

Progressive resistance exercise improves strength and physical performance in people with mild to moderate Parkinson's disease: a systematic review

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Question: Does progressive resistance exercise improve strength and measures of physical performance in people with Parkinson's disease? **Design:** Systematic review with meta-analysis of randomised and quasi-randomised controlled trials. **Participants:** People with Parkinson's disease, regardless of gender or level of disability. **Intervention:** Progressive resistance exercise, defined as involving repetitive, strong, or effortful muscle contractions and progression of load as the participant's abilities changed. **Outcome measures:** Measures of muscle strength (maximum voluntary force production) – either continuous (force, torque, work, EMG) or ordinal (manual muscle test) – and physical performance measures: sit-to-stand time, fast and comfortable walking speeds, 6-min walk test, stair descent and ascent, the Activities-specific Balance Confidence scale, Timed Up and Go test, and the Short Physical Performance Battery. **Results:** Four (quasi-) randomised trials were included, three of which reported data that could be pooled in a meta-analysis. Progressive resistance exercise increased strength, with a standardised mean difference 0.50 (95% CI 0.05 to 0.95), and had a clinically worthwhile effect on walking capacity, with a mean difference of 96 metres (95% CI 40 to 152) among people with mild to moderate Parkinson's disease. However, most physical performance outcomes did not show clinically worthwhile improvement after progressive resistance exercise. **Conclusion:** This review suggests that progressive resistance exercise can be effective and worthwhile in people with mild to moderate Parkinson's disease, but carryover of benefit does not occur for all measures of physical performance. The current evidence suggests that progressive resistance training should be implemented in Parkinson's disease rehabilitation, particularly when the aim is to improve walking capacity. **Review registration:** PROSPERO CRD42012002194. [Lima LO, Scianni A, Rodrigues-de-Paula F (2013) Progressive resistance exercise improves strength and physical performance in people with mild to moderate Parkinson's disease: a systematic review. *Journal of Physiotherapy* 59: 7–13]

Key words: Parkinson's disease, Rehabilitation, Systematic Review, Muscle weakness, Physical therapy techniques

Introduction

Parkinson's disease is a chronic neurodegenerative condition that leads to progressive disability (Poewe and Mahlknecht 2009), reduced health-related quality of life, and high healthcare costs (Weintraub et al 2008, Kaltenboeck et al 2011). It is expected that more than 8 million people worldwide may develop Parkinson's disease in the coming decades (Dorsey et al 2007).

The clinical hallmarks of Parkinson's disease include bradykinesia, postural instability, pathological tremor (5–6 Hz), and stiffness in the limbs and trunk (Kwakkel et al 2007). In addition, several studies have provided evidence that people with Parkinson's disease have reduced muscle strength compared to age-matched controls (Allen et al 2009, Cano-de-la-Cuerda et al 2010, Inkster et al 2003, Nallegowda et al 2004). The dopaminergic deficit in Parkinson's disease causes reduction in the excitatory drive of the motor cortex (Lang and Lozano 1998), which can affect motor unit recruitment and results in muscle weakness (David et al 2012). Correlation studies have demonstrated that muscle strength is related to measures of physical performance such as sit-to-stand (Inkster et al 2003, Pääsuke et al 2004) and gait (Nallegowda et al 2004), and to risk of falls (Latt et al 2009) in people with Parkinson's disease.

Progressive resistance exercise has been suggested as a treatment option to preserve function and health-related quality of life in Parkinson's disease (David et al 2012, Dibble et al 2009, Falvo et al 2008). Consequently, some studies have reported increases in strength after progressive resistance exercise training in patients with Parkinson's disease, and that increased strength can translate into improved measures of physical performance such as gait (6-minute walk and gait velocity), stair-climbing and Timed Up and Go test (Dibble et al 2006, Dibble et al 2009). On

What is already known on this topic: Parkinson's disease causes tremor and reduces mobility and functional performance. People with Parkinson's disease also have reduced strength compared to age-matched controls. Progressive resistance exercise improves strength but it is unclear how large this effect is and whether functional performance is also improved.

What this study adds: Progressive resistance exercise has a moderate effect on strength in people with Parkinson's disease. Some measures of mobility and functional performance also improve, including walking capacity and sit-to-stand time. However, this evidence is derived mainly from trials involving people with Parkinson's disease of mild or moderate severity.

the other hand, a recent study has reported improvements in muscle strength without carryover to gait (6-minute walk), mobility (Timed Up and Go test) and balance (Activities-specific Balance Confidence scale) (Schilling et al 2010).

Recent reviews established a rationale for the use of resistance training and highlight findings related to positive effects of progressive resistance exercise in people with Parkinson's disease. However, meta-analysis was not performed, limiting the conclusions about these effects in such patients (Falvo et al 2008, David et al 2012).

Progressive resistance exercise will only be widely implemented in clinical practice as a therapy for Parkinson's disease if it is found to be effective and worthwhile in terms of improvements in physical performance. Therefore, the research questions of this systematic review were:

1. Does progressive resistance exercise increase muscle strength in people with Parkinson's disease?
2. Does progressive resistance exercise improve functional measures of physical performance?

Method

Identification and selection of trials

Searches of CINAHL (1982 to November 2011), PEDro (to November 2011), LILACS (to November 2011), and MEDLINE databases were conducted without language restrictions. Searches were performed using terms recommended by the Cochrane Collaboration related to Parkinson's disease and randomised or quasi-randomised controlled trials and words related to progressive resistance training (see Appendix 1, available on the eAddenda). Titles and abstracts (where available) were displayed and screened by a single reviewer to identify potentially relevant trials. Full text copies of potentially relevant trials were retrieved and their reference lists were screened. The retrieved papers were assessed for eligibility by two independent researchers blinded to authors, journal, and outcomes, using predetermined criteria (Box 1). Disagreements were resolved by discussion with a third reviewer.

Assessment of characteristics of trials

Quality: The quality of included trials was assessed by extracting scores from the Physiotherapy Evidence Database (PEDro) website. Rating of trials in PEDro is carried out by two trained independent raters, with disagreements resolved by a third rater. The PEDro scale assesses the methodological quality and statistical reporting of a randomised trial against 11 individual criteria (Maher et al 2003). One item relates to external validity and the remaining 10 items can be tallied to give a score from 0 to 10 (de Morton 2009).

Participants: Trials involving patients with Parkinson's disease, regardless of gender or level of disability, were eligible. Age, gender, and severity of the disease was recorded using the Hoehn and Yahr Scale, where reported.

Intervention: The experimental intervention had to be progressive resistance exercise, defined as movement against progressively increased resistance. It had to be of a dose that could be expected to improve strength, ie, it had to involve repetitive, strong, or effortful muscle contractions, and it had to be stated or implied that the intensity was progressed as ability changed.

Box 1. Inclusion criteria.

Research design

- Randomised controlled trial, or quasi-randomised controlled trial

Participants

- Patients with Parkinson's disease (any level of severity – Hoehn & Yahr)
- No surgery

Interventions

- Progressive resistance exercise
- Repetitive effortful muscle contractions

Outcomes

- Measure of muscle strength (voluntary force production)
- Measure of physical performance (sit-to-stand time, fast and comfortable walking speeds, 6-min walk test, stair ascent and descent, the Activities-specific Balance Confidence scale, Timed Up and Go test, and the Short Physical Performance Battery)

Comparisons

- Progressive resistance exercise versus no intervention/placebo
- Progressive resistance exercise plus other therapy versus other therapy

Outcome measures: Continuous measures of muscle strength (eg, force, torque, work, EMG) and physical performance (sit-to-stand time, fast and comfortable walking speeds, 6-min walk test, stair descent and ascent, the Activities-specific Balance Confidence scale, Timed Up and Go test, and the Short Physical Performance Battery) were used in the analysis where available. Otherwise, ordinal measures of strength (eg, Manual Muscle Test) were used. When both limbs were trained, the most affected limb was used in the analysis.

Data analysis

Data were extracted from the included trials by a single reviewer and cross-checked by a second reviewer. Information about the method (design, participants, intervention, and measurements) and outcome data (number of participants and mean and standard deviations of strength and measures of physical performance) were extracted. Where information was not available in the published trials, details were requested from the author listed for correspondence.

All trials reported pre-and post-intervention scores. Post-intervention scores were used in the meta-analysis. When the same methods of measurement were used, the effect size was reported as a weighted mean difference with a 95% CI. When different methods were used, the effect size was reported as Cohen's standardised mean difference with a 95% CI. After confirmation of low heterogeneity with the I^2 statistic, the analyses were performed using The MIX–Meta-Analysis Made Easy program (Bax et al 2006, Bax et al 2008) and pooled estimates were obtained using a fixed effects model.

Table 1. PEDro Scale scores for included trials (n = 4).

Trial	Random allocation	Concealed allocation	Groups similar at baseline	Participant blinding	Therapist blinding	Assessor blinding	< 15% dropouts	Intention-to-treat analysis	Between-group difference reported	Point estimate and variability reported	Total (0-10)
Allen et al (2010a)	Y	Y	Y	N	N	Y	Y	Y	Y	Y	8
Dibble et al (2006)	N	N	Y	N	N	N	Y	N	Y	Y	4
Hirsch et al (2003)	Y	N	Y	N	N	N	Y	N	Y	Y	5
Schilling et al (2010)	N	N	Y	N	N	N	N	N	Y	Y	3

Y = yes, N = no; PEDro = Physiotherapy Evidence Database

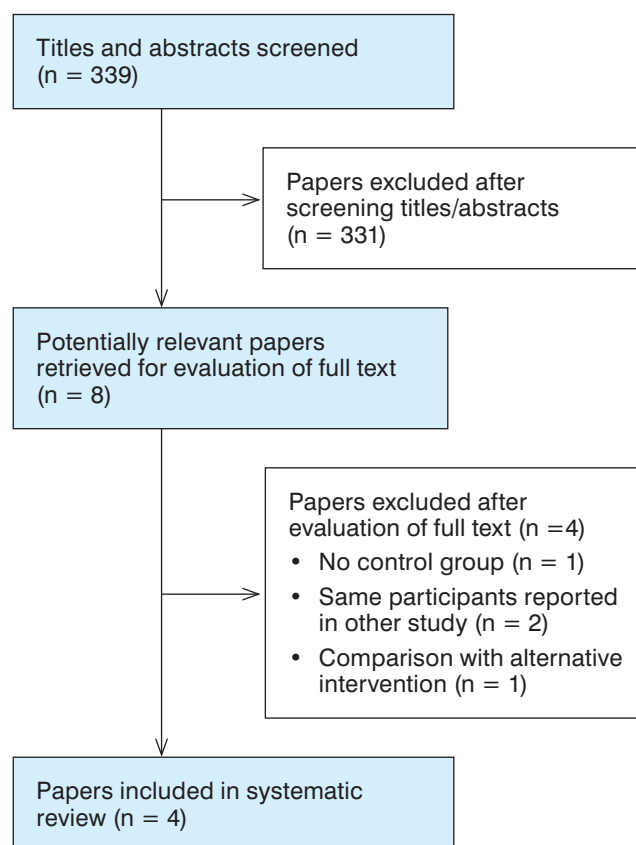


Figure 1. Identification and selection of trials.

Results

Flow of trials through the review

The search strategy identified 339 papers. After screening titles and abstracts, 8 full papers were retrieved. After assessment against the inclusion criteria, 2 randomised trials (Allen et al 2010a, Hirsch et al 2003) and 2 quasi-randomised trials (Dibble et al 2006, Schilling et al 2010) were included in the review. Figure 1 shows the trial selection process.

Characteristics of included trials

Quality: The mean PEDro score of the trials was 5 (Table 1). Two trials were randomised trials that had mean PEDro scores of 8 and 5. True randomisation was carried out in 50% of trials, and concealed allocation, assessor blinding, and intention-to-treat analysis in 25%. No trials blinded participants or therapists, which would have been difficult due to the type of intervention.

Participants: The four trials included 92 people with Parkinson's disease. The mean age of participants across trials ranged from 57 to 75.7 years. The severity of the disease ranged from 1.8 to 2.5 on the Hoehn and Yahr scale. Only three trials reported the Hoehn and Yahr scores (Hirsch et al 2003, Dibble et al 2006, Schilling et al 2010) and only 2 trials reported gender.

Intervention: The trials examined three short-term interventions that ranged from 2 to 3 months (Schilling et al

Table 2. Summary of included trials (n = 4).

Trial	Design	Participants	Intervention ^a	Outcome measures
Allen et al (2010a)	RCT	n = 45 Age (yr) = Exp 66 (SD 10); Con 68 (SD 7) HY = not reported	Exp = Balance exercise + PRE (standing up and sitting down, heel raises in standing, half squats and forward or lateral step-ups onto a block) + Falls prevention advice (booklet) Progression: Initial exercise session: weighted vests 0% or up to 2% of their body weight added to the vest. Subsequent session: the weight in the vest was increased until 15 (hard or heavy) on Borg rating of perceived exertion. 3/week × 24 weeks, 40–60 min Con = Usual care + Falls prevention advice (booklet)	Muscle strength Knee E (strain gauge, <i>kg</i>) Physical performance Sit to stand time (5 reps) (<i>s</i>) Fast walking speed (<i>m/s</i>) Comfortable walking speed (<i>m/s</i>) SPPB (score) Follow-up = 0, 24 weeks
Dibble et al (2006)	Q-RCT	n = 19 Age (yr) = Exp 64 (SD 10); Con 67 (SD 10) HY = Exp 2.5 (SD 0.5); Con 2.5 (SD 0.7)	Exp = PRE of knee leg press + usual care (light calisthenics and stretching, treadmill, cycle ergometer and lifting weights [machines and free weights] with the upper extremities) Progression: Each week 60–70% of the 1 Repetition Maximum weight (13 RPE; somewhat hard) 3/week × 12 weeks, 3 sets of 12 to 15 repetitions Con = Usual care group	Muscle strength Knee E (isokinetic dynamometer, <i>Nm</i>) Physical performance 6-min walk (<i>m</i>) Stair ascent and descent (<i>s</i>) Follow-up = 0, 12 weeks
Hirsch et al (2003)	RCT	n = 13 Age (yr) = Exp 71 (SD 3); Con 76 (SD 2) HY = Exp 1.8 (SD 0.3); Con 1.9 (SD 0.6)	Exp = Balance training + PRE of ankle E, knee E, hip E (Equipment) Progression: 60–80% of 4 Repetition Maximum 3/week × 10 week, 45 min, 1 set of 12 repetitions Con = Balance training, 30 min	Muscle strength Knee E and F, ankle E (pulley system, <i>kg</i>) Physical performance Balance (EquiTest-SOT): Proportion of trials resulting in falls under balance conditions 4 to 6 Follow-up = 0, 10, 14 weeks
Schilling et al (2010)	Q-RCT	n = 15 (9 male) Age (yr) = Exp 61 (SD 9); Con 57 (SD 7) HY = Exp 1.8 (SD 0.3); Con 1.9 (SD 0.3)	Exp = Leg press, seated leg curl, and calf press (Hammer Strength) Progression: 8 repetitions completed for 3 sets: weight ↑5–10% 2/week × 8 weeks, 3 sets of 5 to 8 repetitions Con = Usual care	Muscle strength Knee E (leg press machine, <i>kg</i>) Physical performance 6-min walk (<i>m</i>) ABC (score) TUG (<i>s</i>) Follow-up = 0, 8 weeks

^aOnly the groups related to the current study objectives are shown. RCT = randomised controlled trial; Q-RCT = quasi-randomised controlled trial; PRE = progressive resistance exercise; HY = Hoehn and Yahr; SOT = Sensory organisation test; Exp = experimental group; Con = control group; E = extensors; F = flexors; SPPB = the Short Physical Performance Battery; ABC = Activities-specific Balance Confidence; TUG = Timed Up and Go test; PDQ-39 = Parkinson's disease questionnaire

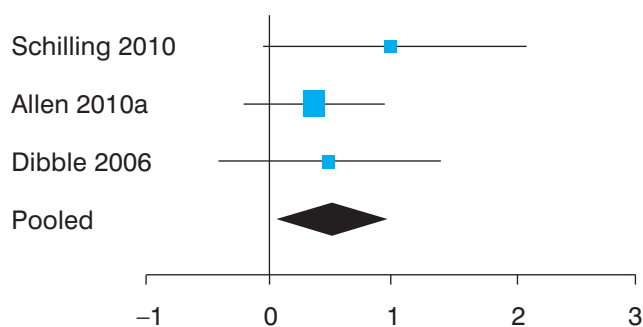


Figure 2. SMD (95% CI) of effect of progressive resistance exercise on strength after 8–24 weeks of training by pooling data from 3 trials ($n = 79$).

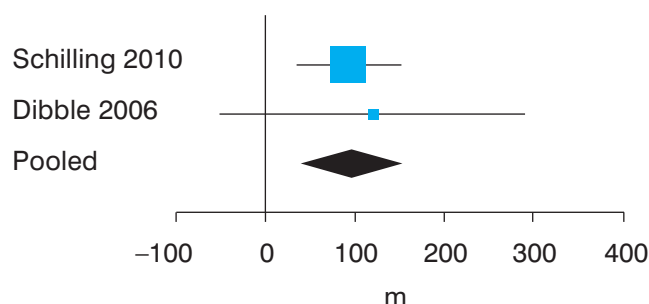


Figure 4. MD (95% CI) of effect of progressive resistance exercise on 6-minute walk test distance after 8–12 weeks of training by pooling data from 2 trials ($n = 34$).

Table 3. Effect of progressive resistance exercise on measures of physical performance.

Trial	Duration of intervention (wk)	Outcome measure	Difference between groups Exp minus Con	
			Mean difference	95% CI
Schilling et al (2010)	8	6-min walk test (<i>m</i>)	93	34 to 152
		ABC Scale (<i>0 worst to 100 best</i>)	6.7	-8.5 to 21.9
		Timed Up and Go test (<i>s</i>)	-1.05	-2.18 to 0.08
Hirsch et al (2003)	10	Balance (EquiTest score)	13	8 to 18
Dibble et al (2006)	12	Stair ascent (<i>s</i>)	-1.5	-3.7 to 0.7
		Stair descent (<i>s</i>)	-1.0	-3.0 to 1.0
		6-minute walk test (<i>m</i>)	122	-51 to 294
Allen et al (2010a)	24	Sit-to-stand time for 5 reps (<i>s</i>)	-1.9	-3.62 to -0.18
		Fast walking speed (<i>m/s</i>)	0.13	-0.08 to 0.34
		Comfortable walking speed (<i>m/s</i>)	-0.01	-0.16 to 0.14
		Short Physical Performance Battery	0.001	-0.17 to 0.18

Exp = experimental group, Con = control group; ABC = The Activities-specific Balance Confidence

2010, Hirsch et al 2003, Dibble et al 2006) and one long-term intervention of 6 months (Allen et al 2010a). Progressive resistance exercise training was carried out over 2–3 days/week. In one trial, intensity was high at 60–80% of the 4 Repetition Maximum with low (1 set of 12) repetitions (Hirsch et al 2003). Two trials used the perceived exertion rating to gradually increase the intensity from very, very light to hard or heavy (Allen et al 2010a, Dibble et al 2006). One trial set the intensity at the maximal effort carried out to volitional fatigue (Schilling et al 2010). Two trials used standard-care controls, ie, people engaged in an existing rehabilitation program appropriate for their disease and impairments, such as walking on a treadmill (Dibble et al 2006) or balance training (Hirsch et al 2003). Participants in the control groups of the remaining trials were instructed to continue their standard care (Schilling et al 2010) or received usual care from their medical practitioner and community services (Allen et al 2010a).

Outcome measures: Strength was reported as a continuous measure of maximum voluntary force or torque production in three trials (Allen et al 2010a, Dibble et al 2006, Schilling et al 2010). The remaining trial only reported submaximal

voluntary force as a strength outcome measure (Hirsch et al 2003).

Physical performance was measured in all four trials. One trial (Schilling et al 2010) used the Timed Up and Go Test, the Activities-specific Balance Confidence scale, and the 6-minute walk test. One trial (Hirsch et al 2003) used the EquiTest Score to measure balance. One trial (Dibble et al 2006) measured physical performance using the 6-minute walk test and the time to ascend and descend stairs. The last trial (Allen et al 2010a) measured sit-to-stand time and walking velocity as separate physical performance outcome measures, along with the Short Physical Performance Battery, which incorporates tests of standing balance, sit-to-stand time, and walking velocity. Table 2 summarises the included trials.

Effect of intervention

Strength: The effect of progressive resistance exercise on strength was examined by pooling post-intervention data from 3 trials involving 79 participants (Dibble et al 2006, Allen et al 2010a, Schilling et al 2010). Progressive resistance exercise increased strength by a standardised

mean difference of 0.50 (95% CI 0.05 to 0.95, $I^2 = 0\%$), as presented in Figure 2. See Figure 3 on the eAddenda for the detailed forest plot. One trial (Hirsch et al 2003) could not be included in the pooled analysis because strength was measured as submaximal, not maximal, voluntary force.

Physical performance: The effect of progressive resistance exercise on the 6-minute walk test distance was examined by pooling post-intervention data from 2 trials (Dibble et al 2006, Schilling et al 2010). Progressive resistance exercise improved walking capacity by 96 metres (95% CI 40 to 152, $I^2 = 0\%$) compared with control, as presented in Figure 4. See Figure 5 on the eAddenda for the detailed forest plot. Four included trials evaluated the effect of progressive resistance exercise on different physical performance outcomes, such as chair rise test and the Short Physical Performance Battery (Table 3). After short-term intervention, statistically non-significant improvements occurred in the Timed Up and Go test (by 1 second), the Activities-specific Balance Confidence scale (by 7 points), and stair ascent/descent time (by about 1 second). After long-term intervention, the Allen et al (2010) trial reported a statistically significant improvement of 1.9 seconds in the sit-to-stand time. The other physical performance measures in that trial showed non-significant improvements, with 0.13 m/s higher fast walking speed, 0.01 m/s lower comfortable walking speed, and 0.001 points higher on the Short Physical Performance Battery.

Discussion

This systematic review provides evidence that progressive resistance exercise can improve strength and several measures of functional ability as well in Parkinson's disease. The results of this systematic review quantify the results of a recent narrative review suggesting positive effects from progressive resistance exercise for patients with Parkinson's disease (David et al 2012). The mean PEDro score of 5 for the trials included in the current review represents moderate quality, suggesting that the findings are believable. This review shows that the implementation of progressive resistance exercise produced a positive and moderate effect size on strength in people with Parkinson's disease (SMD = 0.50). The reasonably consistent results across the trials may reflect that all trials administered progressive resistance exercise at an intensity and duration recommended by the ACSM (2002). The trials included in the current review averaged 15 weeks of progressive resistance exercise (range 8 to 24), and the intensity measured by perceived exertion ratings of 13 (somewhat hard) (Dibble et al 2006) and 15 (hard or heavy) (Allen et al 2010a) was adequate to produce a training effect. Ratings of perceived exertion of 13 and 17 correspond to around 66% and 80% of the voluntary maximal force production, respectively (Borg et al 1970, Lagally and Amorose 2007). Therefore, the perceived exertion ratings of the included trials represented values within the intensity recommended by the American College of Sports Medicine (2002) guidelines for novices (60–70% of 1 Repetition Maximum). These results suggest that therapists should consider including progressive resistance exercise in exercise programs to increase strength in people with mild to moderate Parkinson's disease.

Walking capacity is determined as the distance a person is capable of walking over a long period of time, typically for 6 minutes, as in the 6-minute walk test (Reybrouk

2003). The progressive resistance exercise increased the 6-minute walk test distance by 96 metres. An improvement of 82 metres in the same test has been shown to be meaningful in people with Parkinsonism (Steffen and Seney 2008). However, one of the two trials included in this meta-analysis used progressive resistance exercise associated with exercises such as walking on a treadmill. Consequently, this intervention may have produced task-specific training for gait, thereby increasing the measured effects of the progressive resistance exercise on the walking tests. Therefore, these results should be interpreted cautiously. Further research is required to determine if progressive resistance exercise programs alone can improve the 6-minute walking capacity in people with Parkinson's disease. Although this result is encouraging, the effects of progressive resistance exercise on the physical performance of this population remain unclear.

Some measures of physical performance used in the trials showed non-significant improvement, such as the 7% change in the Activities-specific Balance Confidence scale and the 3% change in walking speed. This minor improvement in physical performance may have been the result of the mild disability of the participants based on their average Hoehn and Yahr scores, which ranged from 1.8 to 2.5. These results are in line with the results of Buchner et al (1996), which suggested that small changes in physiological capacity could have substantial effects on performance in frail adults, while large changes in capacity have little or no effect in mild disability. This has been suggested in stroke patients (Ada et al 2006) and in children with cerebral palsy (Scianni et al 2009), and it may also be true in people with Parkinson's disease. In the trial by Allen et al (2010b), muscle power was more strongly associated with walking velocity and falls than muscle strength in people with mild to moderate Parkinson's disease. It is possible that it is not just the force of muscle contraction that determines the ability of people with Parkinson's disease to perform physical activities; the muscle power may be another important contributor.

The results of this systematic review have suggested that progressive resistance exercise can be effective and worthwhile in people with mild to moderate Parkinson's disease, but carryover of these benefits may not occur in all measures of physical performance. We recommend that progressive resistance exercise should be implemented into clinical practice as a therapy for Parkinson's disease, particularly when the aim is improving walking capacity in such people. ■

eAddenda: Appendix 1, Figure 3 and Figure 5 available at jop.physiotherapy.asn.au

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