight machines)</td>
<td>24</td>
<td>12</td>
<td>Post-treatment</td>
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<tr>
<td>Dibble et al²⁹</td>
<td>Active control group Renew (eccentric</td>
<td>21 (3)</td>
<td>12</td>
<td>Post-treatment</td>
<td>↑*</td>
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<tr>
<td></td>
<td>ergometer</td>
<td>20 (2)</td>
<td>2</td>
<td>Post-treatment</td>
<td>↑*</td>
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<tr>
<td>Mateos-Toset et al²⁵</td>
<td>Upper limb exercises</td>
<td>30</td>
<td>1</td>
<td>Post-treatment</td>
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<tr>
<td>Paul et al¹¹</td>
<td>ST (therapeutic putty) Control group</td>
<td>30</td>
<td>12</td>
<td>Post-treatment</td>
<td>↑</td>
<td>↑/=</td>
<td>↑/=</td>
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<tr>
<td></td>
<td>ST (weight machines)</td>
<td>30</td>
<td>12</td>
<td>Post-treatment</td>
<td>↑</td>
<td>↑/=</td>
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<tr>
<td>Ridge et al¹³</td>
<td>Static cycling</td>
<td>25 (2)</td>
<td>12</td>
<td>Post-treatment</td>
<td>↑</td>
<td>↑/=</td>
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<td></td>
<td>Dynamic cycling</td>
<td>26 (1)</td>
<td>12</td>
<td>Post-treatment</td>
<td>↑</td>
<td>↑/=</td>
<td>↑/=</td>
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<tr>
<td>Schlenstedt et al²²</td>
<td>BAL</td>
<td>20 (5)</td>
<td>12</td>
<td>Post-treatment</td>
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<td></td>
<td>ST (cuff weights, elaticated bands)</td>
<td>20 (3)</td>
<td>12</td>
<td>Post-treatment</td>
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<td>↑/=</td>
<td>↑/=</td>
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<tr>
<td>Shen and Mak²⁴</td>
<td>RST and visual cues ST (weight machines</td>
<td>15 (1)</td>
<td>12</td>
<td>Post-treatment</td>
<td>↑</td>
<td>↑/=</td>
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<td></td>
<td>and cuff weights</td>
<td>14</td>
<td>12</td>
<td>Post-treatment</td>
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<td>↑/=</td>
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<tr>
<td>Shen and Mak²⁵,²⁶</td>
<td>BAL (technology-assisted)</td>
<td>26 (4)</td>
<td>12</td>
<td>Post-treatment</td>
<td>↑</td>
<td>↑/=</td>
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<tr>
<td></td>
<td>ST (weight machines and cuff weights)</td>
<td>25 (2)</td>
<td>12</td>
<td>Post-treatment</td>
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<tr>
<td>Volpe et al²⁷</td>
<td>PKT</td>
<td>17</td>
<td>8</td>
<td>Post-treatment</td>
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<td></td>
<td>Hydrotherapy</td>
<td>17</td>
<td>8</td>
<td>Post-treatment</td>
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</tbody>
</table>

**Notes:** ↑, outcomes improvement; ↓, outcomes decline; =, no outcomes change; ↑*, outcomes significant improvement within group; ↑**, outcomes significant improvement between group. Numbers in bracket represent the drop-out events recorded during follow-up.

**Abbreviations:** ST, strength training; PKT, physiotherapy; mFC, modified fitness counts exercise program; PREP, progressive resistance exercise program; BAL, balance training; RST, repetitive step training; RENEW, Resistance Exercise via Negative Eccentric Work; UPDRS-II, Unified Parkinson’s Disease Rating Scale Part II; UPDRS-III, Unified Parkinson’s Disease Rating Scale Part III; PDQ-39, Parkinson’s Disease Questionnaire; PDQL, Parkinson’s Disease Quality of Life Scale; BDI, Beck Depression Inventory; EEG, electroencephalographic activity.
**Abbreviations:**
- BDI: Beck Depression Inventory
- RST: Repetitive Step Training
- RENEW: Resistance Exercise via Negative Eccentric Work
- UPDRS-II: Unified Parkinson's Disease Rating Scale Part II
- UPDRS-III: Unified Parkinson's Disease Rating Scale Part III
- PDQ-39: Parkinson's Disease Questionnaire
- PDQL: Parkinson's Disease Quality of Life Scale

**Notes:**
- Numbers in bracket represent the drop-out events recorded during follow-up.
- Notes are for personal use only.

**Table 2:** Details of intervention type and outcomes of the articles reviewed

<table>
<thead>
<tr>
<th>Study</th>
<th>Intervention Details</th>
<th>Outcome Type</th>
<th>Physical Parameters</th>
<th>Quality of life parameters</th>
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<td>Limit of stability</td>
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<td>Gait parameters</td>
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<td>Freezing performance</td>
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<td>UPDRS-III</td>
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<td>Aerobic performance</td>
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<td>Flexibility</td>
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<td>UPDRS-II</td>
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<td>PDQ-39</td>
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<td>BDI</td>
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</table>

- **↑:** Outcomes improvement
- **↓:** Outcomes decline
- **=:** Outcomes no change
- ***:** Outcomes significant improvement within group
- ****:** Outcomes significant improvement between group

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consistent with other recent reviews that assessed the effect of strength training on PD.35–45

We would like to point out that, despite the fact that the study intervention included strength training, only six out of twelve articles selected assessed the improvement of muscle strength; moreover, only two studies reported muscle power/strength as primary outcome. Mainly balance, gait parameters, and measure of mobility were assessed. On the
basis of these evidences, it is hard to establish a correlation between strength training and the improvements highlighted. It is worth noting that an improvement in strength correlates positively with physical performance/UPDRS-III results, but the correlation with balance is not well defined.

Despite the encouraging results, our review highlighted the lack of common intent in terms of strength training, control group training, intervention design, and outcomes. Accordingly, further studies are necessary to support the beneficial effects of different types of strength training in PD subjects and to underline the superiority of strength training in people with PD with respect to other training.

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Disclosure
The authors report no conflicts of interest in this work.

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