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Reviews

Parkinson's Disease and Resistive Exercise: Rationale, Review, and Recommendations

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Abstract: Individuals with Parkinson's disease (PD) are not only burdened with disease-specific symptoms (i.e., bradykinesia, rigidity, and tremor), but are also confronted with age-associated progressive loss of physical function, perhaps to a greater extent than neurologically normal adults. Suggestions for the inclusion of resistive exercise into treatment to attenuate these symptoms were made over 10 years ago, yet very few well controlled investigations are available. The objective of this review is to establish a clear rationale for the efficacy of resistance training in individuals with PD. Specifically, we highlight musculoskeletal weakness and its relationship to function as well as potential training-induced adaptive alterations in the neuromuscular system. We also review the few resistance training interventions currently available, but limit this review to those investigations that provide a quantitative exercise prescription. Finally, we recommend future lines of inquiry warranting further attention and call to question the rationale behind current exercise prescriptions. The absence of reports contraindicating resistive exercise, the potential for positive adaptation, and the noted benefits of resistance training in other populations may provide support for its inclusion into a treatment approach to PD. © 2007 Movement Disorder Society

Key words: Parkinson's disease; resistive exercise; exercise training; muscle strength.

Parkinson's disease (PD), a progressive neurodegenerative disorder, is manifested by a loss of dopaminergic neurons from the substantia nigra pars compacta thereby disrupting the basal ganglia circuitry. As a result, individuals present with tremor, rigidity, progressive bradykinesia, and postural instability.[1] Currently, the primary treatment option is administration of anti-Parkinson medications (e.g., levodopa). Unfortunately, levodopa loses effectiveness over time and leads to the appearance and development of dyskinesias.[2] Thereafter, patients and health care providers may consider neurosurgical options (i.e., deep brain stimulation). As these treatments come with obvious risks and limitations, some authors have suggested alternative treatment options to slow disease progression and stimulate movement control.[3] One such option, physical exercise, is generally accepted to improve physical performance and activities of daily living (ADL).[4]

Physical exercise has demonstrated a reduction in mortality rate in individuals with PD[5] and, albeit modestly, a protective effect for PD risk.[6] More immediate effects include improved motor performance, cognitive and functional ability.[7] Specific to PD, these findings may be a result of exercise stimulating the synthesis of dopamine via increased serum calcium levels (for review, see Sutoo and Akiyama 2003).[8] Although this hypothesis is derived from animal models, it is supported by earlier work demonstrating a monotonic relationship between dopamine activity and aerobic exercise workload.[9] While the precise mechanism has not yet been identified, robust effects of exercise are well recognized in this population and inclusion of exercise in the treatment of PD is encouraged.

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Apart from disorder-induced symptoms of PD, individuals are also confronted with the age-associated declines in physical activity, strength, and quality of life. This has led some investigators to denote PD as *accelerated aging*.[10,11] This term may appear appropriate in light of reduced physical activity,[12] greater muscle weakness,[13–15] and lower bone mineral density (BMD)[16] when compared to neurologically normal age-matched individuals. Ultimately, these age- and disease-associated impairments often confer a reduced quality of life.[17] However, the progression of these losses may be attenuated through physical exercise, especially when the exercise includes a resistive component.

Despite recommendations for the inclusion of strength training into PD treatment more than 10 years ago,[10,18] very few well-controlled investigations exist on this topic. This is unfortunate as resistance training in neurologically normal older adults has repeatedly been shown to increase muscle mass, strength, and function,[19] even in nonagenarians.[20] The purpose of this review is to reevaluate the rationale for resistance training, analyze the existing literature, and suggest potential future interventions.

RATIONALE FOR RESISTIVE EXERCISE

Muscle Weakness

Corcos et al.[21] maintain that investigating muscle strength in individuals with PD is essential as strength influences the manner in which muscles are activated and movement speed, and weakness can compromise ability to perform ADLs. Both the former and latter have been reviewed in detail elsewhere regarding normal aging,[19] yet whether PD contributes uniquely to this process is equivocal. Beradelli et al.[22] identified muscle weakness as a secondary cause of bradykinesia due to increasing evidence demonstrating individuals with PD to be weaker than neurologically normal adults in a variety of muscle groups,[23-25] and muscle weakness has been suggested to be a primary symptom of PD.[26] In addition, muscle weakness is recognized as one of the factors contributing to postural instability.[27] Despite these suggestions, some ambiguity remains as to whether individuals with PD are actually weaker than neurologically normal adults due in part to methodological issues, disease severity, and medication status. Medication status (i.e., ON or OFF) is of considerable importance as strength is reduced during periods of withdrawal.[21,27,28] Pedersen and Oberg[28] have suggested that strength measurements may be an appropriate evaluation method of pharmacological therapy as reductions in strength were found to be correlated with disability changes following withdrawal of medication.

Strength may also be delineated into time-related components. It appears that longer latencies are necessary for muscle force production and relaxation in individuals with PD.[14,21] These obvious time-related decrements of force production appear to be related to the pathophysiology of bradykinesia and have led some researchers to stress the importance of the rate of force development for monitoring motor control in PD.[14] Maximal or absolute strength has been shown to be significantly correlated with rate of force development in older adults[29] and individuals with PD,[21] but this has not been noted in all investigations.[14] Interestingly, when controlling for strength, no differences were observed in contraction time of the elbow flexors between individuals with PD and neurologically normal adults.[30] Presumably, if this relationship between strength and speed is robust and trainable, responses to postural disturbances (e.g., balance) and functional capacity may be improved. Some authors have suggested that maximal strength[31] and the rate of force production[32] of the lower extremities is critical during a period of compromised balance, whereby sufficient force is necessary to orient the body's center of mass over the base of support in a short period of time. Elaboration of muscle weakness as it relates to PD is discussed below ("Cross-Sectional Investigations") and presented in Table 1.

Central Manifestations

Cortical afferents arrive at the striatum (caudate and putamen) in anatomically distinct locations, thereby creating unique circuits.[33] In the basal ganglia-thalamocortical motor circuit, afferents from motor regions of cortex (M1, pre-motor, supplementary, and somatosensory) terminate on the striatum (caudate and putamen), which also receives dopaminergic innervation from the substantia nigra pars compacta.[34] Inhibitory projections from the striatum terminate on the globus pallidus external (indirect pathway) and internal (direct pathway) segments, which in turn sends inhibitory projections to the ventral anterior and lateral thalamus. Inhibitory outputs from the globus pallidus internal segment have been suggested to serve two distinct functions: (1) focused selection of the desired movement and (2) inhibition of competing movements.[35]

Functional anatomists suggest motor cortices are not fully activated secondary to abnormal drive from the basal ganglia to the thalamus, thereby impeding the facilitation of desired movement.[36] This impaired cortical activation can lead to inability to sufficiently activate motoneuron pools, thereby affecting recruitment and dis-

charge rate.[18] This may ultimately result in reduced neural drive (i.e., EMG amplitude), and general muscle weakness.[10] Ultimately, these clinical findings may contribute to the progressive deterioration in function observed in these patients. Consistent with these reports are electroencephalographic recordings (e.g., Bereitschaftspotential) reporting underactivation of the cortex in areas ascribable to movement preparation, planning, and execution.[37] Dick et al.[37] also demonstrated that differences between patients and neurologically normal adults were dependent on dopaminergic function. Therefore, it appears that peripheral manifestations (i.e., decreased EMG activity) are centrally-mediated, which may contribute to diminished muscle strength. These observations, in concert with the noted increase in strength due to medication,[38] demonstrate that weakness is clearly due at least in part to central nervous system function.[26]

Following short-term strength training, significant gains in maximal force production occur without concomitant muscle hypertrophy. It is generally agreed that neural adaptations are responsible for this enhancement, which manifests as increased amplitude of the surface electromyographic signal.[39] Griffin and Cafarelli[40] suggest this increase in neural drive, along with lower recruitment thresholds observed subsequent to training, may reflect adaptations at the level of the central nervous system. To quantify this increase in neural drive, some investigators superimpose a supramaximal electrical pulse to contracting muscle (i.e. interpolated twitch) to determine whether the motoneuron pool has been sufficiently activated to produce maximal force.[41] More recent techniques, such as transcranial magnetic stimulation (TMS), have also been used to quantify voluntary activation.[42] Both interpolated twitch and TMS methods may be useful to investigate the potential for chronic adaptation induced by resistance training[43] as well as estimate how well the brain is able to drive muscle contraction.[41] However, TMS methods are unable to definitively establish whether resistance training is capable of affecting the functional organization of the cerebral cortex,[44] despite the well established changes induced via motor learning.[45]

Evoked spinal reflexes, Hoffman-reflex (H-reflex) and V-wave, have also been used following resistance training to assess the excitability of the α-motoneurons and the magnitude of output from descending central pathways, respectively.[46] Following 14 weeks of strength training, Aaagard et al.[46] demonstrated parallel increases in isometric strength and H-reflex and V-wave amplitudes, indicative of enhanced supraspinal drive and motoneuron excitability. Additional indirect lines of evidence pointing toward centrally mediated neural adaptations have also been demonstrated in the literature, including reductions in agonist-antagonist coactivation,[47] and cross-education (i.e., transfer of unilateral training effects to the contralateral limb).[48] It remains to be established whether these adaptations are attainable in individuals with PD. In brief, resistance training may be of therapeutic value to individuals with PD to enhance neural drive to the agonist as well as decrease coactivation, both contributing to improved strength and movement control.

Bone Health

A recent review[49] identified PD as a secondary cause for osteoporosis. Several investigations have associated PD with low BMD,[16] but exist with noteworthy limitations including selection bias, reporting only single BMD sites, and not controlling for influencing external factors.[16] Perhaps the greatest support to date is derived from the Osteoporotic Fractures in Men Study Group (MrOS), where lower BMD at the hip and spine was associated with PD irrespective of physical activity and neuromuscular function.[16] However, PD status was based on self-report questionnaires. Authors from the MrOS promote the potential to lower fracture risk in persons with PD via physical training aimed at reducing bone loss and/or promoting favorable bone augmentation. Consistent with this approach, loads applied to the bone via the muscular system in addition to loading the axial skeleton, which can be accomplished through resistive exercise, have direct effects on bone formation and remodeling, a hallmark of Wolff's Law.[50]

Some investigations have reported low BMD in individuals with PD at the hip[51] and low back,[52] which may be related to the three-fold greater incidence of hip fracture in PD patients compared to age- and sex-matched controls.[53] This high incidence rate of fracture is of serious concern due to its association with disability, pain, and especially mortality.[54] This concern is amplified due to previous reports from Sato et al. demonstrating vitamin D deficiency (i.e., 25-hydroxyvitamin D levels less than 10 ng/mL) in individuals with PD, which may induce conditions of hyperparathyroidism and exacerbate loss of BMD.[55] Compensatory hyperparathyroidism is likely manifested by a lack of exposure to sunlight. This is consistent with previous reports of individuals with PD performing less physical activity,[12] especially after the initial appearance of symptoms.[56] Subsequent well-controlled investigations by Sato et al.[57,58] demonstrated the efficacy of administering biophosphonates (2.5–5 mg/day) and ergocalciferol (1000

IU/day) for 2 years in elderly men and women with PD to improve BMD and reduce hip fracture risk.

The American College of Sports Medicine (ACSM) maintains the efficacy of weight-bearing exercise to promote bone health across the lifespan,[59] and weight-bearing physical activity programs are widely used in the prevention and treatment of osteoporosis.[60] Several reviews and meta-analyses in regards to neurologically normal older adults are available on the utility of resistive exercise.[61–63] In brief, it is intuitive and encouraged to pursue progressive resistive exercise as a viable treatment to improve bone parameters, but an optimal strategy remains to be determined. Presumably, individuals with PD may stand to derive equal benefit from resistive exercise. Moreover, the combination of pharmacotherapy (e.g., biophosphonates, vitamin D) and resistive exercise may confer an even greater benefit for individuals with PD. However, to the knowledge of these authors, such investigations (i.e., combined treatment and/or resistance training alone) are surprisingly absent from the literature regarding bone health outcomes in individuals with PD.

Relationship to Function

Navigating stairs and rising from a chair are performed at an effort level close to maximal force production capabilities in healthy older adults,[64] likely due to substantially lower maximum strength in this group. This group also has inefficient activation (e.g., increased drive to both agonist and antagonist), which likely contributes to fatigue, thereby limiting ADLs. Although Hortobagyi et al.[64] only considered neurologically normal adults, the altered activation patterns they observed have been reported in PD.[10] In addition, fatigue is more pronounced in patients with poorer functional capacity,[65] and is considered one of the three worst self-reported symptoms of PD.[66,67] These myoelectric disturbances and altered bioenergetics are likely associated with muscle weakness in this population, collectively affecting ADLs. As most ADLs involve the lower extremities (i.e., chair-rise, ambulation), weakness of this musculature is of considerable interest, and may also compromise the ability to mount a defense against a postural disturbance.[31,32]

Rising from a chair is an objective measurement used to evaluate functional limitations and is suggested to be a major factor in independence and quality of life in individuals with PD.[68] Sit-to-stand performance in this population is impaired, particularly the time necessary to transition from forward flexion to an extension direction.[69] Further, biomechanical analysis of this task reveals reduced torques and rate of force development at the hip, knee, and ankle as compared to controls.[69] Other investigators have reported a correlation between sit-to-stand time and hip strength ($r = -0.71$),[13] and bilateral leg extension strength ($r = -0.63$)[14] in individuals with PD. Presumably, enhancing the maximal strength and rate of force production in these patients may improve sit-to-stand time. This has recently been observed in consecutive sit-to-stands (e.g., 11% improvement) following 12 weeks of moderate resistance exercise and creatine monohydrate supplementation in individuals with PD (See Table 2).[70]

Gait disturbances are prevalent in PD and are one of the most critical motor impairments[71] as they contribute to falls, loss of independence, and institutionalization.[72] Individuals with PD generally have slower gait velocity, increased stride variability, and increased double support time.[73,74] Increased time spent in double support is associated with increased falls in the elderly, and it may be that those with poor postural stability use increased double support as a compensatory mechanism to help avoid falls.[75] Other features of parkinsonian gait, specifically festination and freezing, may also predispose individuals to falls.[76] Therefore, a clinical assessment of gait is critically important to the welfare of the patient, particularly as disease severity progresses.

Scandalis et al.[73] stated that strength training is generally assumed to improve gait, which has been observed in neurologically normal older adults,[77] yet few investigations are available pertaining to PD. The linear relationship between leg strength and gait speed has been well defined in respect to healthy older men and women, with composite leg strength explaining 17% of the variance in gait speed.[78] Interestingly, nonlinear regression analysis demonstrated that in those with less strength it explained a greater proportion of variance (22%). Recently, Nallegowda et al.[27] demonstrated strength of the ankle, hip, and trunk to be positively correlated with gait velocity in individuals with PD. Similar to neurologically normal adults, ankle strength explained 15% of the variance in gait speed in individuals with PD while ON medication.[27]

Scandalis et al.[73] showed that a simple resistive exercise program increased gait speed in persons with PD, so much so that there was no significant difference in gait speed between persons with PD and controls at the end of the 8-week study. In simple gait tasks, the role of strength and utility of strength training appear to be evident. Even in more complex tasks, such as gait while negotiating obstacles, 24 weeks of progressive resistance training demonstrated 5–15% improvements in stride velocity during obstacle crossing in healthy older adults. Such results were concomitant with strength improve-

ments of 197–285%.[79] These relationships remain to be determined in PD.

CROSS-SECTIONAL INVESTIGATIONS

Several descriptive studies are available that analyze force production capabilities in individuals with PD.[21,26,80,81] These studies unfortunately do not compare persons with PD to neurologically normal age- and sex-matched controls. There appears to be a general agreement that the rate of force production is decreased in individuals with PD, consistent with bradykinesia. To understand the normal effects of aging, comparison with neurologically normal adults is important and is presented in Table 1. Although previous reports have demonstrated weakness to be more pronounced in the more affected limb of individuals with marked laterality of symptoms,[26,80] this was not observed for the investigations presented in Table 1.[13–15,27,82–84] Observed inter-limb differences appear to be velocity-dependent, such that strength differentials between the two sides are more pronounced at greater velocities.[81] Pedersen et al.[83,84] compared high velocity isokinetic measurements of the dorsiflexors between individuals with PD and controls, but no delineation for more or less affected limbs was made.

From Table 1, individuals with PD appear weaker and slower than neurologically normal adults across a spectrum of testing modalities (i.e., isometric, isokinetic, isotonic) and across muscle groups of the upper- and lower-extremities. Interestingly, Pedersen et al.[83,84] examined ankle dorsiflexion strength during concentric and eccentric (i.e., shortening or lengthening) muscle actions separately. Torques for both action types were measured at five[84] or three[83] different velocity settings. As expected, power (Nm/s) decreased proportionally with increasing movement velocity for concentric actions (30°/s = 1,882, 120°/s = 918, 180°/s = 647), which has been supported elsewhere.[80] However, this relationship was not observed for eccentric actions as power remained constant (30°/s = 2,480, 120°/s = 2,628, 180°/s = 2,833). These relationships were also demonstrated in the companion study[84] and earlier work by the same authors.[28] Despite the preservation of eccentric torque, or power, individuals with PD remained weaker than controls. This finding has previously been demonstrated in neurologically normal adults whereby eccentric strength appears to be less influenced by aging.[85] These authors imply that a resistive exercise program composed of a large eccentric component may provide a unique treatment option. Eccentrically biased exercise may be a viable alternative given the muscle can withstand greater forces while lengthening rather than shortening, thus performing more work (work = force × distance). The ability to produce more work via eccentric training rather than concentric training has been recognized previously,[86] and has recently been exploited in individuals with PD.[87]

RESISTANCE TRAINING INTERVENTIONS

Research syntheses evaluating the utility of physical therapy[7] or physical exercise[4] as an appropriate supplement to pharmacological treatment have been documented previously and generally support their inclusion. However, two comprehensive reviews[88,89] concluded there is insufficient evidence to support or refute any form of physiotherapy. These authors present a broad definition of physiotherapy that includes a variety of treatment techniques that may or may not include resistive exercise. Additionally, many investigations fail to adequately quantify the training intervention, which makes interpretation of resistive exercise studies extremely difficult. Said investigations utilize descriptors such as "strengthening exercises" or "exercises for improving strength " to describe the protocol employed.[90,91] This brevity ultimately clouds the interpretation of findings and does not allow for meaningful comparison. To circumvent these limitations, attention must be paid to the acute variables that comprise a resistive exercise prescription (e.g., mode, volume, temporal expression of force, multi- vs. single-joint exercises, rest periods, etc.). Herein, we review those investigations that provide a detailed exercise prescription and do not include those considered ambiguous or those that included only subjective outcomes.[90-93] To the knowledge of these authors, only five well controlled clinical trials are available at the time of this review, and are presented in Table 2.

Postural disturbance or compromised balance in general is considered an intrinsic risk factor for falling in Parkinson's disease.[94] In attempts to improve postural stability, Toole et al.[31] and Hirsch et al.[95] combined 10 weeks of lower extremity progressive resistance training (PRT) and exercises performed on unstable surfaces to promote balance and strength. Although these investigations were similar, Toole et al.[31] randomly assigned patients to treatment PRT and balance exercises (n = 4) or control (no-exercise; n = 3) groups, whereas Hirsch et al. (2003) assigned subjects to treatment (PRT/balance; n = 9) and quasi-control (balance only; n = 6) groups. Exercise volume was greater for Toole et al.[31] than Hirsch et al.[95] (90 repetitions per muscle group per week versus 36 reps/week), but were performed at a lower intensity (60% of 4 repetition maximum [RM] versus 80% of 4RM). As higher loads are widely known to foster the greatest training effect,[96] it is not surprising that the treatment group of Hirsch et al.[95] experienced

TABLE 1. *Cross-sectional investigations (PD and control comparisons)*

Reference	Subjects	Muscles tested/measurement device	Results	Comments
Paasuke et al., 2002[15]	1) 14F PD (72.6 yrs, 1-3 HY)	Knee extensors; UL Isometric knee extension; ON (knee = 90°, hip = 110°)	PD had ↓ MF, ↓ RFD than controls	1) PD patients more deficient in rate rather than absolute force
	2) 12F Con (72.8 yrs)	Analyzed best of three trials	No difference for relative MF	2) RFD reflected in longer chair rise time 3) No strength asymmetry
Paasuke et al., 2004[14]	1) 12F PD (74.3 yrs, 1-3 HY)	Leg extensors; UL and BL Isometric leg extension; ON (knee = 120°, hip = 110°, ankle = 60°)	PD had ↓ BL MF, ↓ relative MF, ↓ RFD than controls	1) PD patients were generally weaker (rate and max) 2) Longer chair rise time
	2) 16F Con (71.7 yrs)	Analyzed best of three trials		3) No strength asymmetry
Koller and Kase, 1986[82]	1) 21M PD (62.5 yrs, 1.2 HY)	Wrist, arm, knee; BL Isotonic measurement on isokinetic device (5 rev)	PD had ↓ BL strength for all muscles than controls	1) PD patients had average 3.1 yrs of symptoms, yet still were weaker
	2) 21M Con (65.2 yrs)	Three patients did not take medication All other patients were ON	PD had ↑ endurance in knee, L wrist, and L arm than controls	2) Greater endurance is likely a function of the reduced load 3) No strength asymmetry
Inkster et al., 2003[13]	1) 10M PD (64.1 yrs, 2.1 HY)	Hip (BL) and knee (UL) extensors Isokinetic hip and knee extension; ON and OFF (45°/s)	PD had ↓ hip and knee MF (torque) than controls	1) No difference ON and OFF for knee torque, but not hip torque 2) Hip torque explained 50-64% variance in sit-to-stand times
	2) 10M Con (65.5 yrs)			3) No strength asymmetry
Pedersen et al., 1997[84]	1) 14M, 11F PD (63.7 yrs, 1-3 HY)	Ankle dorsiflexors; UL Isokinetic ankle dorsiflexion; medication? (0, 15, 30, 120, 180°/s)	PD had ↓ concentric torque at all velocities than controls	1) Eccentric torque is well preserved in PD, especially for women
	2) 19M, 18F Con (60.4 yrs)		Only men had ↓ eccentric torque than controls	
Pedersen et al., 1997[83]	1) 7M, 3F PD (62.3 yrs, 1-3 HY)	Ankle dorsiflexors; UL Isokinetic ankle dorsiflexion; ON Concentric, eccentric, SSC; (30, 120, 180°/s)	PD had ↓ torque for all velocities and muscle action types than controls	1) PD had lower contraction efficiency 2) Authors suggest eccentric torque might be important for dynamic movements
	2) 7M, 4F Con (66.0 yrs)	EMG of anterior tibialis and gastrocnemius	PD had ↑ iEMG for all velocities and conditions except SSC at faster velocities than controls	
Nallegowda et al., 2004[27]	1) 25M, 5F PD (57.7 yrs, 2.7 HY*) HY* = OFF	Ankle dorsi- and plantar-flexion; UL Hip flexion and extension Trunk flexion and extension (90, 120, 150 °/s)	PD had ↓ torque for all measures than controls (ON and OFF) except left ankle dorsiflexion and trunk flexion (ON was NS)	1) PD were weaker at ankle, hip, and trunk for most all measures, regardless of medication 2) Ankle strength for PD correlated with gait velocity
	2) 25M, 5F Con (age-matched)	ON and OFF testing Only concentric torque reported	PD ON had ↑ torque for all measures except right ankle plantarflexion (120°) and dorsiflexion (90°)	3) Authors suggest muscle weakness is a factor for postural instability

M = male, F = female, Con = neurologically normal, HY = Hoehn and Yahr stage, UL = unilateral, BL = bilateral, MF = maximal force, RFD = rate of force development, ↓ = lower, ↑ = greater, ON = patients had taken parkinsonian medication, OFF = patients were on an overnight withdrawal of medication, (?) = unknown, NS = not significant.

large composite strength gains (52%) compared to modest increases (7%) for Toole et al.[31] It should be noted that Toole et al.[31] used isokinetic strength testing, which is not specific to the isotonic training, and may have contributed to moderate training effects.[97] In general, it appears that PRT was effective in improving strength and balance in these experiments and gains were still present 4 weeks after cessation of exercise.[95] The investigation used by Hirsch et al. in Ref. 95 is the only investigation to monitor detraining effects (e.g., knee flexors/extensors) following an intervention in this population.

In the only clinical intervention to include age- and sex-matched healthy controls, Scandalis et al.[73] trained

controls and individuals with PD for 16 sessions. Interestingly, no differences were evident between the groups at baseline or after 8 weeks of training for leg curl, extension, press, and toe raise performance. As both groups improved total exercise volume (repetitions × load) with training, authors suggest that these findings (e.g., no differences at post-testing) demonstrate that individuals with PD can experience improvements similar to those of neurologically normal controls. These findings should be interpreted cautiously as groups were unequal in size (PD = 14, control = 6), the training intensity was moderate, and individuals with PD were likely at an early-stage of their disease progression (Hoehn and Yahr average = 2.5). This study also analyzed gait and observed group differences for stride length and hip velocity that were shorter and slower in individuals with PD at baseline, respectively. After training, only those with PD significantly increased stride length (14.4%) and hip velocity (7.5%). Hip velocity after training for individuals with PD was not different from that of controls. Although this study demonstrated moderate training effects on gait and strength, it must be considered in light of the training protocol which consisted of very few sessions (e.g., 16 sessions) of light-moderate intensity. These improvements further support the significant positive correlation observed between ankle strength and gait velocity in individuals with PD without any intervention.[27]

Dibble et al.[87] had patients perform nontraditional resistance training (eccentric semirecumbent cycling) in addition to standard care exercises for 12 weeks. Subjects were assigned to one of two groups that differed only in their lower extremity resistive exercise (i.e., eccentric cycling or traditional). Eccentric cycling is a model used previously with great success by LaStayo et al. with older adults[86] and cardiac rehabilitation patients.[98] Eccentric cycling offers the opportunity to perform substantial muscular work at low metabolic costs.[86] Further, this allows individuals with PD, or any person, to experience higher workloads otherwise unattainable through traditional modes of exercise. In a traditional exercise, such as a knee extension, the knee is extended against a resistance (concentric) and then flexed back to its starting position (eccentric). To perform multiple repetitions against a constant external resistance, the individual must be able to overcome this resistance during the concentric portion of the exercise. Therefore, it is concentric strength that inevitably creates a ceiling for potential adaptation by limiting workload.[99] In Dibble et al.,[87] individuals assigned to the experimental group (i.e., eccentric cycling and standard care) experienced significant muscle hypertrophy of the quadriceps (6%) in concert with increased knee extensor torque (24%) as well as significant improvements in ambulation and function. Based on these data, it may not be prudent to replace traditional lower extremity resistive exercise with eccentric cycling as no effort was made to match groups on total work. However, eccentric cycling appears to offer a viable treatment option that is both safe and feasible for individuals with PD.[100]

The National Institute for Neurological Disorders and Stroke (NINDS) recently embarked on the largest clinical trial to date for Parkinson's disease, which will be conducted at 51 sites and will evaluate the potential neuroprotective benefits of creatine monohydrate.[101] Creatine (Cr) is a popular ergogenic compound often used in combination with resistive exercise, although NINDS will examine only the efficacy of the compound alone. Nevertheless, a recent randomized placebo-controlled trial combined Cr with PRT for 12 weeks in individuals with PD. All subjects performed exercises for the entire body of moderate to high intensity (70%1RM). Placebo and Cr-supplemented groups both experienced significant improvements in 1RM (9–23%), muscle endurance, accrual of lean body mass, and decreased sit-to-stand times. The Cr-supplemented group demonstrated larger gains for chest press and biceps curl 1RM and sit-to-stand time. Albeit modest improvements may be attributable to Cr, perhaps gains may have been limited due to intervention duration (24 sessions) and training volume (1 set per muscle group).

Investigators are challenged when designing resistive exercise prescriptions that provide a sufficient stimulus for adaptation while considering the exercise capacity of individuals with PD. Fatigue is recognized as one of the major nonmotor symptoms of PD,[102] and may significantly limit exercise capacity. The etiology of fatigue in PD is not well understood, but maybe related to mitochondrial dysfunction. Loss of mitochondria occurs with normal aging thereby impacting exercise performance (i.e., fatigue) and is reversible to some degree through exercise training.[103] Mitochondrial dysfunction contributes to the process of neurodegeneration evident in PD, although it is unclear whether this translates to other tissues such as skeletal muscle.[104]

RECOMMENDATIONS

Resistance training for individuals with PD has generally been shown to be effective in increasing strength, and in some cases mobility, but thus far has been conservatively approached. The investigations presented in Table 2 are short in duration (16–36 training bouts) and frequency (2–3 days/week), and often include only one set of exercises per muscle

TABLE 2. *Resistance training interventions*

Reference	Subjects	Resistance training program	Duration	Outcome measures	Major findings
Toole et al., 2000[31]	1) Bal + RT—4 PD (72.5 yrs, 2.3 HY)	Machine knee flx/ext, ankle inversion 3 × 10 reps at 60% 4RM; 6 s contraction	30 sessions (3 days/wk, 10 wks)	Isok torque knee flex/ext (90°, 180°/s) Isok ankle inversion (120°/s)	1) Modest ↑ strength, likely due to Con subjects performing worse pre–post
	2) Con—3 PD (70.7 yrs, 2.3 HY)	Load readjusted weekly (Balance exercises also performed)		Tested ON	2) Training improved equilibrium
Scandalis et al., 2001[73]	1) RT (PD)—14 (65.5 yrs, 2.5 HY)	Machine leg press/flx/ext, calf raise, ab crunch 1 × 12 reps at 60% 1RM	16 sessions (2 days/wk, 8 wks)	Gait Exercise volume Abdominal endurance	1) Individuals with PD showed similar performance and gains to healthy controls
	2) RT (Con)—6 (62.5 yrs)	Load increased by 5 lbs when 12 reps reached (Both groups performed RT)		Tested OFF	2) Patients, but not controls, had increased stride length and gait velocity
Hirsch et al., 2003[95]	1) Bal—9 PD (75.7 yrs, 1.9 HY)	Machine knee flx/ext, plantarflexion 1 × 12 reps @ 60% 4RM; 6 s contraction	30 sessions (3 days/wk, 10 wks)	4RM knee flx/ext, plantarflexion	1) Bal + RT had greater ↑ strength (52%) compared to Bal (9%)
	2) Bal + RT—6 PD (70.8 yrs, 1.8 HY)	Load increased to 80% in wk 2 and readjusted (Both groups perform balance exercises)		Tested ON	2) Both improved balance
Dibble et al., 2006[87]	1) RT—10 PD (64.3 yrs, 2.5 HY)	Eccentric recumbent cycling Intensity based on RPE, and readjusted weekly	36 sessions (3 day/wk, 12 wks)	Isom knee ext at 60° Quadricep volume (MRI)	1) All measures were significantly greater in RT group
	2)Con—9 PD (67.0 yrs, 2.5 HY)	Ranged 3-5 min (wk 1) to 15-30 min (wk 12) (All groups performed standard care exercises)		6-min walk time (6MW) Stair ascent/descent time Tested ON	2) 6% ↑ volume, 24% ↑ torque, 21% ↑ 6MW, 18% ↑ stair climb
Hass et al., 2007[70]	1) RT + Creatine—10 PD (62.2 yrs, 2.1 HY)	Machine leg ext/flx, calf raises, chest press, lat pulldown, shoulder press, back extension, biceps curl, triceps extension	24 sessions (2 days/wk, 12 wks)	1RM for each exercise Consecutive sit-to-stand Muscle endurance test	1) For both groups; lean body mass ↑, 1RM strength ↑, muscle endurance ↑, sit-to-stand ↑
	2) RT + Placebo—10 PD (62.8 yrs, 2.2 HY)	1 × 8-12 reps at 70% 1RM; 6 s contraction 1 × 8-12 FAST reps at 50% 1RM for leg ext/flx Load progressed when 12 reps achieved		Tested ON	2) Creatine group ↑ sit-to-stand performance, ↑ chest press and bicep strength to a greater degree than placebo

Con = control group, Bal = balance training, RT = resistance training, yrs = age, HY = Hoehn and Yahr stage, flx = flexion, ext = extension, reps = repetition, RPE = ratings of perceived exertion, ON = patients had taken parkinsonian medication, OFF = patients were on an overnight withdrawal of medication, RM = repetition maximum, isok = isokinetic, isom = isometric, isot = isotonic or isoinertial, ↑ = increase.

group.[70,73,95] Although single-set approaches are valuable and recommended (ACSM), recent reports suggest that strength, endurance, and functional gains are greater when volume is increased in older adults.[105] Although no reports exist suggesting that resistive exercise may exacerbate symptoms of PD, considerable attention must be paid to the development and management of fatigue as previously mentioned.[65]

Recommendations for progressive resistance exercise training are available for healthy older adults.[106] In brief, these suggest a program that incorporates concentric and eccentric muscle actions performed via single- or multi-joint exercises, and ordered such that multijoint and larger muscle group exercises precede single-joint and smaller muscle group exercises. Strength-specific recommendations include a training frequency of 2–3 days/wk, a repetition maximum (RM) loading range of 8–12 RM, and 3-min rest intervals for novice exercisers. For more advanced individuals, training frequency is increased to 4–5 days/wk with an eventual emphasis on a 1–6 RM loading range and rest intervals held constant. It is critical to note that the number of acute training variables that can be manipulated creates difficulty in forming a precise exercise prescription. Again, these recommendations were put forth for healthy adults,

and there is currently no accepted model available for individuals with PD, reflecting the paucity of data in this population. Scandalis et al.[73] is the only investigation to compare individuals with PD to neurologically normal controls, demonstrating that improvements were similar between groups. Ultimately, recommendations may in fact be similar for individuals with PD and controls, yet until more data are available this remains speculative.

One may speculate that the eccentric resistive training implemented by Dibble et al.[87] lends favorably to fatigue-related concerns as eccentric (i.e., lengthening) muscle actions require ~20% less oxygen than concentric (i.e., shortening) muscle actions.[107] In addition, eccentric resistive exercise may be of additional benefit due to the preservation of eccentric strength despite aging[85] or PD.[28,83,84] Intuitively, if strength is greater during muscle lengthening, individuals would be able to withstand greater imposed loads. This is critical as higher loads elicit greater adaptation.

Considering that training may be performed safely at a high intensity,[100] such training may also impede the noticeable decline in bone integrity observed in individuals with PD. Current successful approaches have included the administration of biophosphonate and vitamin D supplements to attenuate these conditions,[57,58] but have not included resistive exercise. This appears to be an area ripe for investigation.

Lastly, as PD is a neurodegenerative disorder with altered motor unit behavior,[10] more investigation is needed on the utility of resistance training to promote neural adaptations. From literature in neurologically normal individuals, such modifications are indeed possible.[32,39,40] Unfortunately, no investigation presented in Table 2 quantified surface EMG modifications and/or cortical excitability. Knowledge of neural adaptations, particularly those that are centrally-mediated, that occur via resistance training seemingly would be of great benefit to clinicians and researchers.

CONCLUSIONS

Striatal dopamine loss disrupts pathways responsible for gross movement and presents as bradykinesia, rigidity, and tremor. Secondary to neurotransmitter loss, individuals with PD demonstrate impaired motor function and capacity, as well as muscle and bone weakness. In addition, these individuals are also confronted with the challenges of normal aging. Ultimately, these lead to a reduced quality of life, fear of falling, and "self-chosen home arrest."[71] To this end, resistive exercise has been proposed as a potential therapeutical intervention to attenuate some of these deficiencies, yet very few well controlled trials have been performed. However, interventions that are available have generally increased muscle strength and function. Future clinical interventions should consider high-intensity resistance training with particular emphasis on musculoskeletal and neural adaptations.

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