Rehabilitation and Parkinson’s Disease

Guest Editors: Gammon M. Earhart, Lee Dibble, Terry Ellis, and Alice Nieuwboer
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<tr>
<th>Name</th>
<th>Nationality</th>
<th>Location</th>
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<td>Jan O. Aasly</td>
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<td>Cristine Alves da Costa</td>
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<td>Yoshikazu Ugawa</td>
<td>Japan</td>
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</tr>
</tbody>
</table>
Contents

Rehabilitation and Parkinson's Disease, Gammon M. Earhart, Terry Ellis, Alice Nieuwboer, and Leland E. Dibble
Volume 2012, Article ID 371406, 3 pages

LSVT LOUD and LSVT BIG: Behavioral Treatment Programs for Speech and Body Movement in Parkinson Disease, Cynthia Fox, Georg Ebersbach, Lorraine Ramig, and Shimon Sapir
Volume 2012, Article ID 391946, 12 pages

Volume 2012, Article ID 543426, 7 pages

Altered Dynamic Postural Control during Step Turning in Persons with Early-Stage Parkinsons Disease, Jooeun Song, Susan Sigward, Beth Fisher, and George J. Salem
Volume 2012, Article ID 386962, 8 pages

Is Freezing of Gait in Parkinson's Disease a Result of Multiple Gait Impairments? Implications for Treatment, Meir Plotnik, Nir Giladi, and Jeffrey M. Hausdorff
Volume 2012, Article ID 459321, 8 pages

Posture and Locomotion Coupling: A Target for Rehabilitation Interventions in Persons with Parkinson's Disease, Marie-Laure Mille, Robert A. Creath, Michelle G. Prettyman, Marjorie Johnson Hilliard, Katherine M. Martinez, Colum D. MacKinnon, and Mark W. Rogers
Volume 2012, Article ID 754186, 10 pages

Feasibility, Safety, and Compliance in a Randomized Controlled Trial of Physical Therapy for Parkinson's Disease, Jennifer L. McGinley, Clarissa Martin, Frances E. Huxham, Hylton B. Menz, Mary Danoudis, Anna T. Murphy, Jennifer J. Watts, Robert Iansek, and Meg E. Morris
Volume 2012, Article ID 795294, 8 pages

Volume 2012, Article ID 692150, 8 pages

Volume 2012, Article ID 589152, 7 pages

Lack of Short-Term Effectiveness of Rotating Treadmill Training on Turning in People with Mild-to-Moderate Parkinson's Disease and Healthy Older Adults: A Randomized, Controlled Study, Marie E. McNeely and Gammon M. Earhart
Volume 2012, Article ID 623985, 8 pages
Accuracy of Fall Prediction in Parkinson Disease: Six-Month and 12-Month Prospective Analyses,
Ryan P. Duncan, Abigail L. Leddy, James T. Cavanaugh, Leland E. Dibble, Terry D. Ellis, Matthew P. Ford, K. Bo Foreman, and Gammon M. Earhart
Volume 2012, Article ID 237673, 7 pages

Community Walking in People with Parkinson’s Disease, Robyn M. Lamont, Meg E. Morris, Marjorie H. Woollacott, and Sandra G. Brauer
Volume 2012, Article ID 856237, 8 pages

Volume 2012, Article ID 124527, 10 pages

Exercise and Motor Training in People with Parkinson’s Disease: A Systematic Review of Participant Characteristics, Intervention Delivery, Retention Rates, Adherence, and Adverse Events in Clinical Trials, Natalie E. Allen, Catherine Sherrington, Gayanthi D. Suriyarachchi, Serene S. Paul, Jooeun Song, and Colleen G. Canning
Volume 2012, Article ID 854328, 15 pages

Volume 2012, Article ID 871974, 6 pages

A Review of Dual-Task Walking Deficits in People with Parkinson’s Disease: Motor and Cognitive Contributions, Mechanisms, and Clinical Implications, Valerie E. Kelly, Alexis J. Eusterbrock, and Anne Shumway-Cook
Volume 2012, Article ID 918719, 14 pages

Reliability in One-Repetition Maximum Performance in People with Parkinson’s Disease, Thomas A. Buckley and Christopher J. Hass
Volume 2012, Article ID 928736, 6 pages

Comparing the Mini-BESTest with the Berg Balance Scale to Evaluate Balance Disorders in Parkinson’s Disease, Laurie A. King, Kelsey C. Priest, Arash Salarian, Don Pierce, and Fay B. Horak
Volume 2012, Article ID 375419, 7 pages

The PIT: SToPP Trial A Feasibility Randomised Controlled Trial of Home-Based Physiotherapy for People with Parkinson’s Disease Using Video-Based Measures to Preserve Assessor Blinding, Emma Stack, Helen Roberts, and Ann Ashburn
Volume 2012, Article ID 360231, 8 pages

Gait Difficulty, Postural Instability, and Muscle Weakness Are Associated with Fear of Falling in People with Parkinson’s Disease, Margaret K. Y. Mak, Marco Y. C. Pang, and Vincent Mok
Volume 2012, Article ID 901721, 5 pages
A Manipulation of Visual Feedback during Gait Training in Parkinson’s Disease, Quincy J. Almeida and Haseel Bhatt
Volume 2012, Article ID 508720, 7 pages

Walking Ability Is a Major Contributor to Fear of Falling in People with Parkinson’s Disease: Implications for Rehabilitation, Maria H. Nilsson, Gun-Marie Hariz, Susanne Iwarsson, and Peter Hagell
Volume 2012, Article ID 713236, 7 pages

Impaired Economy of Gait and Decreased Six-Minute Walk Distance in Parkinson's Disease, Leslie I. Katzel, Frederick M. Ivey, John D. Sorkin, Richard F. Macko, Barbara Smith, and Lisa M. Shulman
Volume 2012, Article ID 241754, 6 pages
Early after the turn of the century, much excitement was generated by the reports of Tillerson et al. [1, 2] that exercise appeared to protect against neuronal degeneration in rodent models of toxin-induced parkinsonism. Such findings, coupled with epidemiologic suggestions that persons with a history of moderate to vigorous exercise may have a decreased risk of developing Parkinson's disease (PD) [3–5], led to an exponential growth in research on the effects of physical activity and exercise on PD. Unfortunately, additional follow-up animal studies to the work of Tillerson et al. have failed to yield consistent findings [6–10]. For this reason, it appears that the critical factors associated with neuroprotection remain elusive. With a continued focus on examining the effects of exercise in animal models of parkinsonism, identifying biomarkers of disease progression, and new and innovative outcomes, we look forward to a day when an evidence-based neuroprotection study can be implemented in human idiopathic PD.

Although results from studies of the neuroprotective effects of exercise are mixed, one consistent finding from animal models and human trials is the lack of adverse effects of exercise and physical activity on anatomic and behavioral outcomes. The adverse side-effect profile of exercise as an intervention for those with PD appears to be minimal. As such, we think there is no reason to wait for confirmation of neuroprotection. Rather, evidence is accumulating that exercise and physical activity should be utilized as key tools in the management of PD across the spectrum of disease. Evidence-based approaches to rehabilitation are known to improve physical functioning, strength, balance, gait, and health-related quality of life among people with PD [11–13], but questions remain about whether or not these approaches can substantially impact fall rates [14–16]. This is a key issue, as most individuals with PD are only referred to rehabilitation after the onset of reduced mobility and an increase in falls. As such, the majority of PD rehabilitation care is provided in a tertiary prevention model of care. People with PD are most often not seen earlier in the course of the disease, when rehabilitation could play a key role in secondary preventive care. Secondary prevention would entail addressing early PD signs and symptoms, ideally immediately upon diagnosis, to optimize the condition of the central nervous system as well as other peripheral systems such as the cardiovascular and respiratory systems in order to maximize function and slow progression of disability. Even earlier intervention should be considered, as we think that rehabilitation may ultimately serve a role in primary prevention of PD. Primary prevention would entail treating those without current neurologic signs and symptoms in order to prevent PD from ever developing. Those who are potentially at risk for PD (e.g., leucine-rich repeat kinase 2 (LRRK2) carriers, those with rapid eye movement sleep behavior disorder, anosmia, constipation, abnormal positron emission tomography (PET) scans, etc.) may be excellent candidates for primary prevention.

The presently limited scope of rehabilitation in the management of PD, with utilization of rehabilitation as mainly a tertiary prevention measure, reflects a missed
opportunity on the part of healthcare providers, patient advocacy groups, and patients themselves. All stakeholders in this situation should be advocates for higher expectations and should work together to develop targets for the future of rehabilitation in PD to include primary and secondary prevention and to improve our current provision of tertiary prevention interventions.

From the Spectrum of Rehabilitation Options to Atypical Parkinsonism. In this special issue are several articles that we hope advance the field and move us closer to these future targets. The issue opens with a series of three review articles. The first paper summarizes and synthesizes the nature and features of previous randomized, controlled trials of exercise or motor training in PD, important for the long-term provision of increasing levels of physical activity. The second paper provides a meta-analysis focused on motor learning in upper extremity tasks. The third paper provides an integrated overview of the Lee Silverman Voice Treatment approach to voice and movement therapy, discussing the rationale for the approach as well as the data regarding efficacy. These opening three articles highlight the important roles of speech, occupational, and physical therapy approaches in the rehabilitation of individuals with PD as well as address areas for future research.

Several papers in this special issue relate to gait, balance, and falls, examining the relationship between gait economy and six-minute walk distance, reviewing the literature on the costs of dual-task walking, and providing a new theoretical framework for considering freezing of gait (FOG) including methods to improve overall locomotor performance and methods to target the triggers of FOG. Also included are two randomized, controlled trials designed to improve walking. One compares visually cued walking training on a treadmill to overground walking; the other examines use of rotating treadmill training as a means of improving turning, thereby targeting a known trigger of FOG. Turning is also examined in a paper that describes turning impairments in early PD. This is followed by a paper examining the effects of medications on gait-related mobility and postural control, showing that although pharmacologic intervention enhanced some aspects of mobility, reactive postural responses did not improve. This highlights the need for awareness of postural control deficits and the need to be able to measure these deficits, as is addressed by the next two papers in the issue that present the relative merits of different balance measures across different levels of PD severity and examine the relative effectiveness of different balance measures for prospective fall prediction.

The inextricable link between posture and gait is addressed in a paper that focuses on the coupling of posture and locomotion and suggests this coupling as a specific target for rehabilitation. This link is also highlighted in two papers demonstrating that walking ability is a major contributor to fear of falling in PD, as is knee strength. The latter leads to the suggestion that resistance training may therefore be warranted as an approach to reduce fear of falling. The rationale for progressive resistance training as well as its potential mechanisms are addressed in a review paper, followed by an article examining the reliability of one repetition maximum strength testing in PD.

We conclude the issue with a set of papers addressing the delivery of evidence-based rehabilitation in different settings. These papers include two that are randomized, controlled trials of physiotherapy in outpatient and home-based settings, respectively. These are followed by a paper examining facilitators and barriers to community-based walking exercise among those with PD. Community-based healthcare for PD is also addressed in a paper describing the steps taken to improve the Dutch model of multidisciplinary care. The final paper of the issue demonstrates the effectiveness of multidisciplinary care in an inpatient setting in persons with atypical parkinsonism. All papers in this final section draw attention to the need for a collaborative, cooperative approach to rehabilitation across disciplines, across settings, and with PD and other related disorders.

Ultimately, we believe that there is a need to redefine the role of rehabilitation in PD to include the provision of primary, secondary, and tertiary prevention approaches. Across this spectrum from primary through tertiary care, the application of multidisciplinary approaches is needed to optimize the health, function, and quality of life of individuals at risk for, or who already have, PD. Only then will the full potential of rehabilitation in the management of PD be realized.

Gammon M. Earhart
Terry Ellis
Alice Nieuwboer
Leland E. Dibble

References


Recent advances in neuroscience have suggested that exercise-based behavioral treatments may improve function and possibly slow progression of motor symptoms in individuals with Parkinson disease (PD). The LSVT (Lee Silverman Voice Treatment) Programs for individuals with PD have been developed and researched over the past 20 years beginning with a focus on the speech motor system (LSVT LOUD) and more recently have been extended to address limb motor systems (LSVT BIG). The unique aspects of the LSVT Programs include the combination of (a) an exclusive target on increasing amplitude (loudness in the speech motor system; bigger movements in the limb motor system), (b) a focus on sensory recalibration to help patients recognize that movements with increased amplitude are within normal limits, even if they feel “too loud” or “too big,” and (c) training self-cueing and attention to action to facilitate long-term maintenance of treatment outcomes. In addition, the intensive mode of delivery is consistent with principles that drive activity-dependent neuroplasticity and motor learning. The purpose of this paper is to provide an integrative discussion of the LSVT Programs including the rationale for their fundamentals, a summary of efficacy data, and a discussion of limitations and future directions for research.

1. Introduction

Progressive neurological diseases, such as Parkinson disease (PD) impair speech, swallowing, limb function, gait, balance, and activities of daily living. Even with optimal medical management (pharmacological, surgical) these deficits cannot be controlled satisfactorily in the vast majority of individuals with PD and have a negative impact on quality of life [1–3]. Recently, basic science research in animal models of PD has documented the value of exercise for improving motor performance and potentially slowing progression of motor symptoms and neural degeneration [4–9]. The impact of exercise in humans with PD is being increasingly explored in studies that incorporate key principles that have been identified to drive activity-dependent neuroplasticity (i.e., modifications in the central nervous system in response to physical activity), such as specificity, intensity, repetition, and saliency [9–16]. Collectively, these findings have accentuated the important role of exercise and/or rehabilitation in the overall management of PD. Previously, rehabilitation programs were often administered in later stages of PD or as reactive referrals for secondary impairments, such as aspiration due to swallowing dysfunction, or hip fracture due to falling. Today, such programs are being viewed as therapeutic options to be prescribed early in the course of PD that may potentially contribute to slowing of motor symptom progression [5, 17]. The purpose of this paper is to provide an integrative discussion of the rationale for and the efficacy of one type of rehabilitation approach, the LSVT Programs for speech (LSVT LOUD) and limb (LSVT BIG) motor systems in individuals with PD. We will include the rationale for targeting increased amplitude, the intensive mode of treatment delivery, and recalibration of the sensorimotor system including self-cuing, and attention to action, which may be important for generalization and long-term maintenance of treatment effects. In addition, we will summarize published efficacy data and discuss current limitations and future directions for research.
2. What Is LSVT LOUD?

Nearly 90% of individuals with PD have speech and voice disorders that negatively impact communication abilities [18, 19]. These disorders include reduced vocal loudness, monotone, hoarse, breathy voice quality, and imprecise articulation, perceived as mumbling, and other rate-related features, such as hesitations and short rushes of speech [20, 21]. In contrast to previous medical “chart review” literature suggesting a mid- or late-stage onset of speech and swallowing symptoms in PD [22], more recent investigations with sensitive and valid measures consistently report speech symptoms in early PD (e.g., [23]). Further, self-report data from individuals with PD have indicated that voice and speech changes are associated with inactivity, embarrassment, and withdrawal from social situations [2].

Historically, speech treatment for individuals with PD was viewed as futile, in as much as treatment gains were minimal and short lived [24]. Today, LSVT LOUD is a standardized, research-based speech treatment protocol with established efficacy for PD [25–28]. LSVT LOUD trains the target of vocal loudness in order to (1) enhance the voice source, consistent with improving the carrier in the classic engineering concept of signal transmission [29], (2) use vocal loudness as a trigger for distributed effects (e.g., improved articulation, vocal quality and intonation, and reduced rate) across the speech production system [21, 30–33], (3) recalibrate sensorimotor perception of improved vocal loudness [34], and (4) train a single self-cue and attention to action to facilitate generalization of treatment effects into functional communication. Although LSVT LOUD is a standardized treatment protocol, the materials used during treatment and the homework and carryover exercises are made salient and tailored to each individual to facilitate motivation, engagement and the potential to drive neuroplasticity [13, 35, 36].

In contrast, traditional speech therapy typically involves multiple speech system targets (e.g., respiration, voice, articulation, and rate), is low intensity (1–2 sessions per week, minimal number of repetitions of treatment tasks), and does not systematically address the sensory processing deficits related to self-perception of loudness by individuals with PD (see [37] for summary table contrasting LSVT LOUD and traditional speech treatment) [37, 38]. The LSVT LOUD protocol is summarized in Table 1.

3. LSVT LOUD Outcome Data

Two randomized controlled trial (RCT) studies have been conducted [27, 28]. Data have documented that training increased vocal loudness results in a statistically significant and lasting increase in vocal sound pressure level (SPL) and frequency variability during speech (i.e., unceded conversational speech) as compared to a matched treatment focusing on training increased respiratory support [26–28, 30]. Effect size data for the primary outcome variable of vocal SPL in conversational speech were highly significant immediately posttreatment (1.20) and were maintained at 24 months posttreatment (1.03) [27, 30, 40]. Data providing initial external validation of LSVT LOUD outcomes have been reported by independent labs and reviews [41–45].

In addition, various physiologic changes such as increased movement amplitude of the rib cage (larger excursions) during speech breathing [46], increased subglottal air pressure [26], and improved closure and larger/more symmetrical movements of the vocal folds [47] have been documented in individuals with PD immediately after LSVT LOUD. These findings are supported by perceptual data demonstrating listeners rated improved loudness and voice quality in individuals with PD immediately posttreatment [33]. Subjects in these studies were predominately Hoehn and Yahr stages 1–3 with moderate speech deficits.

Training vocal loudness also has been studied for its distributed effects across the speech production system. In a series of smaller pilot studies (subsets of data from larger study) data have documented improvements in orofacial movements, as reflected in consonant articulation [48], tongue strength and motility [44], speech rate [30], ratings of improved facial expression [49], and improvements in some aspects of the oral phase of swallowing (e.g., reduced oral transit time) [50] even though these functions were not specific targets in therapy. The impact of LSVT LOUD on speech articulation, especially vowels, has been further explored. Vowels are formed and differentiated from each other by the movements of the tongue, lips, and jaw. In individuals with PD, these movements tend to be hypokinetic [51], thus rendering the vowels less distinct physiologically, acoustically, and perceptually, a phenomenon known as vowel centralization. LSVT LOUD has been shown to reduce vowel centralization and improve perceptual rating of vowel quality [31, 32]. This improvement may reflect larger amplitude of movements of the tongue, lips, and jaw, possibly due to overall neural and biomechanical coupling of speech subsystems and increased activation of the entire speech neuromuscular system [52].

Two brain imaging studies using O15 PET in a small number of individuals with PD have documented changes in brain function immediately following LSVT LOUD [53–55]. The most recent study by Narayana et al. [55] examined the neural mechanisms underlying the effects of training increased vocal loudness in ten individuals with PD and hypophonia. Cerebral blood flow during rest and reading conditions was measured by H2 15O-positron emission tomography. Z-score images were generated by contrasting reading with rest conditions for pre- and post-LSVT LOUD sessions, and neural activity was correlated with the corresponding change in vocal SPL (loudness). Narayana et al. [55] hypothesized that brain activation patterns associated with LSVT LOUD training would reflect improved loudness, improved perception of self-generated voice output, and improved attention to action. Further it was hypothesized that these outcomes would likely be mediated via the right hemisphere and involve speech motor and premotor cortical areas (related to increasing vocal loudness), the auditory cortices (related to recalibration of perception of self-produced loudness), and dorsolateral prefrontal cortex (related to improving attention to action). To a large extent, the results of the study are consistent with
### Table 1: Comparison of LSVT LOUD and LSVT BIG treatments.

<table>
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<tr>
<th>LSVT LOUD (e.g., [25, 30])</th>
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<tr>
<td><strong>Target:</strong> LOUD</td>
<td><strong>Target:</strong> BIG</td>
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<tr>
<td>Increased movement amplitude directed predominately to respiratory/laryngeal systems</td>
<td>Increased movement amplitude directed across limb motor system including gait</td>
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<td><strong>Intensity:</strong> standardized</td>
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<td>Dosage: 4 consecutive days a week for 4 weeks (16 sessions in one month)</td>
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<td>Repetitions: minimum 15 repetitions/task</td>
<td>Repetitions: minimum 8–16 repetitions/task</td>
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<td>Effort: push for maximum patient-perceived effort each day (8 or 9 on scale of 1–10 with 10 being the most)</td>
<td>Effort: push for maximum patient-perceived effort each day (8 or 9 on scale of 1–10 with 10 being the most)</td>
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<td><strong>Daily exercises</strong></td>
<td><strong>Daily exercises</strong></td>
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<td>First half of the treatment session (30 min.)</td>
<td>First half of the treatment session (30 min. or more)</td>
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<td><strong>Task 1: Maximum Sustained Movements</strong></td>
<td><strong>Task 1: Maximum Sustained Movements: seated</strong></td>
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<tr>
<td>15 reps: sustain “ah” in Loud good quality voice as long as possible</td>
<td>8 reps: sustain Big “stretch” floor to ceiling (10 sec hold); 8 reps: sustain Big “stretch” side to side (10 sec hold)</td>
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<td><strong>Task 2: Directional Movements</strong></td>
<td><strong>Task 2: Repetitive/Directional Movements: standing</strong></td>
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<td>15 reps each: say “ah” in Loud good quality voice going high in pitch; 15 reps each: say “ah” in Loud good quality voice going low in pitch</td>
<td>16 reps: Forward Big step – 8 each leg; 16 reps: Sideways Big step – 8 each side; 16 reps: Backward Big step – 8 each leg; 20 reps: Forward Big Rock and reach – 10 each side; 20 reps: Sideways Big Rock and reach – 10 each side</td>
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<td><strong>Task 3: Functional Phrases</strong></td>
<td><strong>Task 3: Functional Component Movements</strong></td>
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<td>Patient self-identifies 10 phrases or sentences he/she says daily in functional living (e.g., “Good morning”); 5 reps of the list of 10 phrases. “Read phrases using same effort/loudness as you did during the long “ah”</td>
<td>Patient self-identifies 5 movements he/she does in functional living every day (e.g., Sit-to-stand) Clinician and patient select one simple component of each of these movements 5 reps each of the 5 component movements “Do your movement with the same effort/bigness that you did during the daily exercises”</td>
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<td><strong>Hierarchy</strong></td>
<td><strong>Hierarchy</strong></td>
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<td>Second half of the treatment session (30 min)</td>
<td>Second half of the treatment session (30 min or less)</td>
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<td>(i) Designed to train rescaled amplitude/effort of movement achieved in daily exercises and functional phrases into in context specific and variable speaking activities (ii) Tasks increase complexity across weeks (Words-phrases-sentences-reading-conversation) and can be tailored to each patient’s goals and interests (e.g., golf versus cooking) (iii) Tasks progress in difficulty by increasing duration (maintain LOUD for longer periods of time) amplitude (loudness, within normal limits), and complexity of tasks (dual processing, background noise, and attentional distracters)</td>
<td>(i) Designed to train rescaled amplitude/effort of movement achieved in daily exercises and functional component movements into in context specific and variable movement activities (ii) Complex multilevel tasks that progressively become more difficult over the 4 weeks and can be tailored to each patient’s goals and interests (e.g., basic bathroom skills versus going out to dinner or shopping) (iii) Tasks progress in difficulty by increasing duration (maintain BIG for longer periods of time) amplitude (bigness/effort, within normal limits), and complexity of tasks (multisteps, dual processing, background noise, and attentional distracters) (iv) BIG walking is included as part of hierarchy on a daily basis. Time and distance will vary across patients, hierarchy goals, and weeks of therapy</td>
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<td><strong>Shaping techniques</strong></td>
<td><strong>Shaping techniques</strong></td>
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<td>Goal: train vocal loudness that is healthy and good quality (i.e., no unwanted vocal strain or excessive vocal fold closure) Technique: shape the quality and voice loudness through use of modeling or tactile/visual cues. “Watch me and do what I do.” Minimal cognitive loading: behavior is not achieved through extensive instructions or explanations, which are often too complex for patient to generalize outside of treatment room, but rather the patient is trained through modeling</td>
<td>Goal: train movement bigness that is healthy and good quality (i.e., no unwanted strain or pain, impingement, or awkward biomechanics) Technique: shape the quality and movement bigness through use of modeling or tactile/visual cues. “Watch me and do what I do.” Minimal cognitive loading: behavior is not achieved through extensive instructions or explanations, which are often too complex for patient to generalize outside of treatment room, but rather the patient is trained through modeling</td>
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these hypotheses. These initial neural findings underlying LSVT LOUD outcomes are being further examined and verified in ongoing imaging studies as discussed in ongoing research.

4. What Is LSVT BIG?

Individuals with PD perform movements that are hesitant (akinesia), slow (bradykinesia), and with reduced amplitude (hypokinesia). Changing from one motor program to another (set-shifting) may be disturbed and sequencing of repetitive movements may occur with prolonged and/or irregular intervals and reduced and/or irregular amplitudes [56]. External cues may exert disproportionate influences on motor performance and can trigger both motor blocks and kinesia paradoxica [57]. In LSVT BIG, training of amplitude rather than speed was chosen as the main focus of treatment to overcome bradykinesia/hypokinesia because training of velocity can induce faster movements but does not consistently improve movement amplitude and accuracy. Furthermore, training to increase velocity of limb movements may result in hypokinetic (reduced) movement amplitude [58, 59]. In contrast, training of amplitude not only results in bigger, but also in faster and more precise movement [58, 59]. The goal of LSVT BIG is to overcome deficient speed-amplitude regulation leading to underscaling of movement amplitude at any given velocity [59–61]. Continuous feedback on motor performance and training of movement perception is used to counteract reduced gain in motor activities resulting from disturbed sensorimotor processing [62].

Most current therapies rely on compensatory behavior and external cueing in order to bypass deficient basal ganglia function [58, 63–70]. In contrast, other protocols focus on retraining of deficient functions. Task-specific, repetitive, high-intensity exercises for individuals with PD include treadmill training [71], training of compensatory steps [72] walking [73], and muscle strengthening [74, 75]. LSVT BIG belongs to the latter restorative approaches and is aiming to restore normal movement amplitude by recalibrating the patient’s perception of movement execution. LSVT BIG differs from other forms of physiotherapy in PD in its training of movement amplitude as a single treatment parameter (both single motor target and cognitive cue) through high effort, intensive treatment with a focus on recalibrating sensory perception of normal amplitude of movements. The standardized protocol of LSVT BIG was derived directly from LSVT LOUD and is summarized in Table 1.

5. LSVT BIG Outcome Data

Presently two trials on the effectiveness of LSVT BIG have been published.

A noncontrolled study assessed effects of LSVT BIG in 18 individuals with PD [76]. Data documented that after four weeks of training, subjects demonstrated a modest (12%–14%) increase in velocity of walking and reaching movements.

In the recently published rater-blinded Berlin LSVT BIG Study improvement in motor performance was compared in 60 individuals with PD, randomly assigned to receive LSVT BIG, Nordic Walking (as group treatment) or domestic training without supervision [60]. Mean improvement of UPDRS motor score in subjects receiving LSVT BIG was 5.05 at four-month followup. In contrast, the UPDRS motor score slightly deteriorated in control groups undergoing training in Nordic walking with the same amount of supervised sessions and in subjects who received domestic training receiving a 1-hour instructional lesson and no further supervision by a therapist. The beneficial outcome in LSVT BIG was also reflected by improvements in further assessments including a standard time-up and go task and 10-meter walk. According to Schrag et al. [77] a change of five points is the most appropriate cutoff score for the minimal clinical important change (MCIC) of the UPDRS motor score for all Hoehn and Yahr stages from Stage I to III. The degree of change in UPDRS motor score after LSVT BIG can thus be assumed to be clinically relevant. There is no established definition
of the MCIC for the secondary motor assessments, but the observed 10–15% improvements in timed test of mobility are likely to have functional impact.

The Berlin LSVT BIG Study is one of the few studies comparing specific types of physiotherapy with both active comparators and inactive controls. Sage and Almeida [78] reported more improvement in the UPDRS motor score and other motor tasks with exercises designed to improve sensory attention and body awareness when compared to lower-limb aerobic training. Mak and Hui-Chan 2008 [79] found better outcomes in the Sit-and-Stand task when subjects received training including sensory as compared to conventional exercise. In both studies individuals without active interventions did not improve. In the Berlin LSVT BIG Study outcomes differed clearly between active interventions. Intensive one-to-one training (LSVT BIG) was found to be more effective than Nordic walking delivered as group training. Although differences in training techniques may also have influenced results, it is likely that the specific protocol of LSVT BIG and, possibly, individual face-to-face interaction between patient and therapist, was more crucial for successful outcomes than total exercise time. Further studies are needed to explore differences in cost-effectiveness between the more expensive individual LSVT BIG training, group treatments, and self-supervised domestic exercise.

6. Unique Fundamentals of LSVT Programs

6.1. Target: Amplitude. We hypothesize that training-induced increases in movement amplitude target the proposed pathophysiological mechanisms underlying bradykinnesia/hypokinesia—inadequate muscle activation [62]. The muscle activation deficits that occur in bradykinesia are believed to result from inadequate merging of kinesthetic feedback, motor output, and context feedback within the basal ganglia, necessary to select and reinforce an appropriate gain in the motor command [62, 80]. Although the target is increased amplitude, it is important to note that the end result in speech and movement amplitude output (louder voice/bigger movements) is within normal limits. The cue of “loud” or “big” is used to simply drive increased motor output across the motor systems for more normal amplitude. The role of the speech, physical, or occupational therapist is to shape the amplitude into healthy, good quality movements (see Shaping in Table 1). Post-LSVT LOUD videotape data [47] and perceptual ratings of voice [33] indicate improved laryngeal function and voice quality rather than vocal hyperfunction or deterioration in voice posttreatment. Ratings of motor performance after LSVT BIG also indicated a trend towards normalization and no exaggeration or overcompensation of movement amplitudes [60, 76, 81].

The idea of targeting amplitude in rehabilitation for individuals with PD is not new. Training vocal loudness (amplitude) is consistent with approaches recommended for treating motor speech disorders that (a) create a single motor organizing theme, (b) have a maximum impact on other aspects of speech production, and (c) increase effort across the speech mechanism [81–83]. Further, many physical therapy programs have amplitude as a component of therapy either as exercise principles or by using external cues (e.g., [84, 85]). The unique element of training amplitude in LSVT Programs is that it is the exclusive focus. We hypothesize that a single, overlearned cue (louder voice/bigger movements) may minimize cognitive load and mental effort [86] and possibly facilitate maintenance and generalization of treatment strategies outside of the therapy room. This hypothesis is yet to be formally tested and is an area for future research. For example, testing the impact of dual task functioning on the ability of individuals with PD to maintain improved amplitude before/after LSVT Programs would elucidate the ability of these individuals to learn a new self-cue for amplitude.

6.2. Mode: Intensive, High Effort Therapy. The training mode of LSVT Programs is consistent with some principles that promote activity-dependent neuroplasticity [11, 87] including (a) specificity, targeting bradykinesia/hypokinesia through increasing amplitude of motor output, (b) intensity, increased dosage of treatment, (c) repetition, increased repetition of tasks (minimum 15 repetitions) within treatment sessions and home practice, and (d) saliency of treatment tasks, individualized hierarchy and carryover assignments for active practice of desired goals, interests and abilities of each person [9–16]. Further, we recognize that acquisition of the motor skill (e.g., louder voice, bigger movements) alone may not be sufficient for sustained neuroplasticity (i.e., sensorimotor map reorganization, synaptogenesis) [14] or for carryover and long-term maintenance outside the therapeutic environment. Therefore, a direct translation of the structured motor exercises (daily exercises) into functional daily activities is emphasized in treatment with the goal of facilitating generalization outside of the treatment room (see Table 1 Hierarchy, Carryover and Homework). In addition, emphasis is placed on establishing life-long habits of structured homework practice of voice/movement exercises that continue beyond the one-month of treatment. Finally, simply using the louder voice or bigger movements in daily living provides additional practice, as summarized by this patient quote,

“in my normal everyday life, I just exaggerate my movements. I keep things big when I reach for things, or when I bend or when I walk; and when I talk—I keep my voice loud.”

6.3. Recalibration: Addressing Barriers to Generalization. Sensorimotor processing deficits during speech and movement have been well documented [37, 38, 88–91]. From our own clinical observations, it appears that addressing the motor deficit in isolation is not sufficient for lasting treatment outcomes that generalize beyond the treatment room [34]. Thus, the LSVT Programs are designed to train individuals with PD to recalibrate their motor and perceptual systems so that they are less inclined to downscale (reduce amplitude) speech and limb movement parameters after treatment.

Figure 1 illustrates our hypothesized model for amplitude rescaling and recalibration in LSVT Programs. In short,
Figure 1: We hypothesize that pretreatment (a), individuals with PD have reduced amplitude of motor output, which results in soft voice and small movements. Due to problems in sensory self-perception they are not aware of the soft voice and small movements, or they do not recognize the extent of their soft voice and smaller movements. As a result, no error correction is made and individuals continue to program or self-cue reduced amplitude of motor output. They are “stuck” in a cycle of being soft and small. The focus in treatment (b) is on increasing the amplitude of motor output by having individuals with PD produce a louder voice and larger movements. Individuals are then taught that what feels/sounds/looks “too loud” or “too big” is within normal limits and has a positive impact on daily functional living. Therefore at the end of treatment, individuals habitually self-cue increased amplitude of motor output and have attention to action. Now they are in a cycle of a louder voice and bigger movements.

The hypothesized concepts underlying recalibration in LSVT Programs have yet to be systematically tested in pre/posttreatment experiments. However, there is evidence that cognitive training is possible in individuals with PD [92], including training in motor attention to action and performance under multiple tasks [93, 94]. Moreover, the ability to speak in a louder voice two years after intervention as compared to pretreatment levels [27] support the ability of LSVT-LOUD-trained individuals to self-monitor vocal loudness at some level.
7. Limitations of LSVT Programs

There are a number of limitations to the scope of research on LSVT Programs and we have highlighted some of the key areas below. First, there is a need to better define prognostic variables for who will respond best to LSVT Programs and what outcomes can be expected in individuals with a variety of factors, such as depression, dementia, apathy, orthopedic complications, and dyskinesias, as well as atypical PD and post-DBS surgery. While the majority of LSVT outcome data have been reported on individuals with idiopathic PD, single subject, case study and small group designs have documented post-LSVT-LOUD improvements in individuals after neurosurgery and with atypical parkinsonism [95–97]. However, these outcomes may not be of the same magnitude as those observed in individuals with mild-to-moderate idiopathic PD and these individuals may require more frequent follow-up treatment sessions to maintain improvements over time. Furthermore, LSVT LOUD outcomes in individuals with significant rate disorders, such as palilalia, and individuals who have severe speech disorders secondary to high-frequency DBS stimulation have been poor. Data examining LSVT BIG in atypical and post-DBS populations are not available. Second, studies examining the optimal dose-response relationships for LSVT Programs across idiopathic PD, atypical PD, and individual post-DBS are needed. The standard dose of LSVT Programs is 16 individual 60-minute sessions within one month. There is one dose-response study for LSVT LOUD that examined the impact of an extended treatment protocol (LSVT Extended, LSVT-X) [98]. Specifically, individuals received in-person treatment two days a week and completed home practice sessions the other two days a week for 8 weeks of treatment. Outcome data immediately posttreatment were comparable to the standard dosage. Of note, the treating clinicians completed daily calls and extensive home-practice monitoring to ensure that all subjects completed all home sessions. Ongoing work is examining alternative dosages of LSVT BIG, additional dose-response relationships need to be defined. Third, the spread of effects across the speech production system has been reported following LSVT LOUD. These studies should be further advanced and studies are needed to evaluate the spread of effects or transfer effects from large body movements to fine motor functions, balance, or dual tasks following LSVT BIG. Fourth, the practical and financial feasibility of delivering intensive treatment in LSVT Programs must be addressed. Physical immobility and geographical constraints are barriers which limit patient accessibility to intensive treatment. Fifth, the maintenance and enhancement of long-term treatment effects also are areas of need. While LSVT LOUD outcome data report maintenance of treatment effects for two years after one month of treatment, we believe outcomes can be further optimized. The long-term effects of LSVT BIG need to be established. Strategies to maximize compliance with continued home practice and the timing of optimal follow-up treatment intervals need to be defined. Finally, the hypothesized concepts underlying sensory calibration as well as understanding neural mechanisms of treatment-related change need to be systematically studied and validated. Only then can we fully understand what elements of treatment contribute to improvement in speech and movement functioning. These limitations will continue to guide our future research with some areas already being addressed as discussed below.

8. Current and Future Research Directions

Our ongoing work in LSVT LOUD is addressing questions related to the importance of the treatment target versus the mode of delivery. Specifically, we are comparing two treatment targets: vocal loudness training (LSVT LOUD) versus orofacial/articulation training (LSVT ARTIC) and the effects on measures of speech intelligibility, speech acoustics, facial expression, and swallowing. The two treatments are standardized and matched in terms of mode of delivery (e.g., dosage, sensory recalibration, homework, and carryover assignments). LSVT LOUD focuses on training healthy vocal loudness across speech tasks (sustained vowels, high/low vowels, functional phrases, and speech hierarchy), with focused attention on how it feels and sounds to talk LOUD, whereas, LSVT ARTIC focuses on high-force articulation or enunciation across speech tasks (diadochokinesis, contrastive pairs, functional phrases, and speech hierarchy), with focus on how it feels to have high-effort enunciation. Preliminary data examining single-word intelligibility in noise conditions [99] and facial expressions utilizing the Facial Action Coding System (FACS) [100] revealed significant improvements from pre to posttreatment in the LSVT LOUD group only. More extensive analysis is ongoing. In addition, this study includes comprehensive neuropsychological profiles of subjects and may shed some light on the impact of factors such as age, stage of disease, depression, dementia, or other nonmotor symptoms on treatment outcomes.

The impact of DBS on speech is an urgent area of research. Tripoliti and colleagues [101] are assessing the reasons for the heterogeneous speech outcomes following DBS-STN by involving simultaneous quantitative measures of pre- and postsurgical speech functioning and details of surgical and stimulator optimization. Knowledge gained from these studies is likely to facilitate development of treatment approaches for speech problems in individuals with DBS-STN either before surgery (as preventative) or after surgery (as rehabilitation). Our laboratory is looking at the impact of additional weeks of treatment on speech outcomes for individuals with PD after DBS.

Advances in computer and web-based technology offer potentially powerful solutions to the problems of treatment accessibility, efficacious dosage delivery, and long-term maintenance in rehabilitation [102–104]. Preliminary studies have documented the impact of telepractice and software programs on treatment availability for LSVT LOUD and suggest that such technology may be effective [42, 105–108] and increase the feasibility of intensive dosage and long-term followup. In addition, a study by Tindall et al. [105] completed a cost analysis comparing in-person delivery of LSVT LOUD versus telepractice delivery. The computed
mean amount of time and money for individuals with PD across these two modes of delivery was reported. The live delivery mode required 51 hours for 16 visits (travel and therapy time), $953.00 on fuel/mileage expenses, and $269.00 for other expenses (e.g., food). In contrast, the telepractice delivery option required 16 hours of time (therapy, no travel) and no additional costs for fuel/mileage or other expenses. To further enhance accessibility, a software program designed to collect acoustic data and provide interactive feedback as it guides the patient through the LSVT LOUD exercises has been developed. Outcome data document that treatment effects are comparable when half of the sessions were delivered by software [109]. These studies need further validation. While telepractice has not been explored for delivery of LSVT BIG, there are studies that have documented the feasibility of remote measuring of activities of daily living [110] and ongoing trials examining the delivery of physical therapy via telepractice in patients after stroke [111]. Thus, future applications of both telepractice and software programs/gaming technology to increase accessibility and feasibility of LSVT BIG is possible. The use of technology is not LSVT specific and may have the ability to increase accessibility, enhance effectiveness, and reduce financial burden of many intensive rehabilitation programs for people with PD.

Understanding neural mechanisms of both speech and movement disorders in PD as well as mechanism of treatment-related change are of great promise to help improve treatment outcomes. As part of our ongoing work we are examining neural changes (PET imaging) in individuals with PD across the LSVT LOUD, LSVT ARTIC, and Untreated groups. Hypothetically, intensive practice of speech enunciation by the LSVT LOUD regimen should strengthen cortically mediated speech articulation in PD, beyond the improvement associated with LSVT LOUD. To our knowledge, this will be the first imaging study of comparison speech treatments in individuals with PD including long-term followup (3 months). Developing parallel imaging studies before/after LSVT BIG is of great interest to us both in terms of understanding reorganization of brain activation patterns following treatment but also to understand differences between using amplitude to treat speech versus limb motor systems.

Finally, whereas studies of movement and limb/gait exercise in animal models of PD have contributed immensely to the literature, there have been no analogous models for studying vocalization deficits. Today, emerging models of vocal motor deficits following dopamine depletion in rodents (rats and mice) and songbirds offer promise for the feasibility and value of these models [112–114]. Viable animal models of vocalization patterns associated with PD may allow us to accelerate the acquisition of the neurobiological and behavioral evidence to improve our understanding of voice/speech deficits in PD and document the therapeutic value of early interventions to slow voice/speech symptom progression in human PD.

Collectively these ongoing studies have the potential to improve our understanding of the underlying mechanisms of speech-treatment-related changes in individuals with PD and will help guide treatment improvements. Future research will address the underlying bases for treatment-related changes that have a beneficial impact on speech and movement and thus quality of life in individuals with Parkinson disease.

Disclosure

L. Ramig and C. Fox receive lecture honoraria and have ownership interest in LSVT Global, Inc. They are in full compliance with Federal Statute (42 C.F.R. Part 50, Subpart F) and the University of Colorado-Boulder Policy on Conflict of Interest and Commitment.

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References


Parkinson’s Disease


Improving Community Healthcare for Patients with Parkinson's Disease: The Dutch Model


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Because of the complex nature of Parkinson's disease, a wide variety of health professionals are involved in care. Stepwise, we have addressed the challenges in the provision of multidisciplinary care for this patient group. As a starting point, we have gained detailed insight into the current delivery of allied healthcare, as well as the barriers and facilitators for optimal care. To overcome the identified barriers, a tertiary referral centre was founded; evidence-based guidelines were developed and cost-effectively implemented within regional community networks of specifically trained allied health professionals (the ParkinsonNet concept). We increasingly use ICT to bind these professional networks together and also to empower and engage patients in making decisions about their health. This comprehensive approach is likely to be feasible for other countries as well, so we currently collaborate in a European collaboration to improve community care for persons with Parkinson's disease.

1. Background

The number of patients with Parkinson's disease (PD) and related forms of parkinsonism is increasing in all ageing societies [1]. In Western Europe's five, and the world’s 10 most populous nations, the number of individuals with PD over the age of 50 was between 4.1 and 4.6 million in 2005; these numbers will be doubled by 2030 [1]. Likewise, the costs related to PD care will increase dramatically. PD is a very complex disorder, characterised by a wide array of both motor and nonmotor problems for which medical care alone is insufficient [2–6]. As a reflection of this complexity, no less than 18 different disciplines (e.g., physiotherapy and psychology) may be involved in PD care [7–9]. However, patients often have no access to the allied healthcare required [10]. Moreover, the involvement of various disciplines requires close collaboration and integration of medical and nonmedical care. Great challenges remain in the way multidisciplinary care is best realized for Parkinson patients. But, where to start? The purpose of this paper is to share the various steps we have taken (Figure 1), as they are likely to be feasible for application in other countries.

2. Stepwise Improvement of Community Health Care

Step 1 (gaining insight into current care). Detailed insight into the current provision of allied healthcare, as well as barriers and facilitators for optimal care, was lacking. As a first step, we therefore aimed to evaluate current care. Surveys involving more than 500 PD patients and 300 allied health professionals were used to gain this insight [11, 12]. The results revealed that on average therapists treated as few as three individual PD patients a year. Therapists also reported that they had only limited expertise in treating PD. A major barrier for improvement was the absence of guidelines to
Figure 1: Steps of the Dutch model to improve community healthcare for Parkinson’s disease.

support these therapists in providing optimal treatment. Most patients were referred by their neurologist. However, referring physicians had no information about the benefits of, for example, physiotherapy in PD, and were unable to find therapists with PD-specific interest or expertise. Finally, therapists of different disciplines (e.g., speech and language therapy, occupational therapy, and physiotherapy) were often unaware of each other’s treatment possibilities. Moreover, communication about a common patient (e.g., on treatment goals and timing of interventions) was very poor. As trends have been found towards positive effects of integrated care programs in the chronically ill [13] this needed to be improved. Therefore, our next step was to create a regional Parkinson, multidisciplinary expert centre.

Step 2 (creation of a regional expert centre). In order to offer expert care to PD patients and their carers, a regional Parkinson’s expert centre was initiated. The centre serves as a tertiary referral centre for a large catchment area, by offering critical revision of the diagnosis (if needed supported by ancillary investigations), recommendations with respect to drug treatment and stereotactic neurosurgery, and individually tailored multidisciplinary treatment advice. The centre also initiates and coordinates clinical trials and disseminates the newly acquired knowledge. The centre is part of the neurology department of one of the eight Dutch university medical centres. Several comparable initiatives have meanwhile arisen across the country.

Step 3 (development of evidence-based guidelines). Next, we started to develop evidence-based guidelines for allied healthcare. As physiotherapy is the most applied allied healthcare discipline in PD care, we first developed a guideline that targeted physiotherapy for PD. Conform international standards for guideline development, practice recommendations were developed based on the results of a systematic literature review, clinical expertise, and patient values. The recommendations were graded according to the level of evidence available [14]. The guideline was authorized and distributed by our national professional organisation for physiotherapy, the Royal Dutch Society for Physical Therapy (KNGF). Likewise, guidelines for speech
and language therapy and for occupational therapy were developed, authorized, and distributed [15]. For other disciplines, for example, dieticians, the development of guidelines has recently started. The guidelines provide decision support for everyday clinical practice.

3. ParkinsonNet

As dissemination does not automatically lead to implementation, we developed a multifaceted implementation strategy: ParkinsonNet. ParkinsonNet not only aims to implement the guidelines, but also to reorganise allied healthcare to increase the patient volume of therapists, make expert healthcare professionals visible to other professionals as well as to patients, and support communication amongst health care professionals involved in PD care as well as between professionals and patients. To set up a ParkinsonNet, first a region needed to be defined.

Step 4 (definition of a parkinsonNet region). Members of the ParkinsonNet team (at the regional expert centre) together with the coordinating neurologist of a general hospital defined the catchment area for which the ParkinsonNet needed to be developed. Within this geographic area, a local community of allied health professionals with Parkinson-specific expertise was created. The key points in this process were selection, training, communication, and transparency (Figure 1, steps 5 to 8).

Step 5 (selection of dedicated professionals). To succeed in increasing the patient volume, a relatively small number of therapists were selected for each regional ParkinsonNet. To allow the networks to evolve slowly, the Dutch networks were set up with a maximum of one physiotherapist for every 20,000 residents in the specific region, and one speech and occupational therapist for every 40,000 residents. These numbers were based on the preferred patient volume as reported by therapists (i.e., 15), the estimated number of PD patients in the Netherlands, the current referral pattern of physicians (more patients are referred to physiotherapy in comparison with occupational therapy or speech and language therapy), and the number of residents in the predefined region.

For selection, all allied health professionals in a specific region were informed about the benefits, requirements, and costs for participation. In all regions, the numbers of physiotherapists interested in participation exceeded the required number, making a selection required. Professionals working in the same neighbourhood were therefore asked to arrange self-selection. Only when this was not successful, the ParkinsonNet team made the selection based on motivation, bio sketch and current function in regional PD care. In the selection process we tried to reach a good geographical dispersion in the region. This, as an evaluation under Dutch PD patients and allied health professionals, revealed that they both were prepared to travel up to 15 minutes.

Step 6 (training based on guidelines). All allied health professionals selected for a future network participated in the same 3-day (for the first networks this was a 4-day), interactive course. Here they were trained to treat PD patients according to the evidence-based guidelines. The program entailed both mono- and multidisciplinary classes. Participating neurologists and PD nurse specialists were informed about the referral criteria and main treatment options of the allied health professions included in their regional ParkinsonNet. For physiotherapists, a guideline-based electronic patient record was developed to further support their clinical decision taking. During the course, physiotherapists were trained to use this patient record.

Step 7 (supporting communication). Starting at the course, networking was supported. For example, professionals from a specific region shared a table during lunch and together prepared and completed educational tasks during the course. After the course, continuation of network meetings takes place during three-monthly regional seminars and a yearly ParkinsonNet congress (see Step 9). Concerning communication about common patients, the development of regional communication plan was facilitated. In addition, a secured web-based community is used to enhance communication, both within the ParkinsonNet as with hospital professionals.

Step 8 (transparency). Patients, medical and nonmedical care professionals were informed about the ParkinsonNet. The location of the specialized therapists is visualized by web-based sources and printed folders. Moreover, structured and preferred referral to ParkinsonNet therapists by neurologists was supported by using standardized referral forms, including objective referral criteria. So, participating therapist were enabled to attract a large number of patients. A certification system, supported by professional societies, was developed to guarantee the quality of therapy provided by health professionals participating in these networks.

Step 9 (continuous education and exchange of knowledge). Each regional ParkinsonNet organises, if needed with support by the ParkinsonNet team, three-monthly seminars to for example, practice skills, discuss cases, and to enhance (multidisciplinary) collaboration within the region. Every year, the ParkinsonNet team organises a national ParkinsonNet congress with national and international speakers and a wide variety of Parkinson’s related workshops (e.g., on cognitive functioning, sleep, nutrition, and exercise and the brain). In addition, through a secured web-based community, up-to-date information is shared by the ParkinsonNet team.

4. Scientific Evaluation ParkinsonNet

In 2004, the first, multidisciplinary ParkinsonNet was designed and tested for its feasibility [17]. This ParkinsonNet included neurologists, a PD nurse specialist, physiotherapists, occupational therapists, and speech and language therapists. Given its feasibility and the enthusiasm of the participants, a cluster-randomized trial was designed to further evaluate ParkinsonNet. For feasibility purposes of the trial, eight ParkinsonNets were developed which only included the most used allied healthcare in PD, that is, physiotherapy.
Theses clusters were compared with eight clusters where care remained unchanged. The trial, in which 699 PD patients participated, showed that the quality of care increased and the volume of patients per therapist more than doubled within as little as six months while considerably saving costs [18]. In addition, evaluation of the connectedness of healthcare professionals within the ParkinsonNet showed that especially therapists treating more than nine PD patients a year were associated with stronger connectedness with other health professionals than those treating less than 10 PD patients a year. As connectedness between professionals is known to influence clinical decision making and the coordination of patient care [19], this knowledge is of high importance to the size of future networks.

5. National Coverage ParkinsonNet

Supported by these positive results, ParkinsonNet was endorsed by professional healthcare organizations and the national patient society. In 2010 national coverage within the Netherlands was achieved by 65 unique networks (Figure 2). The size of the networks is related to the population density of the specific regions. In addition to increase in number of networks, many additional disciplines have been added to the ParkinsonNet. Currently, throughout the Netherlands, 1885 care professionals are participating, amongst which 57 neurologists, 107 PD nurse specialists, 809 physiotherapists, 317 occupational therapists, 318 speech and language therapists, 89 dieticians, 76 elderly care physicians, 62 psychologists, 31 social workers, and 4 sex therapists.

6. Multidisciplinary Guidelines

In addition to the monodisciplinary guidelines, a multidisciplinary guideline has been developed in a joint collaboration among professional organizations of 18 medical professions, the patient society, and two national healthcare knowledge and quality institutes [7]. The multidisciplinary guideline includes recommendations not only for daily medical and nonmedical practice, as an update of the NICE guidelines [8], but also for network care. Specifically these recommendations, concerning collaboration, expertise, communication, and finances were lacking in the existing guidelines [20], even though they are of high importance. For example, in outpatient neurology, dissatisfaction with communication is related to noncompliance [21]. As part of the support for collaboration, the guideline provides a detailed overview of impairments, limitations, restrictions, and external factors related to PD (Figure 3) [7]. For this overview the common language of the International Classification of Functioning,
Disability, and Health (ICF) was used [16]. So far, an ICF for neurology combining three neurologic disorders was available, but not for PD specific [22]. This PD-specific classification can further improve communication in relation to patient functioning between health care workers, researchers, and social policy makers.

7. Empowering Patients

Traditionally, the relationship between patients and their healthcare providers is fairly paternalistic, with healthcare providers making decisions (with the best intentions) and patients simply carrying out instructions. Some patients appreciate this role. However, many patients wish to have more control over their own care [23] and patient preferences may differ from what doctors focus on [24]. The guideline supports patient empowerment, for example, by teaching therapists how to get to the treatment goal in “partnership” with the patient. This, however, will not be sufficient [25]. Increasingly, the Internet can provide solutions to support patient empowerment [26]. To further support patients within ParkinsonNet regions to participate in medical decisions made about their health, we developed a web-based “portal to empower patients.” The portal provides patients with information necessary to make choices in their own health care process. For example, this includes actual and controlled information about all treatment options. In addition, patients are enabled to easily find a specialized health care professional within their community, based on transparent background information (e.g., the number of PD patients treated by a professional, or the education received to increase Parkinson-specific knowledge and expertise). Another tool for patients will be the opportunity to build their own virtual network of care providers, supporting information sharing and collaboration between all participants.

8. International Collaboration

As described, one of our first steps to improve PD care was the development of an evidence-based physiotherapy guideline [14]. An external quality evaluation of all Parkinson guidelines available worldwide, by the Dutch Institute for Health Care Improvement (CBO), showed that this guideline is one of the few which is of good quality [7]. In addition, to date, it is still unique in its field. As a consequence, internationally there is a lot of interest for using the guideline. The Association for Physiotherapists in Parkinson’s Disease Europe (APPDE; http://www.appde.eu/) therefore endorses the guideline and its implementation. Currently, we are updating the guideline, in a joint collaboration among 19 European physiotherapy associations, members of the European Region of the World
Confederation for Physical Therapy (ER-WCPT). This will lead to a first European guideline for physiotherapy in Parkinson’s disease in 2012. As a first step in the guideline development, surveys have been set out Europe-wide \( (n = 10,000) \) to gain insight into current care, barriers met in delivering this care, possibilities for improvements and to identify those therapists interested to become members of a PD expert’s network. Perhaps this is another first step towards improving community healthcare (Figure 1). The results of the survey will be used to develop key questions for the European guideline. In addition, the results will support the participating countries to further structure their guideline implementation plans.

At the same time, possibilities for using the ParkinsonNet concept for implementation of the guideline are being explored in several European countries as well as in the United States. The approach seems applicable to other countries with a similar population density and health care system (e.g., compensation of physical therapy). Through these future networks, also the guidelines for occupational therapy and for into English in collaboration with the National Parkinson Foundation (http://www.parkinson.org/), can be implemented and thus leading to multidisciplinary Parkinson’s networks in many countries.

9. Conclusions

Given the complex nature of PD, many disciplines will be involved in Parkinson care. Aiming for optimal Parkinson care, in the Netherlands, care for persons with Parkinson’s has been changed stepwise. The Dutch approach seems applicable to other countries, be it with adaptations based on population density and health care organization.

References


Research Article

Altered Dynamic Postural Control during Step Turning in Persons with Early-Stage Parkinson’s Disease

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1. Introduction

Postural control is the ability to alter the magnitude and patterns of segmental kinematics (e.g., trunk and limb movements) in order to direct body position in response to external mechanical demands imposed during static and dynamic tasks such as turning [1, 2]. Functional independence, and consequently quality of life, is compromised in individuals with postural control deficits. Persons with early-stage Parkinson’s disease (EPD), Hoehn and Yahr stage 1 and 2, may not demonstrate overt clinical symptoms and may describe only minimal levels of functional impairment, such as reduced gait velocity and stride length, during simple movement tasks including straight walking [3, 4]. However, they often demonstrate altered postural control during standing tasks [5] and report difficulty with turning [6]. Turning difficulty becomes a sensitive indicator of a higher prevalence of freezing and falling in persons with advanced PD (Hoehn and Yahr stage ≥3 with moderate to severe symptoms) [7, 8].

The demands of turning present unique challenges to individuals with impaired postural control as they are required to initiate a state of disequilibrium during single limb stance in order to change directions during an ongoing movement [9, 13]. This disequilibrium is created by increasing the distance between the body’s COM and the center of pressure (COP; the equilibrium point of the distribution of the resultant ground reaction force applied to the base of support). An increased distance between these two points not only creates momentum necessary to turn, but also requires increased neuromuscular control (e.g., neural drive,
muscle forces, and joint power) to redirect and control this momentum. Alterations in turning strategies are thought to reflect an individual’s inability to meet these increased neuromuscular demands. For example, when compared to healthy controls, persons diagnosed with advanced PD utilize postural control strategies that include longer turning times [14] along with a greater number of smaller steps [8, 14] to complete a turn. These postural adjustments serve to decrease the body’s momentum, reduce the distance between the COM and the COP, and in turn decrease the neuromuscular demands. While alterations in postural control strategies have been observed in individuals with advanced PD, they have not been characterized in individuals diagnosed with EPD.

Individuals diagnosed with EPD do report difficulty turning [6]. However, in contrast to individuals diagnosed with advanced PD, they do not frequently exhibit observable movement impairments that could impact turning such as shuffling gait, freezing episodes, and en bloc movements. [3, 4, 15, 16]. A more detailed evaluation of postural control strategies employed by individuals diagnosed with EPD during turning is needed. However, more traditional measures of postural control that relate the distance between the positions of the COP and COM may not be sensitive enough to detect differences between individuals diagnosed with EPD and healthy controls because they do not take into account the dynamic nature of the turning task. During dynamic tasks it is important to consider not only the position of the COM but also the magnitude and direction of the COM velocity in relation to the COP [17, 18].

Despite self-reports of difficulty turning in persons with EPD, studies to date have not characterized the postural control strategies used during turning in this cohort. Early identification of these strategies may be used to develop effective intervention protocols that (1) improve turning capabilities and (2) increase balance confidence in persons with EPD. Therefore, the purpose of this study was to characterize the differences in postural control during a step turn activity, between persons with EPD and healthy age-matched control (HC) participants. We hypothesized that, compared to HC participants, persons with EPD would demonstrate a dynamic postural control strategy that reduced the demands on the neuromuscular system. Specifically, we hypothesized that when accounting for the position, magnitude and velocity of the COM persons with EPD would demonstrate shorter distances between the COP and the eCOM than healthy controls during both phases of a step turn at 90 degrees. Moreover, this will be accomplished by both decreasing their COM velocity and the distance between their COP and the COM.

2. Methods

2.1. Participants. Fifteen persons with EPD and 10 HC subjects participated. Participant characteristics are provided in Table 1. A fellowship-trained movement disorder specialist confirmed diagnosis of idiopathic PD in our participants, performed the Unified Parkinson’s Disease Rating Scale (UPDRS), and determined Hoehn and Yahr stage for each individual participant. Participants that had pharmacological treatment were stable and tested while they were on their routine therapy (Table 2). At the time of testing, none of the participants exhibited any fluctuations in motor ability throughout the day, dyskinesia, dystonia, or other signs of involuntary movement.

The inclusion criteria for the early PD group were the following: (1) age ≥18 years old, (2) able to ambulate at least 14 meters (time not measured) without a walker or other devices, (3) diagnosed with PD within 3 years [19], (4) Hoehn and Yahr stages 1-2 (indicating EPD), and (5) stable on PD medications. Healthy control participants were age and gender-matched to the participants in the early PD cohort. Participants were excluded from the study for the following: (1) surgical intervention for persons with PD, (2) Mini-Mental State Exam (MMSE) score <24 [20], (3) comorbidities affecting gait (e.g., diabetes, musculoskeletal injury, arthritis, vestibular disorders), (4) severe vision problems, and (5) pregnancy.

2.2. Protocol. All testing took place in the Musculoskeletal Biomechanics Research Laboratory at the University of Southern California (USC). Procedures were explained to each participant and each participant signed an informed consent form approved by the Institutional Review Board of the USC. Participants were instructed to walk straight at a “self-selected, comfortable pace and turn at the designated stanchions at a right angle” toward their dominant leg and then continue walking in the new direction (Figure 1). Prior to testing the dominant leg was determined as the leg they would use to kick a ball as far as possible. No other instructions were given to the participants. The subjects

Table 1: Mean and standard deviation of participant’s characteristics.

<table>
<thead>
<tr>
<th></th>
<th>EPD (n = 15)</th>
<th>HC (n = 10)</th>
<th>Differences (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>62 (9.1)</td>
<td>60 (8.5)</td>
<td>2 (−5.49; 9.49)</td>
</tr>
<tr>
<td>Height (m)</td>
<td>1.68 (0.07)</td>
<td>1.72 (0.09)</td>
<td>−0.04 (−0.11; 0.03)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>68.9 (12.1)</td>
<td>74.8 (17.2)</td>
<td>−5.9 (−17.99; 6.19)</td>
</tr>
<tr>
<td>Approach gait velocity (m/s)</td>
<td>1.35 (0.14)</td>
<td>1.46 (0.14)</td>
<td>−0.11 (−0.23; 0.01)</td>
</tr>
</tbody>
</table>

Mean (Standard Deviation).
EPD: persons with early-stage Parkinson’s disease.
HC: healthy control participants.
Table 2: Dosage of Parkinson’s medications.

<table>
<thead>
<tr>
<th>Participant number</th>
<th>Medication</th>
<th>Dosage</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>P01</td>
<td>Levodopa/carbidopa</td>
<td>25–100 mg</td>
<td>3x/day</td>
</tr>
<tr>
<td>P02</td>
<td>De Novo</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pramipexole</td>
<td>1 mg</td>
<td>3x/day</td>
</tr>
<tr>
<td>P03</td>
<td>Rasagiline</td>
<td>1 mg</td>
<td>1x/day</td>
</tr>
<tr>
<td></td>
<td>Levodopa/carbidopa</td>
<td>50–200 mg</td>
<td>3x/day</td>
</tr>
<tr>
<td>P04</td>
<td>De Novo</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pramipexole</td>
<td>1.5 mg</td>
<td>3x/day</td>
</tr>
<tr>
<td></td>
<td>Selegiline</td>
<td>5 mg</td>
<td>2x/day</td>
</tr>
<tr>
<td></td>
<td>Rasagiline</td>
<td>1 mg</td>
<td>1x/day</td>
</tr>
<tr>
<td>P05</td>
<td>Amantadine</td>
<td>100 mg</td>
<td>2x/day</td>
</tr>
<tr>
<td>P06</td>
<td>De Novo</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Rasagiline</td>
<td>1 mg</td>
<td>1x/day</td>
</tr>
<tr>
<td></td>
<td>Trihexyphenidyl</td>
<td>4 to 6 mg</td>
<td>1x/day</td>
</tr>
<tr>
<td>P07</td>
<td>De Novo</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pramipexole</td>
<td>1.5 mg</td>
<td>3x/day</td>
</tr>
<tr>
<td></td>
<td>Selegiline</td>
<td>5 mg</td>
<td>2x/day</td>
</tr>
<tr>
<td></td>
<td>Rasagiline</td>
<td>1 mg</td>
<td>1x/day</td>
</tr>
<tr>
<td>P08</td>
<td>Rasagiline</td>
<td>1 mg</td>
<td>1x/day</td>
</tr>
<tr>
<td>P09</td>
<td>Levodopa/carbidopa</td>
<td>150 mg</td>
<td>3x/day</td>
</tr>
<tr>
<td>P10</td>
<td>Pramipexole</td>
<td>0.75 mg</td>
<td>3x/day</td>
</tr>
<tr>
<td></td>
<td>Rasagiline</td>
<td>1 mg</td>
<td>1x/day</td>
</tr>
<tr>
<td>P11</td>
<td>Pramipexole</td>
<td>1.5 mg</td>
<td>3x/day</td>
</tr>
<tr>
<td></td>
<td>Rasagiline</td>
<td>1 mg</td>
<td>1x/day</td>
</tr>
<tr>
<td>P12</td>
<td>Levodopa/carbidopa</td>
<td>25–100 mg</td>
<td>4x/day</td>
</tr>
<tr>
<td>P13</td>
<td>Levodopa/carbidopa</td>
<td>25–100 mg</td>
<td>3x/day</td>
</tr>
<tr>
<td></td>
<td>Rasagiline</td>
<td>0.5 mg</td>
<td>1x/day</td>
</tr>
<tr>
<td>P14</td>
<td>Pramipexole</td>
<td>0.5 mg</td>
<td>3x/day</td>
</tr>
<tr>
<td></td>
<td>Pramipexole</td>
<td>1.5 mg</td>
<td>3x/day</td>
</tr>
<tr>
<td>P15</td>
<td>Selegiline</td>
<td>5 mg</td>
<td>2x/day</td>
</tr>
<tr>
<td></td>
<td>Trihexyphenidyl</td>
<td>2 mg</td>
<td>3x/day</td>
</tr>
</tbody>
</table>

Figure 1: Laboratory setup. Dashed line: starting point; A: first trigger; B: second trigger; black square: force plate (AMTI 1.2 m × 1.2 m, 1560 Hz). Two stanchions were placed at the midpoint of each force plate. Starting point to A: 1 m. A to B: 2.4 m. B to force plate: 0.6 m. Force plate to stanchions: 0.6 m.
started 1 meter from the first timing trigger. They then walked for an additional 2.4 meters before walking through the second timing trigger, which was located 0.6 meters in front of the force plate.

A total of 10 turning trials were recorded for each participant. The first three successful trials during which they used a step turn strategy were considered for analysis. A step turn is defined as a change in direction opposite to the pivot foot [10, 13]. Ninety-degree turns were selected for analysis because these types of turns are associated with the navigation of corridors, street corners, and other common walking activities. Moreover, Sedgman and colleagues reported that the majority of turns experienced during activities of daily living were between 76° and 120° [21].

Kinematic data were sampled at 60 Hz using a motion analysis system (Vicon 612, Oxford Metrics Ltd., Oxford, England). Reflective markers (14 mm spheres) were placed bilaterally on the skin over specific anatomical landmarks including the anterior, posterior, and lateral cranium, acromion processes, anterior and posterior shoulders, greater tubercles of humerus, medial and lateral humeral epicondyles, radial styloid process, ulnar head, third metacarpophalangeal joints, 7th cervical vertebrae, sternoclavicular notch, iliac crest, anterior superior iliac spines, posterior superior iliac spines, L5-S1 joint, medial and lateral femoral epicondyles, medial and lateral malleoli, first and fifth metatarsal heads, and first proximal/distal phalanx. Additionally, cluster markers were placed with a band over the upper arms, lower arms, thighs, shanks, and shoe heels. Reflective markers were identified manually within the VICON Workstation software and then imported into Visual 3D software (C-Motion, Rockville, MD). 3D marker coordinates were lowpass filtered at a cut-off frequency of 6 Hz.

Kinetic data were captured using 1.2 m × 1.2 m AMTI (Advanced Mechanical Technologies, Inc., Newton, MA, USA) force platform at 1560 Hz. The size of the platform allowed for quantification of ground reaction forces throughout the entire task. Kinematic and kinetic data were interfaced to the same microcomputer allowing for synchronization of data.

2.3. Data Analysis. Dynamic postural control during turning was quantified using the method previously described by Hof (1) [17]. It was defined as the difference between the COP and an extrapolated COM calculated to account for the position, magnitude and velocity of the COM:

\[
\text{Dynamic Postural Control} = \text{COP} - \left(\text{COG} + \frac{\text{COMvel}}{\sqrt{\left(\frac{g}{l}\right)}}\right).
\]  

The COP was determined from the forces and moments obtained from the force platform. The position of the total body COM was defined using the weighted sum of the COM of all 15-body segments. Based on Winter [22], instantaneous velocity of the total body COM (COMvel) was computed from the linear total body COM positions (COMpos):

\[
\text{COMvel}_n = \frac{[\text{COMpos}_n + 1 - \text{COMpos}_{n - 1}]}{\Delta t},
\]

where, \(n\) is the event frame, and \(\Delta t\) is the time between event frames.

The center of gravity (COG) represents the vertical projection of the body’s COM. It was calculated based on the medial-lateral and the anterior-posterior locations of the COM. The COM velocity was divided by the natural frequency of the limb. The natural frequency was calculated as \(\sqrt{\left(\frac{g}{l}\right)}\) where \(g\) is the acceleration of gravity and \(l\) is the length of the leg measured from the ankle joint center to the COM. The extrapolated COM (eCOM) was calculated as sum of the COG and the new COM velocity term:

\[
e\text{COM} = \left(\text{COG} + \frac{\text{COMvel}}{\sqrt{\left(\frac{g}{l}\right)}}\right).
\]

The turning cycle was defined from heel strike of the approach step to heel strike of the acceleration step and was broken into 2 phases. Phase 1 was defined from heel strike of the approach step to heel strike of the pivot step. Phase 2 was defined from heel strike of the pivot step to heel strike of the acceleration step (Figure 2). The dependent variable dynamic postural control was measured as the peak distance between the COP and the eCOM. Peak distance between the COP and the COG, and the peak COM velocity were identified for each phase. These measures were considered in the case in which dynamic postural control differed between groups, as alterations in both position and velocity can affect this measure of dynamic postural control. The average approach gait velocity across three successful trials was calculated over the 2.4 meters between the first trigger (A) and the second trigger (B) during turning (Figure 1). The single- and double-limb gait cycle phases were determined using force plate contact and the vertical velocity of the virtual center of each foot [23].

2.4. Statistical Analysis. To determine if differences in our dependent variable, dynamic postural control, existed
between persons with EPD and HC participants across turning phases, a $2 \times 2$ (group $\times$ phase) ANOVA was performed. In the case in which differences in dynamic postural control were found between groups, independent $t$-tests were performed to determine if group differences existed in the input variables used to calculate dynamic postural control, position of the COG relative to the COP, and the COM velocity within each phase. All statistical analyses were performed using SPSS 15.0 (Chicago, IL) with an alpha level set at 0.05.

### 3. Results

Participant characteristics and approach gait velocity are provided in Table 1. There were no significant group differences for age, height, weight, or approach gait velocity ($P > 0.05$). In the EPD group, average time since diagnosis was $18.2 \pm 13.9$ months, average H&Y score was $1.9 \pm 0.3$, and average UPDRS motor score was $21.2 \pm 6.7$. Average UPDRS gait and postural stability subscores were $0.1 \pm 0.4$ and $0.3 \pm 0.5$, respectively.

No significant group by phase interaction was found for dynamic postural control ($F = 0.584$, $P = 0.453$). Main effects of group and phase are found for dynamic postural control. Persons with EPD demonstrated statistically significant smaller peak COP-eCOM distances compared to HC participants during both Phase 1 (20.6% difference; $0.34 \pm 0.05$ versus $0.41 \pm 0.06$ m; $P < 0.01$) and Phase 2 (21.1% difference; $0.38 \pm 0.06$ versus $0.46 \pm 0.07$ m; $P = 0.01$) of the step turn (Figure 3(a)). The peak distance between the COP and the eCOM always occurred during single limb stance within each of the phases.

Compared to control participants, persons with EPD demonstrated statistically significant smaller peak COP-COG distances during both Phase 1 (30.8% difference; $0.13 \pm 0.03$ versus $0.17 \pm 0.03$ m; $P < 0.01$) and Phase 2 (28.6% difference; $0.21 \pm 0.05$ versus $0.27 \pm 0.04$ m; $P < 0.05$; Figure 3(b)).
Although there was no significant difference in the average approach gait velocity between groups, persons with EPD exhibited significantly slower peak COM velocity when compared with control participants during phase 1 (14% difference; 0.64 ± 0.10 versus 0.74 ± 0.10 m/s) and phase 2 (35% difference; 0.41 ± 0.11 versus 0.63 ± 0.08 m/s; \( P < 0.05 \); Figure 3(c)) of the turning cycle.

4. Discussion

This study identified differences in dynamic postural control strategies in persons with EPD during step turning activities compared to HC participants. Using the eCOM, we were able to account for not only the position of the COM but also the magnitude and velocity. This is particularly important during turning as the momentum of the COM is needed for forward propulsion and redirection. We found that persons with EPD utilized shorter distances between the COP and the eCOM during both phases of the turning cycle. For both phases the group differences were noted during single limb stance. This suggests that during a time in which postural control demands are greatest, individuals with EPD adopt a strategy that aims to decrease these demands. It is also important to note that the differences observed in postural control between the groups appear to be largely driven by alterations in magnitude, not timing, suggesting that individuals with EPD are not adopting an entirely new strategy but merely scaling the strategy typically used to turn (Figure 3).

Persons with EPD appeared to scale both position and velocity of the COM: factors used to calculate postural control in this study. Both the shorter peak distance between the COP and the COG, and the slower peak COM velocity exhibited by individuals with EPD during the turn limit the disequilibrium experienced by the individual. Both of these adjustments have the potential to decrease neuromuscular demands. A smaller COP-COG distance reduces the moment arm created for the body weight vector acting around the centers of joint rotation, and thus the magnitude of the muscular force required to control the COM [24]. Additionally, a slower COM velocity reduces the momentum of the COM and decreases the muscular force required to decelerate and redirect the COM.

These alterations are consistent with what has been observed in persons with more advanced PD (longer turning time and smaller steps) during turning [8, 14, 25]. The current data support self-reports of “difficulty in turning” from persons with EPD [6]. Our findings are similar to those reported by researchers investigating other transitional movement patterns in persons with more advanced PD, namely gait initiation and sit-to-walk activities. For example, Martin and colleagues [26] reported a shortening of the separation between the COM and the COP during gait initiation in persons with PD, compared to healthy older adults. Moreover, Buckley and colleagues [27] reported that compared to healthy control subjects, persons with PD utilized a conservative movement strategy that limited separation of COP-COM during sit-to-walk transitions. We demonstrated that when we challenged individuals with EPD with a turning task, alterations in postural control similar to those seen in more advanced stages were observed. This is of particular importance since this group does not commonly demonstrate obvious signs of gait disturbance [3, 4].

Although the current findings describe adjustments in postural control in individuals with EPD, they are not sufficient to tease out whether or not the COP-eCOM difference is a primary deviation or a secondary compensation of the disease. The reduced COM velocity demonstrated by our participants is in agreement with previous reports of slower turning velocity in persons with PD (i.e., task-specific bradykinesia) [14, 25]. As discussed, our data demonstrate that persons with EPD utilize a scaled motor control strategy that limits separation of the COP and the eCOM. This could be due to lack of neuromuscular control of the COM, limb and trunk position, or the result of bradykinesia or rigidity-primary deviations associated with compromised basal ganglia function. Alternatively, the findings may also be the result of secondary compensation of the disease. For example, this strategy could be adopted due to the inability to generate appropriate momentum or the presence of neuromuscular deficits, which limit adequate muscular force production [26, 28]. While we did not directly measure muscular force, our findings are consistent with reports of reduced lower extremity force generation in persons with PD [29]. In aggregate, the cross-sectional designs of the previously mentioned studies and the absence of strength measures in the current study limit our ability to tease out whether or not the shorter COP-eCOM differences are primary deviations related to a lack of neuromuscular control or secondary compensation of the disease. Future studies that incorporate longitudinal designs and strength measures will ultimately be required to delineate these underlying factors.

A limitation of the study is that we only examined one walking speed, one turning direction, and one turning angle. Specifically, the participants were instructed to walk at their self-selected, comfortable pace and then turn to their dominant side at the stanchions and continue walking in the new direction. Although the instructions for participants to walk at their “self-selected, comfortable pace” were instituted in order to assess participants during their most frequently utilized walking speeds, these instructions are likely to have increased the variability of walking speed across subjects. It is not clear, however, if increased walking-speed variability would also increase the variability of our primary outcome variable, COP-eCOM, because participants may select a safe turning strategy that preserves COP-eCOM distance, independent of walking speed. Moreover, individuals will often have to modify their movement speed (either slowing or speeding-up) during ADLs in response to external/environmental conditions (e.g., weather, traffic lights, ground/floor frictional characteristics, obstacles, etc.). Thus, future studies should examine the effects of speed on postural control during turning in persons with PD, and include trials “as fast as possible”, “as safe as possible”, and at other predetermined speeds. Additionally, in order to navigate successfully, people must turn both right and left and negotiate a variety of turning angles (although the majority of turns experienced during ADLs
are between 76° and 120°) [21]. These additional directions and turning angles should also be examined in future study designs.

This study also did not examine the influence of medication on turning behavior and COP-eCOM. Participants that had pharmacological treatment were stable with no fluctuations of PD symptoms and tested while they were on their routine therapy. At the time of testing, none of the participants exhibited dyskinesia, dystonia, or other signs of involuntary movement. Thus, whether or not COP-eCOM distances would have been different had the participants not been on their routine therapy cannot be inferred from the current investigation. In a recent report, Hong and Earhart reported that although medication significantly improved UPDRS scores and walking velocity, it did not statistically significantly alter turning performance [30]. The authors went on, however, to report that “there was evidence for [turning] improvements particularly with respect to the amplitudes of relative rotation between segment rotations with effect sizes ranging from 0.42 to 0.70.” They noted that their “…results suggest that only certain features of impaired turning may be responsive to anti-Parkinson’s medication.” The participants in the Hong and Earhart study were older and had more advanced PD than participants in the current study—making extrapolation of their findings to the current investigation difficult. We hypothesize, however, that medication effects on turning in persons with early PD will be less evident. Additional studies investigating the influence of medication on COP-eCOM during turning will be needed in persons with EPD to test this hypothesis.

Despite these limitations, the results of the current study provide important additional evidence that functional impairments can be detected even in the early stages of the disease, when clinical signs of gait disturbance are often absent [5, 31]. Taken together, these reports suggest that identifying the movement limitations associated with PD requires examination of more complex tasks that increase the challenge to the neuromuscular system, such as turning and gait initiation. The findings also suggest that the peak COP-eCOM distance generated during turning activities may be a useful index for quantifying disease severity and intervention effectiveness. In order to determine whether the postural control strategies during step turning are sensitive to disease severity, additional studies that examine individuals across a broader range of disease severity will be necessary. Additionally, studies will be needed to delineate the influence of rehabilitation interventions on postural control during turning in persons with EPD.

5. Conclusion

Compared to HC participants, persons with EPD altered their postural control strategies (shorter distance between the COP and the eCOM) during the step turn. Persons with EPD appear to decrease their overall movement amplitude (i.e., COM displacement, velocity) suggesting that dynamic postural control during turning is altered even in the early stages of PD.

Acknowledgments

The authors gratefully acknowledge Dr. Petzinger for help with subject recruitment and patient evaluations and providing recommendations and guidance in the development of the study. This study was supported by a Magistro Family Foundation Research Grant, the Grant-in-Aid Award at American Society of Biomechanics, and the James Zumberge Research and Innovation Award.

References


Review Article

Is Freezing of Gait in Parkinson’s Disease a Result of Multiple Gait Impairments? Implications for Treatment

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Several gait impairments have been associated with freezing of gait (FOG) in patients with Parkinson’s disease (PD). These include deteriorations in rhythm control, gait symmetry, bilateral coordination of gait, dynamic postural control and step scaling. We suggest that these seemingly independent gait features may have mutual interactions which, during certain circumstances, jointly drive the predisposed locomotion system into a FOG episode. This new theoretical framework is illustrated by the evaluation of the potential relationships between the so-called “sequence effect”, that is, impairments in step scaling, and gait asymmetry just prior to FOG. We further discuss what factors influence gait control to maintain functional gait. “Triggers”, for example, such as attention shifts or trajectory transitions, may precede FOG. We propose distinct categories of interventions and describe examples of existing work that support this idea: (a) interventions which aim to maintain a good level of locomotion control especially with respect to aspects related to FOG; (b) those that aim at avoiding FOG “triggers”; and (c) those that merely aim to escape from FOG once it occurs. The proposed theoretical framework sets the stage for testable hypotheses regarding the mechanisms that lead to FOG and may also lead to new treatment ideas.

1. Introduction

In a recent comprehensive review on the pathogenesis of freezing of gait (FOG), Nutt et al. describe several competing hypotheses that have been put forth to explain this episodic gait disturbance that mysteriously affects many, but not all patients with Parkinson’s disease (PD) [1]. For example, when comparing the gait of PD patients who suffer from freezing (PD + FOG) with that of patients who do not suffer from the symptom (PD-FOG), we identified several gait properties that were abnormally altered in PD + FOG patients, even in the interictal period [2], that is, functional walking periods in between freezing episodes. We suggested that impairments in the regulation of the gait cycle (i.e., poor control of rhythmicity [3], impaired bilateral coordination of stepping [4], and increased asymmetry [5]) operate in the background, perhaps with executive function deficits, to set the stage for FOG that occurs in response to “triggering events” (e.g., turning). Some researchers highlighted the ideas that impairments in dynamic postural control while walking [6] and in step scaling [7–10] are related to the presence of FOG in PD. Other investigators underscore the importance of transitions and some suggest that visual-spatial processing is involved in the pathogenesis of FOG [11, 12]. In short, a number of different, apparently competing theories have been put forth to explain this disabling phenomenon.

Nutt et al. astutely point out that the extant hypotheses may not necessarily be exclusive [1]. In this paper, we take a closer look at this idea and show how multiple gait impairments may take place simultaneously and lead to FOG. More specifically, we propose that motor control mechanisms
of two or more gait features associated with FOG may interact with each other and, under certain circumstances, deteriorate synergistically. Once the level of deterioration crosses some imaginary “redline” or critical threshold, FOG occurs.

In the following paragraphs, we introduce the theoretical framework underlying the hypothesis that synergism in the malfunction of the control of different gait features can cause an overall effect on gait performance that leads to freezing episodes in patients with PD. In particular, we describe how two seemingly independent gait features may both deteriorate when challenged, thereby increasing the propensity for FOG. We illustrate this with respect to step length scaling and gait symmetry. Then, we discuss the clinical implications of this viewpoint.

2. Theoretical Framework: Combined Effect of Changes in Background Levels of Gait Parameters Associated with FOG Determines the Occurrence of FOG Episode

Figure 1 heuristically illustrates the concept that a FOG episode occurs when the overall gait performance is no longer sufficient to support functional gait. The overall gait performance is an expression of the combination of multiple control mechanisms; each one addresses a different aspect of walking. In Figure 1(a), the simultaneous behavior of five gait features associated with FOG in PD are depicted: (1) bilateral coordination of gait (BCG)—the control of the antiphase left-right stepping pattern; (2) gait symmetry—the control of producing similar motor program outputs to both legs, for example, equal swing times, equal step lengths (The converse of gait symmetry, gait asymmetry, GA, is a more readily measureable and can be quantified by contrasting the function of one leg with that of the other); (3) step scaling—the distance covered by each step; (4) Dynamic postural control—as expressed, for example, by center of pressure movements; and (5) Gait rhythmicity—as expressed, for example, by stride-to-stride variability (higher variability reflects lower rhythmicity).

According to the proposed conceptual model, the individual performance in each of these domains (a) is not constant and varies over time and (b) in some instances, performance of a given feature may be influenced by another gait feature. For example, during the time period 10–20 (arbitrary units), all gait features associated with FOG maintain a fairly constant level and operate seemingly independent from each other. Similarly, when the dynamic postural control deteriorates (at time 60–70), other gait features are not influenced.

On the other hand, other gait circumstances may yield stronger dependency between different gait features. This is illustrated, for example, in the time periods 20–30 and 40–50. Deteriorations in gait symmetry are accompanied with deteriorations in step length scaling, with a suggestion that BCG may also be influenced in the 40–50 time window.

Malfunctions in gait parameters that are associated with FOG can influence the propensity for FOG not only after gait has started, but even during the preparation for walking (e.g., start hesitation that occurs prior to the initiation of walking). In these circumstances, the motor control system is not able to raise a specific gait parameter to a functional level, a fact which may also influence other gait features and result in increased propensity for FOG (lower trace in Figure 1(a)).

Theoretically, the interrelationships between different gait features and in particular gait features associated with FOG in PD can be described by the following analytical formulation:

\[ X_k(t) = \sum_{i=1, i \neq k}^{n} f_i(t, X_i), \]  

where \( X_k \) represent any one of the gait parameters associated with FOG and \( n \) is the number of gait features that are associated with FOG. Equation (1) emphasizes that each gait parameter associated with FOG is influenced by any of the others, and this dependency varies with time, that is, varies with the changing “circumstances.” Furthermore, the relationship between any given pair of FOG associated gait parameters is not identical (i.e., different functions, \( f_i \), determine the dependence). In the case of one pair, it might be strong, while for another pair the association may be weaker.

The thick curve in Figure 1(b) represents the compound gait performance which is the combination (not necessarily linear) of all individual gait features associated with FOG. Denoting this parameter by \( X \), the following analytical relationship can describe the relationship between \( X \) and any individual \( X_i \):

\[ X(t) = F(X_1, X_2, \ldots, X_n). \]  

According to this proposed framework, as long as the overall gait performance is maintained above a border line (i.e., a threshold), functional gait is maintained. However, once the overall gait performance deteriorates below the “threshold,” FOG occurs. As illustrated, the deterioration of gait performance and the resultant FOG may take place as a result of poor control of one or more individual gait features associated with FOG. The duration of the FOG episode is dependent upon the ability to restore the control over the gait feature(s) that deteriorates.

3. An Example: Do the “Sequence Effect” and Gait Asymmetry Converge?

The theoretical concept depicted above can be exemplified by probing the possibility that step scaling and gait asymmetry are related to each other and to FOG. Indeed, we suggest that insight into the pathogenesis of FOG can be gained by taking a closer look at the “sequence effect,” one of the five primary hypotheses summarized by Nutt et al. [1]. Iansek et al. first described the sequence effect and its potential contribution to FOG [8]. In a follow-up study that was designed to experimentally control the “background” step length, Chee et al. [7] found that when patients were cued to walk at a markedly reduced step length, FOG became
Figure 1: Freezing of gait and gait features deterioration. (a) Quality of performance of gait features associated with FOG (thin lines in top 5 traces) may vary over time (hypothetical data). Similarly the level of interaction between these gait features may vary with time and in response to different circumstances or provocations (see text). BCG—Bilateral coordination of gait. (b) The combination of the performances of the individual gait features dictates whether FOG will occur or whether functional walking will be maintained. If the overall performance deteriorates below a certain threshold (horizontal line), then gait freezes (FOG zone). Deterioration in the overall gait performance can be an expression of malfunction of single gait feature associated with FOG (see text). In some cases, the deterioration of one gait feature can cause the deterioration of one or more gait features as portrayed in (a). FOG—Freezing of gait, a.u.—arbitrary units.
the healthy control subjects who did not exhibit the sequence effect had much lower values of asymmetry (5.1% and 7.3%, resp.; see Figure 2(b) for single calculations done for single trace only). While not definitive, this finding supports the idea that more than one gait feature may be deteriorating in association with FOG. Further studies are needed to address the possibility that in reduced step length conditions, gait asymmetry increases among patients who experience FOG just prior to FOG, potentially another ingredient needed to produce the faulty state that leads to FOG.

Indeed, if we seek to develop the optimal rehabilitation program for FOG, it is critical to move beyond a description of the phenomena and to try and identify cause and effect. Examination of the data in the zigzag trace (depicted in Figure 2(a)) shows that across the strides, step length is not correlated with step length asymmetry (Spearman’s $\rho = -0.24$, $P = 0.43$). There is, however, a strong inverse relationship between step length and the level of asymmetry seen in the preceding stride (Spearman’s $\rho = -0.76$, $P = 0.005$): relatively increased values of asymmetry tend to precede relatively smaller step lengths in the next stride (Figure 2(c)). In fact, Fasano et al. [13] have recently drawn similar conclusions from their findings on gait freezing during treadmill walking with unbalanced subthalamic nucleus deep brain stimulation (STN-DBS; see below): “During poorly coordinated gait, information from the leg with the shorter stride length... might conflict with the internal cueing of the opposite leg and cause the leg with the longer stride to decrease stride length...” In PD patients, however, the strategy might further destabilize gait and induce a vicious circle of progressively shorter step length (“sequence effect”), resulting in FOG. Therefore, our findings indicate a possible link between two apparently unrelated pathogenetic theories of FOG: poor interlimb coordination and the “sequence effect” [13].

While intriguing, further work is, nonetheless, needed to determine if these findings actually reflect causality. Still, it appears that there may be more to the sequence effect than meets the eye and it may be an oversimplification to assume that a sole factor is behind the mysterious phenomenon known as FOG. This example demonstrates how multiple gait deficits, for example, asymmetry, a reduced step length,
and a further decrease in the step length, are apparently simultaneously related to FOG. Acting alone, they may not always be sufficient to cause FOG. Moreover, during walking periods that are not interrupted by FOG, these gait deficits are not necessarily strongly related to each other.

Further support for this idea (i.e., that the level of interdependency between the two gait features is not constant) was obtained by revisiting data recently collected [14]. In a study in which we evaluated bilateral coordination of alternating hand tapping, we found that stride length was not significantly correlated with gait asymmetry or the phase coordination index [15] in PD patients with or without FOG ($P > 0.422$).

Turns may be another example of this principle. Turns are an activity of daily living that frequently leads to FOG [16–18]. Turns also place high demands on bilateral coordination. In addition, during a turn, step length reduction may be exacerbated due to the need to reduce the step length of the inner leg. The two effects, high demand on bilateral coordination and reduced step length, may superimpose to cause FOG. These and additional interfering effects such as attention loading should be studied in light of the possibility that they work synergistically.

4. Clinical Implications: How to Address the Multifactorial Aspects of Freezing of Gait?

Treating freezing of gait in PD is very complicated and to the best of our knowledge no “magic bullet” has yet been identified. On the other hand, a conceptual approach acknowledging that synergy and multiple influences between gait control mechanisms have an impact on FOG may enable researchers to generate some new thinking about treatment opportunities as well as mechanisms. This raises an interesting, practical question: what should be the targets of treatments designed to reduce FOG?

Keeping in mind the theoretical idea that the overall gait performance and the propensity to FOG is the product of a combination of individual gait features associated with FOG (Figure 1(b)), we turn now to discuss what may affect the individual gait features in a way that the compound gait performance moves from the functional zone to the FOG zone. Figure 3(a) illustrates two instances (“triggers”) that “push” gait from the functional zone to the FOG zone (denoted by black arrows). This might reflect one of many triggers such as dividing attention while walking, something that has been associated with FOG [19–21]. When a patient’s focus of attention is diverted from walking, the likelihood for freezing will increase since the attention demanding task is being dealt with at the expense of gait control. In fact, all of the five gait features associated with FOG that were described in Figure 1(a) have been shown to deteriorate when subjects with PD perform a dual task [22–25]. It is important to note that triggers of FOG are likely to be less effective if the baseline overall performance of gait is enhanced (in Figure 3(a), compare the dotted trace to solid trace). This fact is supported by the observation that freezing episodes are less frequent during the “ON” phase of the medication cycle as compared to the “OFF” phase [16]; in the “ON” phase, many features of gait improve, enhancing overall gait performance.

Taking these considerations into account it, seems that interventions for the rehabilitation/treatment of FOG should address one or more of the following aspects: (a) improving the overall, background gait performance, in particular gait features associated with FOG, in order to perform within the “envelope” of the functional gait zone; (b) improving the response to the occurrence of FOG provoking triggers; (c) minimizing the impact of freezing on gait regulation. Below is a brief review of recently proposed therapeutic approaches addressing these elements.

4.1. Improving Baseline Gait Performance to Reduce FOG Propensity. Fasano et al. [13] took advantage of the fact that in patients with bilateral implementation of electrodes for STN-DBS asymmetric stimulation of the subthalamic nuclei can result in modulation of the symmetry and coordination between legs. They examined the gait of subjects with PD who suffer from the FOG symptom and showed that uneven stimulation (stimulation voltage decrease in the better functioning brain side) improved BCG as compared to the regular prescribed stimulation (by about 60%). The frequency of FOG episodes decreased 10-fold and their duration decreased more than 20-fold. Additional gait features (e.g., cadence and stride length) improved as well. This study illustrates how improving baseline performance of gait feature associated with FOG (i.e., BCG and stride length) can result in a significant reduction in FOG.

Physiotherapy interventions may also be effective in changing usual-walking gait parameters. For example, treadmill training can be beneficial in increasing stride length, but not cadence (i.e., rhythmicity) [26]. However, the long-term carry-over effects of treadmill interventions still remain to be seen.

4.2. Targeting the Triggers for FOG. From a theoretical point of view, there are two potential types of triggers that can drive the gait control system to such poor management that FOG will more likely occur. The first one is attention shifts (already mentioned above). It is, therefore, reasonable to assume that an intervention that trains the subject to improve his/her performance in dual tasking conditions will result in the reduction of the FOG burden. To the best of our knowledge, only a few studies administrated dual-task (DT) based intervention in subjects with PD. Results published so far are supportive of this notion. For example, Canning et al. [27] and Yogev-Seligmann et al. [28] found improvements in gait speed in response to DT training which was maintained in the retention phase. Other investigators observed improvements in stride length [29]. If training improves DT gait speed and stride length, overall performance is likely to move away from the FOG threshold.

The second type of FOG triggering circumstances are related to transitions between walking trajectory types. These triggers which may shift the locomotion control to the FOG zone (e.g., the transition from straight line walking to turning) are a reasonable goal for intervention.
circumstances that challenge one or more of the gait features associated with FOG can cause malfunction in that gait feature that will lead to overall deterioration (i.e., “trajectory triggers”). For example, changing trajectories from straight line walking to turning poses high demands on BCG since gait control now produces different motor programs to the axial (inner) and the pivotal (outer) leg; this mismatch challenges coordination. In addition, the step length reduction seen in the inner leg challenges the step scaling control and may trigger the sequence effect. Likewise, walking through narrow passages may lead to slowness of gait and reduction in step length since choosing a leading leg for passing through the passage is both an attention and coordination demanding situation.

If effective training results in adaptation of the motor system to rapid accommodation of the post-transition gait task, then the transitioning effect (i.e., between two gait patterns) may have lesser impact on gait. In a pilot study, Hong and Earhart [30] used a rotating treadmill to extensively expose subjects with PD who suffer from FOG to circular walking. Following this training, the two subjects who participated in the study exhibited substantial improvement and immediate reduction in freezing episodes. The authors suggested that after “practice of externally cued turning, a motor pattern appropriate for turning may become more automatic, facilitating the ease of switching between straight walking and turning. This may be the mechanism of improved turning ability and reduced freezing following rotating treadmill training” [30]. Perhaps, carefully designed gait training programs for particular conditions (e.g., narrow passages) will improve the response of the patient to changing gait patterns required spatial circumstances that would otherwise impact on multiple gait features and likely provoke FOG.

4.3. Assistive Device for Alleviating the FOG Symptom. In recent years, wearable mobility measures were used in studies that documented locomotion patterns in patients with PD [31]. The compound gait performance which sustained functional gait or “falls” into the FOG zone (Figures 1 and 3) can be a subject of quantification. This quantification may be achieved by the analysis of data recorded by mobility measures. If such quantification can take place in real time, it might be possible to identify gait deterioration into the FOG zone. Then, an automated response in the form of external cue can be elicited to help the patient to restore functional gait. This concept is heuristically illustrated in Figure 3(b). The two arrows point to the places in which gait performance cross the negative threshold into the FOG zone. If efficient automatic detection device will identify these points and elicit external cue, then the subject utilizing the information from the external cueing will restore functional gait (dashed lines departing from the solid line) more rapidly. A good “candidate” for effective external cue is the rhythmic auditory stimulation which has been proven effective in improving gait in subjects with PD (for review Lim et al. [32]).

In a pilot study, we demonstrated the feasibility of this strategy [33, 34]. Within a 3-second delay, a wearable device based on set of accelerometers identified in real time more than 200 FOG episodes with technical sensitivity >70% and specificity of >80%. These promising results open the venue for assistive devices to ameliorate the FOG symptom, rather than to treat it.
5. Summary

This paper addresses the problem of FOG in PD from a slightly different angle. The conceptual framework states that more than one gait control mechanism may be impaired in association with FOG and that the control of gait features associated with FOG may, under certain circumstances or triggers of FOG, interact. Paradoxically, this rather complex nature of the potential pathogenesis of FOG in PD motivates pursuing more than one scheme of intervention with several degrees of freedom. While curing the symptom seems out of reach at the moment, recent findings support the promise that sooner rather than later, the symptom will be curtailed during the daily living of patients with PD.

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References


Review Article

Posture and Locomotion Coupling: A Target for Rehabilitation Interventions in Persons with Parkinson’s Disease

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Disorders of posture, balance, and gait are debilitating motor manifestations of advancing Parkinson’s disease requiring rehabilitation intervention. These problems often reflect difficulties with coupling or sequencing posture and locomotion during complex whole body movements linked with falls. Considerable progress has been made with demonstrating the effectiveness of exercise interventions for individuals with Parkinson’s disease. However, gaps remain in the evidence base for specific interventions and the optimal content of exercise interventions. Using a conceptual theoretical framework and experimental findings, this perspective and review advances the viewpoint that rehabilitation interventions focused on separate or isolated components of posture, balance, or gait may limit the effectiveness of current clinical practices. It is argued that treatment effectiveness may be improved by directly targeting posture and locomotion coupling problems as causal factors contributing to balance and gait dysfunction. This approach may help advance current clinical practice and improve outcomes in rehabilitation for persons with Parkinson’s disease.

“…postural activity should be regarded as a function in its own right and not merely as a component of movement…”

James Purdon Martin

1. Introduction

Disorders of posture, balance, and gait associated with falls and related injuries are among the most debilitating symptoms of advancing Parkinson’s disease (PD). In his seminal studies of these clinical sequelae in patients with postencephalitic Parkinsonism entitled The Basal Ganglia and Posture published over forty years ago, the British neurologist James Purdon Martin documented with great detail the disorders of postural fixation, righting reactions, and locomotion that similarly often accompany the progression of idiopathic PD [1]. His observations on facilitating functional movements—by gently rocking patients prior to chair rising or gait initiation, by placing bold transverse lines on the walking surface, or through the use of vision to compensate for proprioceptive deficits—influenced the development of current rehabilitation approaches. Purdon Martin later summarized his perspectives on the integration of posture and movement by emphasizing that “…postural activity-should be regarded as a function in its own right
2 Parkinson’s Disease

..." [2]. He concluded that all of the conditions on which stepping and consequently locomotion depend (e.g., antigravity support of the body, equilibrium, propulsion) are postural in nature and that even stepping, which prevents the body from falling forward, serves a postural function.

Although neurophysiological studies in both quadrupeds and humans have indicated that the control of posture and locomotion is interdependent at many levels of the central nervous system (CNS) encompassing multiple supraspinal and spinal networks [3–6], the ways by which locomotion may be affected by prevailing postural conditions are not well understood. This is particularly relevant to the problems of postural instability and gait disorders that accompany advancing PD. Such problems are especially evident when patients with PD attempt to perform complex whole body posture and locomotion sequences during functional activities such as gait initiation, sit-to-stand and other transfers, turning while standing and walking, and in ongoing gait. During such tasks, hesitation delays or “freezing” episodes are frequently observed, and the normal pattern of spatial and temporal sequencing between postural and locomotor elements of the task is either absent or disrupted [7]. Thus, the question arises as to whether or not at least some of the difficulties with locomotion experienced by individuals with PD are attributable to a dysfunction of the neuronal networks that mediate the coupling between posture and locomotion. This issue appears to have important implications for current rehabilitative interventions. For example, current physical therapy and rehabilitation interventions for posture, balance, and gait disorders in PD mainly focus on separate aspects of the problems such as posture and balance training [8, 9] or gait training [10–14]. However, impaired coupling between posture and locomotion could contribute to gait and mobility disorders, due not only to biomechanical limitations but also to adaptive changes in neural control. For example, De Nunzio et al. have recently demonstrated that alternate rhythmic vibration during quiet stance of bilateral paraspinal muscles affecting trunk posture produced a cyclic transfer of the center of pressure mimicking the one accompanying body progression during walking [15]. When vibration was applied to the trunk musculature during gait, walking velocity, cadence, and stride length increased in both patients with PD and controls [16]. In contrast, no effects on gait were observed when leg muscles (soleus and tibialis anterior) were similarly vibrated. Since the paraspinal muscles contralateral to the single support stance leg play a role in the stabilization of trunk posture during stance, these results suggest that proprioceptive feedback from postural muscles can be used to improve the coupling of posture and locomotion elements of the gait cycle, thus facilitating performance of the task in people with PD.

The purpose of this perspective and review is to present a framework with supportive research findings to advance the viewpoint that focusing rehabilitation interventions on individual or isolated components of posture, balance, or gait disorders in persons with PD should be reevaluated. Instead, it is argued that the emphasis in intervention approaches ought to be shifted towards therapeutic training programs

that directly target impairments in posture and locomotion coupling as a causal factor contributing to balance and gait dysfunction.

2. Conceptual and Theoretical Model

The difficulties with performing complex whole body posture and locomotion sequences during functional activities such as gait initiation [17–21], turning [22, 23], sit-to-stand [24, 25], and ongoing walking [16, 26] are commonly accompanied by timing delays in the coupling between postural movements of the body segments and the goal-intended locomotion action (e.g., stepping release, step redirection change in turning while walking, seat-off in chair rise, continuous walking). The conceptual and theoretical framework for developing intervention approaches that target impairments in posture and locomotion coupling is illustrated by focusing on the initiation of gait. During gait initiation, an anticipatory postural adjustment (APA) phase normally precedes and accompanies the initiation of the stepping phase [27–30]. For forward stepping, these APAs involve a sequence of muscle activations and changes in the ground reaction forces (loading of the initial swing leg and unloading of the initial stance leg) that move the net center of pressure beneath the feet backward and toward the initial swing limb. This motor sequence, which ends after heel off, produces the forces and moments necessary to propel the body center of mass (COM) forward and towards the single stance limb prior to stepping.

Compared with healthy control subjects, the mediolateral (M-L) and anteroposterior (A-P) ground forces characterizing APAs in patients with PD are abnormally prolonged in duration and reduced in amplitude with a delay in the sequencing between the beginning of the APA and step onset [17, 18, 31, 32]. This delay may include abnormal pauses that disrupt the posture-movement coordination and may precipitate freezing of gait (FOG). While the APA is normally almost always present during voluntary stepping, it may often be absent in patients with PD [17, 19, 20]. In such cases, hesitation delays are readily observable. Thus, the normal spatial and temporal coordination between the APA and stepping components of gait initiation is disrupted in PD in association with start hesitation and FOG.

In gait initiation, the anticipatory nature of the postural-step coordination appears to involve a role for motor prediction. A forward internal model (Figure 1) is a neural mechanism that predicts (estimates) the future state of a system given the current (actual) state and the sensorimotor control signals [33–37]. The use of a forward model for coordination between posture and locomotion could operate such that the neural circuits for initiating stepping would normally be actively delayed until the APAs that generate the weight transfer from bipedal to single leg support have achieved single stance limb loading [38, 39]. This transition in stance support reflects a change in the body center of mass-base of support (COM-BOS) relationship. Thus, using internal and external feedback information, the forward model would determine if the APAs have achieved the sufficient anticipated postural state (e.g., COM position and
motion relative to the BOS) before initiating the gait cycle and finishing the postural phase.

In Figure 1, the integrated networks for posture and locomotion are activated in parallel [38–41] to generate a posture command for segmental orientation and balance and a step command. These motor outputs will modify the COM-BOS relationship. If an external mechanical or sensory event that assists with the APA by facilitating weight transfer is applied early in the postural adjustment phase, sensory information about the limb loading conditions, together with an efference copy of the motor commands sent to the forward model estimating the anticipated limb loading conditions, can be used by the CNS to modify the two commands in advance based on an internal representation of the body. Sensory information produced by movement can also be used online to modulate posture and movement via external feedback mechanisms. Conceivably, the posture assistance provided by external mechanical effects and/or sensorimotor enhancement could decrease the completion time of the weight transfer compared with the predicted time of completion without assistance and/or improve the fidelity of the information associated with the changes in limb loading reflecting postural state conditions during the APA. Based on a mismatch between the predicted and actual limb loading conditions determined from the forward internal model, the initiation release of stepping would be advanced in time and occur earlier. Reinforcement of the posture-locomotion coordination with posture-assisted locomotion (PAL) training could lead to adaptive changes in the internal model for step initiation.

The mechanisms contributing to impaired gait initiation in PD are poorly understood. It has been hypothesized that postural instability and gait dysfunction in PD result from alterations in the output of the basal ganglia to the pedunculopontine nucleus (PPN) in conjunction with the progressive degeneration of the large cholinergic neurons of this nucleus [42, 43]. The PPN has important inputs to regions of the mesencephalic extrapyramidal area and pontomedullary reticular formation that play a role in the pattern generation for locomotion and integration of posture and movement [44]. Alternatively, it has been proposed that impaired gait initiation results from dysfunction of the basal ganglia and a resulting suppression or underactivity of the supplementary motor area [45–47], a region of the frontal cortex critically involved in the planning and preparation for movement. Models of posture and movement coupling [38, 40], such as the model presented in Figure 1, often emphasize that the voluntary command to initiate movement, including the timing signal, must be integrated with brain stem and spinal centers that mediate the control of posture. Accordingly, the supplementary motor area may play a role in providing feedforward information about the internal model to both the basal ganglia and posture and locomotion control regions in the brain stem. The fact that levodopa can often improve gait initiation and locomotion in patients with off-medication impairment [48] provides evidence that
alterations in basal ganglia output to both cortex and brain stem likely play a role in both the triggering of movement initiation and coupling of posture and locomotion. However, in advanced disease, posture and gait abnormalities often become resistant to levodopa replacement therapy, suggesting that the progressive degeneration or dysfunction of nondopaminergic regions of the neuraxis [49], such as the PPN, becomes the principal pathology that mediates the disordered coupling between posture and locomotion.

In PD, difficulties with achieving the postural prerequisites for stepping could contribute to gait initiation delays, “start hesitation,” and FOG. With postural assistance, the usually prolonged APA duration and reduced amplitude accompanying PD could be, respectively, shortened and increased to enhance posture requirements and allow an earlier step onset time. Thus, the rationale for the PAL training approach is that the expected limb loading conditions associated with weight transfer to the single stance limb are enhanced (e.g., achieved earlier and more effectively) compared with what would usually be expected without the assistance. If patients with PD retain the capacity to adapt their putative internal model for stepping with PAL training, then it might be possible to remodel the timing sequence and other characteristics of posture and locomotion components of gait initiation.

### 3. Experimental Support

#### 3.1. Postural Assistance with Weight Transfer Acutely Enhances Posture and Locomotion Coupling and Performance during the Initiation of Stepping

A first study examined the influence of a lateral postural assist on step initiation in patients with PD and healthy controls [18]. Subjects performed self-paced rapid forward steps. In one condition, the APA was assisted shortly after onset (i.e., triggered by a 5% change in loading force from baseline beneath the initial swing leg) with a lateral pull applied to the pelvis (toward the initial stance side) by a motor-driven robotic system. Ground reaction forces and whole body kinematics were recorded to characterize the APA (extracted from the mediolateral center of pressure displacement) and step characteristics (derived from the first stepping leg ankle marker displacement). Overall, persons with PD (Hoehn and Yahr stage mean = 2.0) [50] tested off anti-parkinsonian medications had a longer APA duration and longer first-step duration than control subjects. With the postural assistance, the APA duration for both groups was shorter, the step onset time relative to the APA onset was earlier, and the speed of the first step became faster (i.e., step duration decreased while step length did not change) for PD subjects (Figure 2). These improvements in stepping performance could be related to the influence of a sensory cue provided by the waist-pull stimuli. This possibility was assessed in a tug condition that was delivered in the same way as the posture assist but involved a displacement that was reduced to 25% of the assist waist-pull. The tug resulted in a stimulus that gave very little mechanical assistance with the lateral weight transfer but provided a vigorous stimulus to the pelvic area that could conceivably have been used as a timing cue to facilitate stepping. No changes in performance from baseline were observed when a tug stimulus cue was presented (Figure 2).

This ruled out that the posture assist was attributable to sensory cueing. It is also possible that stepping practice alone could have accounted for the findings. A separate practice group is needed to definitively account for this possibility. However, the fact that a block of trials without mechanical assistance or sensory cues was always presented either as the second to last block or last block of trials and that these trials did not differ from the initial baseline for any of the measurements provides evidence that the effects of the postural assist could not be attributed to practice alone.

These findings indicated that rapid step initiation could be acutely enhanced through external assistance that facilitated weight transfer and thereby modified posture and locomotion coupling in individuals with early stage PD while off of their anti-parkinsonian medication as well as in healthy older people. In addition to the mechanical effects of the robotic assistance that contributed to passively shortening the APA duration and first-step onset timing, the neural networks for initiating stepping could have been acutely triggered and modified in interaction with the enhanced sensory feedback providing information about the expected or actual state conditions (e.g., center of mass position and motion relative to base of support) associated with the evolving APA [38] (Figure 1).

Applying assistive mechanical displacement laterally at the pelvis indirectly modifies the loading forces beneath the feet that influence sensory inputs for posture and gait control [51]. Therefore, it is conceivable that if loading force information is important for timing the release of the gait cycle and other locomotion characteristics, then APA and step parameters should also be modifiable by directly manipulating the loading forces during gait initiation. Alterations in limb loading may also be important because of past work demonstrating that patients with PD may show abnormalities in load receptor-mediated proprioception during stance and gait [52]. Moreover, if limb loading information is important for the control of step initiation as in ongoing gait, then healthy individuals would also be expected to demonstrate modifications in stepping when limb load input is perturbed. Hence, we have extended our waist-pull posture-assisted locomotion approach by developing a controllable, vertical dropping-elevation perturbation system to induce changes in posture and locomotion coupling [53].

Eight patients with PD (modified Hoehn and Yahr Stage score 2.5 to 3.0) [50] and eight healthy control subjects performed rapid self-triggered step initiation with the impending single stance limb positioned over a pneumatically actuated platform. All subjects had been experiencing start hesitation or FOG. In perturbation trials, the APA was either assisted by moving the stance limb ground support surface vertically downward (DROP) or resisted by moving it upward (ELEVATE), shortly after the onset of the APA phase. Overall, patients with PD demonstrated a longer APA duration, longer time to first-step onset, and slower step speed than controls. In both groups, the DROP of the stance limb reinforced the intended APA kinetic changes...
Parkinson’s Disease 5

Figure 2: The group mean values plus 1 SD for (a) APA duration, (b) first-step onset time relative to APA onset, and (c) first-step duration in control subjects (CS: white bars) and subjects with Parkinson’s disease off medication (off: gray bars). The four experimental conditions are initial baseline trials without postural assistance (Baseline), trials with lateral postural assistance (Postural assistance), follow-up trials without postural assistance (No assistance), and trials with a mechanical tug that provided no direct postural assistance (Tug). Data from [18]. †Significant differences between groups. ***Significant difference between the postural assistance condition (ASSIST) and the others.

for lateral weight transfer (i.e., significant reduction in APA duration and increase in peak amplitude) and resulted in positive changes in step characteristics (i.e., earlier time to first-step onset and faster step) compared with other conditions (Figure 3). In contrast, during ELEVATE trials that opposed the intended weight transfer forces, both groups rapidly adapted their stepping to preserve standing stability to the detriment of step characteristics by decreasing step length and duration and increasing step height and foot placement laterally. These findings suggest that sensory information associated with limb load and/or foot pressure occurring prior to the release of stepping modulates the spatial and temporal parameters of posture and locomotion in interaction with a centrally generated feed-forward mode of neural control. Moreover, impaired step initiation in PD may at least acutely be enhanced by augmenting the coupling between posture and locomotion through changes in limb load proprioception.

3.2. Training-Induced Changes in Postural and Locomotion Coupling and Performance during Step Initiation. From a rehabilitation standpoint, it would be important to know whether longer-term changes in posture and locomotion coupling are achievable with training. It is generally acknowledged that patients with PD can improve their motor performance through practice training, but that they may
achieve less improvement and take longer to change their performance than healthy adults [54, 55]. Thus, it is conceivable that posture-assisted training could be applied to adaptively remodel the coupling between posture and locomotion in PD. We have recently completed a feasibility intervention study aimed at determining the effects of PAL training using mechanosensory limb load assistance (i.e., drop of support surface on single stance side) compared with sensory enhancement of weight transfer (i.e., vibration of support surface on single stance side) on posture and locomotion coupling and performance during step initiation in patients with PD.

Seven subjects (mean age = 72.9 years) with moderate PD (modified Hoehn and Yahr Stage score 2.5 to 3.0) [50] and on medications received baseline testing followed by twice weekly PAL training for six weeks. For each training session, the drop assist group performed 50 self-initiated rapid stepping trials where the stance limb ground support surface was moved vertically downward by 1.5 cm over 100 ms shortly after the onset of the APA phase (change in single stance limb load vertical force by 5% from baseline standing) similar to our earlier study [53].

A second group (mean age = 75.3 years) consisted of eight subjects with moderate PD (modified Hoehn and Yahr Stage score 2 to 3) [50] who received vibration assist training through mechanical vibration stimulus (200 Hz over 100 ms) of the single stance side support surface applied at the same relative time point during the early APA phase as the stimulus for the drop assist group. These PD subjects were tested on medications and followed the same testing and training schedule as the drop assist group.

Immediate posttesting completed after the six-week training phase indicated several training-associated improvements in kinetic APA and stepping kinematic variables. First,
FIGURE 4: The group mean values plus 1 SEM for initial swing limb APA (a) rate of loading force and (b) peak loading force amplitude measured at baseline prior to posture assist locomotion (PAL) training (pre), immediately after training (post), and six weeks after the completion of training (ret) PD subjects in drop assist and vibration assist training groups. Unpublished data.

for APA characteristics (Figure 4), both the rate and peak amplitude of the loading force beneath the initial swing limb for lateral weight transfer prior to stepping were, respectively, significantly increased, by 53% and 44% across both training groups. Follow-up testing occurring six weeks after the completion of training showed that these increases were retained. Second, significant group by time of testing interactions for first-step kinematic data (Figure 5) showed that both step speed and length were, respectively, increased by 54% and 38% for the vibration assisted group between the baseline and immediate posttest and remained greater at retention testing. First-step height (Figure 5) was also increased by 17%–25% for both groups between pretesting and both posttesting periods.

Although systematic investigation of the accuracy of the following observations has yet to be addressed, two aspects of the approaches appear to be important for successful implementation. First, the triggering of the posture enhancement stimulus should be activated by the subject’s self-initiated postural action, and, second, the time of delivery of the event should occur shortly after the onset of the posture event. This self-triggered and early event timing might enable the external information to be incorporated into the forward control of the posture and locomotion sequence.

4. Implementation of Posture-Assisted Locomotion Rehabilitation

4.1. Targeting Posture and Locomotion Coupling in the Rehabilitation of People with Parkinson’s Disease. Better understanding of posture and locomotion coupling problems has significant relevance for physical therapy practice. To date, there has been a lack of interventions to directly address posture and locomotion coupling problems. Interventions such as PAL hold promise for specifically enhancing or assisting with the posture requirements that precede and accompany locomotion and other movements in order to improve the spatial and temporal coupling. Ultimately, the goal is to enhance posture and locomotion coupling to improve performance in functional activities, foster greater quality of life, and decrease fall risk.

Two recent reviews [56, 57] point out that while mounting progress has been made with providing some evidence for the effectiveness of current exercise rehabilitation approaches on balance and gait outcomes in PD, considerable gaps remain in the evidence base for specific interventions and in identifying the optimal content of exercise interventions. Part of the challenge in effectively addressing these gaps in knowledge is in formulating conceptual and theoretical frameworks and models that take into account the complexities or influential factors. Greater focus on the ways that the interrelationship or coupling between posture, balance, and locomotion elements advantage and constrain functional performance would appear to be one such area where rethinking the framework for intervention development may be useful for advancing clinical practice.
been identified for the sequencing between the anticipatory forward weight transfer phase and the intended vertical ascent phase of sit-to-stand [24] or between anticipatory segmental body rotations that steer the COM prior to foot redirection in gait turning have been observed in PD patients [23]. These temporal disruptions are very analogous to the temporal disruption of posture and locomotion coupling seen for gait initiation. Application of the PAL approach through mechanical and/or sensory enhancement of the early postural phase may trigger an earlier release of subsequent movement and possible enhancement of overall performance. Improvement in stepping patterns using vibratory sensory stimulation of the trunk postural muscles during ongoing walking in persons with PD and healthy controls, as demonstrated by De Nunzio et al. [16], provides a promising example of posture-locomotion coupling applicable to intervention. Impairments in the interaction between posture and whole body movement tasks will need further investigation to support the hypothesized view of impaired coupling of posture and goal-intended components of action in individuals with PD.

5. Summary

In this perspective and review, we have advanced the view point that approaches to rehabilitation interventions that focus on changing separate isolated components for posture, balance, and gait in persons with PD may have limited effectiveness due to the importance of posture and locomotion coupling. Alternatively, there is neurophysiological and experimental support for the idea that posture and locomotion are highly integrated components of action that require understanding of how these control functions are interactively coupled. Moreover, there is evidence to indicate that individuals with PD have particular problems with coupling or sequencing posture and locomotion during complex whole body movements that are associated with falls. Expanding or shifting current conceptual and theoretical models of rehabilitation beyond posture/balance and gait-centered intervention focuses by incorporating posture and locomotion coupling problems as a target for rehabilitation outcomes may help to optimize and improve the effectiveness of current clinical practice in this important area of rehabilitation for persons with PD.

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References


Feasibility, Safety, and Compliance in a Randomized Controlled Trial of Physical Therapy for Parkinson’s Disease

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Both efficacy and clinical feasibility deserve consideration in translation of research outcomes. This study evaluated the feasibility of rehabilitation programs within the context of a large randomized controlled trial of physical therapy. Ambulant participants with Parkinson’s disease (PD) (n = 210) were randomized into three groups: (1) progressive strength training (PST); (2) movement strategy training (MST); or (3) control (“life skills”). PST and MST included fall prevention education. Feasibility was evaluated in terms of safety, retention, adherence, and compliance measures. Time to first fall during the intervention phase did not differ across groups, and adverse effects were minimal. Retention was high; only eight participants withdrew during or after the intervention phase. Strong adherence (attendance > 80%) did not differ between groups (P = .435). Compliance in the therapy groups was high. All three programs proved feasible, suggesting they may be safely implemented for people with PD in community-based clinical practice.

1. Introduction

Physical rehabilitation in Parkinson’s disease (PD) is a growing field of investigation. Although a number of small randomized controlled trials (RCT) have reported some benefits of physical rehabilitation programs for people with PD [1–5], the outcomes of recent systematic reviews remain equivocal [6–8]. There are many excellent examples of clinical trials, particularly those evaluating rehabilitation outcomes (e.g., [2, 4, 9]). The existence of such rich literature highlights the importance of ensuring high levels of adherence and compliance with therapy protocols, as well as carefully tracking attrition and adverse responses [10]. This manuscript addresses that gap.

The conduct of clinical research presents challenges; trial outcomes can be influenced by many variables related to the rigor of research methods employed, such that even carefully planned and well-funded clinical trials can fail to yield high-quality data or allow results to be translated into practice. In addition, exercise modalities aimed at strengthening and preventing falls may present safety risks to the potentially frail and debilitated participants enrolled in physical rehabilitation clinical trials.

Participant retention has been identified as an issue in a number of previous randomized controlled trials of physical rehabilitation in PD, particularly those studies involving an inactive control group [11, 12]. It has been suggested that offering an alternative therapy as a control intervention may improve retention in nonpharmacological randomized clinical trials [11]. Without the option of blinding participants to group allocation within a physical rehabilitation clinical trial, the challenge becomes developing alternative therapy programs that offer participants an equivalent participation experience whilst minimizing overlap with the content of the active intervention.
Adherence and compliance are key variables influencing the outcome of clinical trials in PD [13]. Within the context of a physical rehabilitation trial, it is important to establish not only when participants attend (adherence; [1, 13]), but what activities they complete during their attendances, that is, the extent of their engagement with the program (compliance; [13]). Adherence and compliance, therefore, reflect the adequacy and appropriateness of therapy content for the sample and should be considered within the design of a clinical trial by the development of appropriate therapy and training protocols.

To date, few trials of physical rehabilitation programs for PD have reported adherence and compliance data (e.g., [14]). Fewer studies have described in detail the strategies used or recommended to maximize adherence and compliance in this patient group. The purpose of this paper is to report the safety, retention, adherence, and compliance rates of a large RCT investigating the efficacy of physical rehabilitation to reduce falls and improve mobility in people with PD. In addition, strategies to improve adherence and compliance will be described, and implications for future research will be discussed.

2. Methods

2.1. Study Design. We conducted a single blind randomized controlled trial to evaluate the effectiveness of two methods of physical therapy combined with falls education to improve mobility and decrease falls in people with PD, relative to a control intervention [15]. Ethical approval was gained from the relevant Ethics Committees, and all participants provided written informed consent.

2.2. Participants. A convenience sample of 210 participants with idiopathic PD was recruited between 2006 and 2009 throughout Melbourne, Australia from neurologists and therapists working in clinics and rehabilitation centers, from PD support groups and from community newspaper advertisements. Eligible people were those who: (i) had a confirmed diagnosis of idiopathic PD; (ii) were able to walk (Hoehn and Yahr (HY) Stages 0-IV [16]); (iii) had a Mini Mental State Examination (MMSE) score ≥24; (iv) were willing and able to attend the therapy and assessment program. Exclusion criteria were other medical conditions that could limit or prevent exercising safely at the required intensity, other prior neurological conditions affecting gait, and dementia.

After screening and consent, participants were randomized to one of three groups: progressive strength training (PST) combined with falls prevention education; movement strategy training (MST) combined with falls prevention education; or a control group (life skills; LS).

2.3. Intervention. The programs were delivered by clinical staff employed in outpatient settings. All staff delivering the intervention completed 2.5 hours training on the therapy protocols, conducted by the study chief investigators. The interventions were delivered in a once weekly two-hour session for 8 weeks to groups of 3-4 participants. The PST and MST interventions were delivered by a physical therapist, and the LS program was delivered by occupational therapists or social workers. An allied health assistant also attended sessions as required to provide general assistance. In addition, all participants were provided with a home exercise program to be completed independently or with carer/family assistance once a week.

The interventions are described in detail elsewhere [15, 17]. To summarize, the PST program comprised seven strengthening exercises for core muscle groups of the lower limbs and trunk, in accordance with the principles of PST [18]. Exercises were progressed by adjusting the number of sets and repetitions, by adding more weights to the vest, by increasing the Thera-band (stretch elastic band) resistance and by adjusting the step or chair height. Exercises were individually tailored and progressed, taking into account factors such as age, fitness level, comorbid health conditions such as arthritis or back pain, and self-reported exercise difficulty according to the Borg Perceived Exertion Scale [19]. The individualized home exercise program was recorded on a standardized home exercise sheet template each week by the therapist. A booklet with photos of each exercise, a gym step, vest with weights, and Thera-band were supplied for use at home during the intervention phase.

The MST program comprised the individualized teaching of training strategies to enhance movement performance, improve balance and mobility, and to prevent falls, according to the principles outlined by Morris et al. [20–22]. Participants practised using strategies such as attention, verbal, and external cues while performing seven functional tasks such as sit to stand, moving from chair to chair, standing and reaching, or walking and turning, either in single or dual task conditions. A booklet with photos and details of each exercise was provided to each participant. Exercises were individually tailored to the functional level of each participant, and progression of each task varied according to need and ability. A home exercise program tailored to the individual’s level was prescribed each week by the therapist.

Both the PST and MST groups received 10–15 minutes of structured falls education component at each weekly session, incorporating an overview of risk factors and strategies to prevent falls. This was based upon the content of the booklet: Don’t fall for it. Falls can be prevented!—A Guide to Preventing Falls for Older People booklet [23].

The control intervention comprised guided discussion sessions on PD-related topics such as the impact of PD on the individual and family, fatigue management, relaxation, medication, communication, and community services. The LS session did not include any content related to falls education, exercise, walking, or balance. Therapists also suggested activities such as reflection activities and relaxation practice to be completed once a week at home.

2.4. Outcome Measures. All participants were tested by trained blinded physical therapist assessors at baseline (T1), one week after the 8-week intervention (T2), and at 3 months (T3) and 12 months (T4) after intervention. The primary outcome measure was falls over 12 months
after-intervention, as detailed previously [15]. Secondary outcome measures included measures of mobility, activity limitations, and quality of life.

2.5. Outcome Measures for the Intervention Phase. Intervention therapists recorded key details of therapy delivered after each session using custom designed forms. The therapy record for the intervention groups indicated compliance with key therapy concepts. For the MST group, this reflected the individual tailoring of activities to address functional movement difficulties. For the PST group, the record detailed the exercises, number of repetitions and sets, weights, and Thera-band resistance level. All participants were screened weekly at the intervention sessions for new adverse events, including new muscle soreness related to therapy. Falls were monitored using a Falls Calendar protocol [15]. This required people to enter falls on a calendar as they occurred and to telephone a falls hotline to answer questions relating to fall circumstances and consequences. Falls Calendars were completed during the intervention phase and for 12 months following intervention.

For the purposes of this study, feasibility was adopted as an umbrella term, encompassing the constructs of safety, retention, adherence, and compliance. Safety during the intervention phase was monitored by: (i) structured weekly screening by the intervention therapists for any new soreness lasting longer than 48 hours related to therapy; (ii) recording of adverse events that occurred during therapy; and (iii) fall rate during the intervention phase. Retention was defined in several ways: (i) the proportion of participants who attended the first post-intervention assessment; (ii) the proportion of participants who returned post-intervention Falls Calendars (reflecting the primary outcome measure of the overall trial); (iii) the proportion of participants who completed all follow-up assessments compared to the number who completed baseline assessments (note that this measure is the opposite of “dropouts”). Adherence considered the consistency of participant attendance at the intervention/control sessions. Compliance to the intervention was determined by the progression of exercises within each of the two intervention groups as evidenced by therapy records.

2.6. Data Analysis. Demographic data were gathered for each group for variables such as age, sex, disease duration, past history of falls, and comorbidities. Kaplan-Meier survival analysis was used to examine time to first fall during the intervention phase of the trial and compared between groups using Mantel-Cox log rank test. Between-group comparisons of adherence were assessed using an independent samples one-way Kruskal-Wallis test. Data were analysed using IBM SPSS version 19.0 (SPSS Corp, Chicago, Ill, USA) or STATA 8 (Stata Corp, College Station, Tex., USA) statistical software.

3. Results

3.1. Participants. Two hundred ten participants (140 men, mean age (SD) of 67.9 (9.6), range 44–89 years) were randomized. Participants generally had mild to moderately severe PD, reflected by a median modified HY stage (IQR) of 2.5 (2-3) and mean (SD) disease duration of 6.7 (5.6) years. Activity limitations, as measured by the Unified Parkinson’s Disease Rating Scale (UPDRS) Part II activities of daily living, were also mild (mean (SD); 11.6 (5.9)). One hundred sixteen participants (55%) reported having falls over the previous 12 months, of whom 74 (64%) were repeat fallers. Freezing of gait was reported by more than half of the participants. Arthritis was the most commonly reported health condition, present in 92 (44%) of the sample, and 48 (23%) participants had a history of cancer or heart disease. The majority of participants were taking levodopa preparations or a combination of PD medications, with 19 on no PD-pharmacotherapy. One hundred fourteen (54%) participants were prescribed four or more medications, with 89 (42%) taking psychotropic medication.

3.2. Delivery of Interventions. The interventions were undertaken in four different outpatient centers located in different regions of Melbourne. Across the three years of the RCT, 8 physical therapists delivered the MST, 10 physical therapists delivered the PST and 6 occupational therapists or social workers delivered the LS program. Therapist professional experience varied markedly from new graduate (<1 year) to highly experienced (>30 years).

3.3. Safety. The safety of the interventions was assessed in three ways and is reported in Table 1. Structured weekly screening during the intervention phase identified new soreness lasting longer than 48 hours in 28 individuals (PST n = 18; MST n = 10). Seven individuals reported more than one episode of soreness (PST n = 6; MST n = 1). Typical reports included a transient increase of preexisting low back, hip or knee pain related to osteoarthritis, resolved by a modified program or over-the-counter medication. Fewer than one quarter of these participants attended a health service practitioner because of new soreness. No new soreness was reported to persist beyond the intervention phase and require intervention.

Secondly, three incidents occurred during the actual intervention sessions. Two MST participants reported single episodes of dizziness with subsequent medical assessment that were resolved without intervention or sequelae. A single participant from the PST group fell during the therapy session, with no reported injury. None of these incidents resulted in any ongoing consequence.

The third safety evaluation examined falls in 203 participants during the intervention phase. Fifty-eight people fell during this phase: (PST n = 10, MST n = 24, LS n = 24). Falls frequency varied markedly; 32 people fell once or twice; 19 fell between 3 to 9 times; 7 fell 10 or more times. The median time to the first fall during the intervention phase was 14 days in the PST group and 9 days in the MST and LS groups. The time to first fall did not differ significantly between groups; Log rank test (Mantel Cox), Chi square = 2.08, df = 2, P = 0.353.
3.4. Retention. Three aspects of retention of participants were considered related to attendance at the three post-therapy assessments and the return of Falls Calendars. The study protocol had allowed for a drop-out rate of 15% when determining the required sample size. Seven participants, six in the LS group and one in the MST group, withdrew prior to the intervention phase after being randomized to a group. Reasons for withdrawal included poor health (LS n = 2), a preference for the exercise group (LS n = 1), unable or no longer wanting to attend (LS n = 2, MST n = 1), and deceased (LS n = 1). Eight participants withdrew from the study during or after the intervention phase and did not return Falls Calendars during the 12 months follow-up phase. Six of these withdrew from the LS program, two due to health reasons, one as they did not want to continue (unspecified reason), one because he felt the group was “depressing”, and two as they were not exercising or receiving falls education. One participant withdrew from PST for health reasons, and one participant from the MST group died of unrelated causes. One hundred ninety-six (93%) of the participants completed the T2 assessment at the end of the 8-week intervention phase (PST n = 69; MST n = 68; LS/control n = 59; see Table 2).

Retention throughout the full trial period was high. One hundred ninety-five participants (93%) returned one or more Falls Calendars during the 12-month follow-up period (PST n = 69, MST n = 67, LS n = 59). One hundred eighty-four participants (88%) provided falls data for the entire 12 months (PST n = 65, MST n = 65, LS n = 54). In the final evaluation of retention, 775 assessments of possible 840 (210 × 4 occasions) were completed (92%). Participation at the final T4 assessment as a percentage of the total number randomized showed 93% of people in the PST group were reassessed, 91% of MST and 79% of participants in the LS program.

### Table 1: Safety during the intervention phase.

<table>
<thead>
<tr>
<th></th>
<th>PST</th>
<th>MST</th>
<th>LS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of fallers (n)</td>
<td>10</td>
<td>24</td>
<td>24</td>
</tr>
<tr>
<td>Falls frequency: median (IQR)</td>
<td>0 (0)</td>
<td>0 (0-0)</td>
<td>0 (0-0)</td>
</tr>
<tr>
<td>Falls frequency: range (n)</td>
<td>0–7</td>
<td>0–24</td>
<td>0–52</td>
</tr>
<tr>
<td>Median time to first fall (days)</td>
<td>14</td>
<td>9</td>
<td>9</td>
</tr>
</tbody>
</table>

### Table 2: Assessments attended across the course of the trial.

<table>
<thead>
<tr>
<th>Assessment</th>
<th>PST n (% of randomized)</th>
<th>MST n (% of randomized)</th>
<th>LS n (% of randomized)</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1 (Baseline assessment)</td>
<td>70 (100)</td>
<td>69 (100)</td>
<td>71 (100)</td>
</tr>
<tr>
<td>T2 (1 week after intervention phase)</td>
<td>69 (98.6)</td>
<td>68 (98.6)</td>
<td>59 (83.1)</td>
</tr>
<tr>
<td>T3 (3/months after intervention phase)</td>
<td>67 (95.7)</td>
<td>64 (92.8)</td>
<td>54 (76.1)</td>
</tr>
<tr>
<td>T4 (12 months after intervention phase)</td>
<td>65 (92.9)</td>
<td>63 (91.3)</td>
<td>56 (78.9)</td>
</tr>
</tbody>
</table>

3.5. Adherence. Eight participants were randomized, but did not attend any therapy sessions (PST n = 0, MST n = 2, LS n = 6). Adherence data are reported for the participants who attended at least one intervention session (PST n = 70, MST n = 67, LS n = 65). Ninety percent of the PST participants attended between 6 and 8 sessions, with 3 participants (4%) attending fewer than 5 sessions. Ninety-three percent of the MST participants attended 6–8 sessions, with 2 participants (3%) attending fewer than 5 sessions. Seventy-eight percent of the LS participants attended between 6 and 8 sessions, with six participants (9%) attending fewer than 5 sessions. Participation attendance (as defined by attendance at ≥6 sessions or 75%) did not differ across the three groups (independent samples Kruskal-Wallis, P = .435). The PST group attended 82.5% of available sessions, the MST group 90.5%, and the LS group 87.0%.

3.6. Compliance

3.6.1. Progressive Strength Training Group. A review of the therapy records indicated that 89% of the participants were able to complete all seven suggested exercises within the 2-hour session. The remaining 11% were able to complete six exercises. Increasing the number of repetitions and/or sets was the most common form of progression, with 97% of participants (68 of 70) progressing in this manner. Eighty percent (56 of 70) of the participants used the vest with weights during the appropriate exercises. Of these, only 5 participants (9%) did not increase the weights across the course of the intervention. Both the step platform and Thera-band (to resist trunk extension/rotation) were used by all participants. Thera-band resistance was increased for 57% of participants.

3.6.2. Movement Strategy Training Group. A review of the available therapy records (n = 64, missing data = 3)
indicated that over 86% (55/64) of the participants were able to routinely complete six or all seven activities within the 2-hour period. Increasing the number of repetitions and sets was the most common form of program progression, in conjunction with increasing the difficulty of the task. Progression of the task was highly variable according to each individual’s task performance. For example, standing and reaching to an object in front of the participant may have progressed to moving the object further away, standing and placing an object down on the ground or up on a high shelf, to moving a heavier or more cumbersome object. Similarly, walking a straight line with long steps might have progressed to walking with a secondary motor task, with a secondary cognitive activity, to an obstacle course; standing up from a chair may have progressed by altering the height or compliance of the chair, or to standing up with an object in hand or standing up and walking off.

4. Discussion

The primary RCT described in this paper investigates the ability of two types of physical therapy to prevent falls in community-dwelling people with PD. The current secondary examination of feasibility demonstrates that these therapy programs can be successfully implemented within the context of an RCT. It also suggests they are feasible and may be safely translated to clinical practice.

4.1. Safety. As it was possible that these physical therapy programs might present safety risks, the first aspect of feasibility considered was the safety of the two active interventions. Both physical therapy interventions carried potential risks, either inherent in their content or specific to the population being treated. Each intervention aimed to extend participants to a high level of activity and performance, as high intensity exercise has been shown to be achievable in people with PD [24, 25]. The possibility, thus, existed of some consequent muscle soreness and/or joint stiffness, leading to the definition of a treatment-related minor adverse event as “soreness that lasted more than 48 hours or required attendance at a health professional.” Falls risk was potentially increased by aspects of the MST program that targeted and challenged aspects of motor performance such as balance, reach, and stride length. The PST program explicitly encouraged participants to work with increasing weights and resistance, potentially risking muscle, and joint problems. Participants were primarily older people (mean age 67.9 ± 9.7 years), potentially carrying a relatively high proportion of orthopedic conditions (osteoarthritis, osteoporosis) and other comorbidities [26]. Further, PD itself is strongly associated with impaired balance and increased falls risk [1, 27]. Finally, there was the possibility that increased confidence, as a result of intervention, might increase activity or risk taking and result in further falls. Evaluation of the safety of these interventions was therefore of key importance.

During the intervention, no adverse events with sequelae were reported. There were no injuries during the therapy sessions. Only 36 instances of “increased soreness > than 48 hours” occurred after the 1367 sessions attended, many in individuals with a history of back pain or osteoarthritis. A number of people were unsure whether it was the intervention or concurrent activities such as gardening or exercise that had triggered the soreness, and a visit to a health professional was necessary in fewer than one quarter of the instances reported. These results support the safety of the PST and MST programs in an older population with mild-moderate disability with a range of comorbidities.

There were no group differences between the time to first fall during the intervention phase. This suggested that neither working to improve participants’ functional motor performance in the MST group nor increasing their functional strength in the PST group may have led them to undertake risky behaviors and fall as a result of overconfidence. We conclude that both therapy programs can be safely implemented in this population.

4.1.1. Retention. A key factor in achieving meaningful results from an RCT is the retention of adequate participant numbers. Retaining participants from any older population in a clinical trial over 12 months or more can be difficult [12, 13]. The retention level in the current trial exceeded expectations in all three measures relating to post-intervention assessment and Falls Calendar data. Falls data for the full twelve months were available from 184 (88%) participants. This compares very favorably with returns of 78% over 6 months in people with PD [27] and over 75% return of monthly falls questionnaires in elderly fallers [28].

The other measures of retention, attendance at T2 and attendance at all 4 assessments over baseline attendance (14 months from randomization), achieved greater than 90 percent retention, very similar to the 92% achieved over 6 months by Tickle-Degnan et al. [29]. Two other RCTs in PD reported differing retention rates over 12-months as measured by attendance at assessments. Only 51 percent of people with PD in one 12 month randomized controlled crossover trial attended all three of the assessments [12], whereas results equivalent to ours were found in a much smaller (n = 56) study of Qigong with almost 94 percent of people returning for their 12 months assessment [30].

Differential attrition between intervention and control groups can affect the equivalence of the groups achieved by randomization at the outset of a trial [31, 32]. In most cases, attrition tends to be greater in the control group [12, 30], although sometimes the intervention carries a level of adverse effects that may cause more people to drop out of the active group [33, 34]. Whilst more participants were lost to follow up in our control group than in the therapy groups, the differences were small. The provision of a control intervention that was similar in duration, group dynamics, and relevance to the exercise interventions appeared to optimize retention and may have limited dropouts.

4.1.2. Adherence. Adherence, as defined by session attendance during the intervention phase, was also satisfactory with over 80% of available sessions attended by each group.
Two smaller RCTs in PD (n = 68 and 116 resp.) reported adherences of 93% [2] and between 86% and 92% over 6 weeks intervention periods [2, 29]. Other reports of adherence in the literature are either over much longer periods [12, 14, 30], in different populations (e.g., [13, 28]), or involved physical therapy in the home setting [1, 9]. The determinants of satisfactory adherence rates are likely to be complex. There may be a degree of selection bias, as people who are willing to participate in research may be more likely to adhere to a program than those who refuse. Other factors such as locale, professional supervision by physical therapists, and social interaction may be relevant [35].

4.1.3. Compliance. Evaluation of therapist and participant compliance to the protocol interventions is important to interpreting the key results of a trial. It also determines how effectively the interventions can be implemented as treatments in the wider context. Despite this, it is seldom reported. In our study, over 85% of participants were able to complete all or nearly all of the prescribed exercises, despite a mean age of 68 years and mild to moderate signs of PD (median modified HY of 2.5). Only one other paper, to our knowledge, reports the ability of people with PD to comply with the content of a therapy intervention to reduce falls [14]. In this small RCT (n = 48), compliance with 6 months of exercise therapy performed primarily at home was evaluated. Only 25% of participants were able to complete all prescribed exercises, with another 25% completing fewer than half of them, possibly because motivation may be different when exercising alone.

We believe compliance with therapy content was enhanced by the booklet of photographically illustrated exercise descriptions provided to each participant in the two exercise groups. Enlarged photographs were also placed at exercise stations in the various therapy locations to improve the accuracy of exercise performance, and correct performance was further facilitated by the presence of both a physical therapist and a trained assistant. The therapy protocol clearly directed that each participant should be working at a hard but achievable level (modified Perceived Exertion Scale levels [19]) that should have fully engaged participation.

The strong compliance with content may also reflect the participants’ relationship with and confidence in the treating therapists as well as the therapists’ confidence in the trial exercise protocol. Importantly, the therapist was always the final judge of how the participant was to perform each activity and at what level, supporting their professional skill and understanding. As this level of compliance with program content was achieved by a number of different therapists of widely varying years of clinical experience, it appears that the content was well defined and easy to implement.

Although not formally assessed, many individuals from our three groups volunteered that they had enjoyed their participation. In part, this probably reflected the supportive relationships and camaraderie that developed between group members, reducing social isolation [36]. It was informally observed that group members supported each other despite differing levels of disability. Such information sharing has been reported as a desired outcome in PD [36]. These factors are likely to have enhanced adherence and compliance in the therapy groups.

An important aspect to designing a randomized controlled trial is setting up the control group. Ideally, a control group should be exposed to similar duration and intensity of contact time as the intervention group, meeting the needs for education, attention, and socialization. The results of this study suggest that the LS program fulfilled these aims. The group’s focus on PD specific topics [36] such as medication management, fatigue management, and communication was a strong point, building on the camaraderie and mutual support provided by members to each other. Control groups can often suffer from poor retention and adherence [12], particularly if they are simply a “wait list” group. Our results and others [11, 37] suggest that participant-relevant education helps improve group participation, particularly if social interaction and support within the group can be fostered. We conclude that guided small group discussions on topics of relevance can be recommended as a viable control program in the design of controlled clinical trials.

5. Conclusions

In the rehabilitation literature, there are few reports of the feasibility, safety, and adverse events associated with physical therapy for people living with Parkinson’s disease. Our results address this gap and show that, when combined with a falls education program, strategy training and strength training can be safely implemented in a community-based sample of people with idiopathic PD. We also found that a life-skill social and education program was an effective control intervention that maintained interest without providing the active ingredients of therapy. Protocols could be easily followed by clinicians with varying levels of expertise, allowing for replication in future trials throughout the world.

Acknowledgment

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Research Article

Improved Dynamic Postural Task Performance without Improvements in Postural Responses: The Blessing and the Curse of Dopamine Replacement


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Introduction. Dopamine-replacement medications may improve mobility while not improving responses to postural challenges and could therefore increase fall risk. The purpose of this study was to measure reactive postural responses and gait-related mobility of patients with PD during ON and OFF medication conditions. Methods. Reactive postural responses to the Pull Test and performance of the Functional Gait Assessment (FGA) were recorded from 15 persons with PD during ON and OFF medication conditions. Results. Persons with PD demonstrated no significant difference in the reactive postural responses between medication conditions but demonstrated significantly better performance on the FGA when ON medications compared to OFF. Discussion/Conclusion. Dopamine-replacement medications alone may improve gait-related mobility without improvements in reactive postural responses and therefore could result in iatrogenic increases in fall risk. Rehabilitation providers should be aware of the side effects and limitations of medication treatment and implement interventions to improve postural responses.

1. Introduction

Parkinson disease (PD) is the most prominent of the hypokinetic disorders [1, 2]. The cardinal features of PD are tremor at rest, rigidity, hypokinesia, and postural instability [3, 4]. Postural instability and falls constitute major reasons for the serious complications in advanced PD [5, 6]. Falls are associated with high morbidity, mortality [7], and diminished quality of life [8, 9]. Current estimates report that up to 70% of those with PD fall each year, and 13% fall more than once a week [5, 10].

The majority of persons with PD will be treated with dopamine-replacement medications and the benefits of these medications on overall motor function and mobility are well established [11, 12]. However, limitations of dopamine replacement do exist. One of these limitations is the minimal effect of dopamine-replacement medications on postural instability [13–15]. Coupling the benefits of increased gait-related mobility and the limitation that postural instability is dopamine-resistant raises the possibility that fall risk may increase through increased exposure to postural challenges.

With such a high incidence of falls and the apparent dopamine-resistant nature of postural instability, an understanding of the extent and character of how postural responses and gait-related mobility respond to dopamine-replacement medication is critical for optimal rehabilitative treatment.

Despite the apparent paradox between dopamine replacement effects on postural responses and gait-related mobility, to our knowledge, no studies have systematically examined these variables in detail. As an initial step in exploring this postural response—mobility paradox, we sought to examine the potential differential effect of dopamine replacement on postural instability and gait-related mobility. This study had the following objectives: (1) quantitatively measure the kinematic characteristics of reactive postural responses and gait-related mobility in persons with PD during both ON and OFF medication conditions and (2) examine the specific components of gait-related mobility (e.g., on level surface, speed, with change in head position, with pivots, over obstacle, with narrow support, with eyes closed, backwards, and steps) that were dopamine-responsive. Based on previous research [13, 14], we hypothesized that dopamine...
replacement would not improve the kinematics of reactive postural responses. In contrast, we hypothesized that dopamine replacement would improve performance on gait-related mobility, but only through the improvement of specific components of the Functional Gait Assessment (FGA).

2. Methods

2.1. Selection of Participants. Potential participants were a sample of convenience recruited through referral from local neurologists or response to advertisement in a PD support group newsletter. The inclusion criteria were a medically confirmed diagnosis of idiopathic PD, a stable and neurologist-optimized medication regime that included dopamine replacement as well as other anti-Parkinson medications, and the ability to independently ambulate in the community with or without an assistive device. PD participants were excluded from the study if they had a history of medical conditions (orthopedic, cardiovascular, or otherwise) that would limit their ability to participate in the study procedures.

2.2. Measures. The most common research paradigms to examine medication effects on postural instability utilize sliding or rotating force plates that induce postural sway. While having high degrees of internal validity for research purposes, these paradigms lack external and ecological validity because the floor sliding or rotating underneath a person is not commonly encountered in daily life. Additionally, many of these studies limit their analysis to the components of sway while the base of support remains fixed omitting analysis of protective steps [11, 16]. Therefore, rather than using measures that lacked ecological validity, we selected the Pull Test because of its wide use in clinical neurology practice. Clinically, the Pull Test became the most widely used tool for clinical evaluation of postural instability in patients with PD when it was incorporated into the Unified Parkinson Disease Rating Scale (UPDRS) [17] in 1987. However, current research suggests the Pull Test in isolation is not accurate in predicting fallers, especially in the ON medication state [5, 18]. Also, the Pull Test has no formal consensus on its exact execution and low intra- and interrater consistency [5, 19]. Despite these concerns, the Pull Test is one of the only clinical balance test that examines reactive postural responses and provides insight into postural reflexes without being confounded by other aspects of mobility [7]. In order to examine postural responses, without being corrupted by mobility, the Pull Test is performed by pulling the subject’s shoulders posteriorly inducing a protective stepping response. To our knowledge, no studies have kinematically examined the Pull Test to explore the temporal and spatial characteristics in response to interventions such as dopamine replacement.

Ideally, community ambulation and monitoring of fall risk would provide direct measurement of gait-related mobility including step counts [20], variability of ambulatory activity [21], episodes of instability, and falls. Although some research groups have demonstrated monitoring within limited tasks or environments [22, 23], sustained multiday measurement is not technologically feasible at this time and is subject to a multitude of confounding influences [24]. Because of these concerns, we selected a clinical measure that is comprised of a set of posturally challenging gait tasks that a person with PD may encounter during community mobility (the FGA [25]). Previous research has suggested that the FGA may have greater ecological validity to postural challenges during community mobility than the Pull Test [26–28]. Furthermore, the FGA was selected because previous research has documented its validity in people with Parkinson disease [18, 29], vestibular disorders [25], as well as other neurologically impaired populations [30]. The FGA was administered in a standardized location as described in the original publication [25] and is comprised of 10 items each worth a maximum of 3 points for a total possible score of 30. Higher scores are indicative of more stability during-specific balance tasks.

2.3. Procedures. Prior to testing, approval for the study was obtained from the Institutional Review Board (IRB) at the University of Utah. After recruitment, the purposes and procedures of the study were explained and all subjects signed an IRB approved consent form. After obtaining consent, demographics and disease specific variables were obtained from each participant.

All testing was conducted at the Wellness and Rehabilitation Clinic and the Motion Capture Core Facility at the University of Utah, Department of Physical Therapy, and took place on two separate days.

For both days of testing, the clinically defined OFF medication condition was induced by having the participant off their dopamine-replacement medications for at least 12 hours prior to testing and is consistent with CAPIT guidelines for OFF medication testing [31]. After completing OFF medication testing, participants took their medication and rested for 1 to 1.5 hours and were retested in a clinically defined ON medication condition.

On the first testing day, the motor subsections of the UPDRS and FGA, during both ON and OFF medication conditions, were conducted by one physical therapist that had undergone standardized training on performance of the UPDRS. Because of the significant medication effects, the tester was not blinded to medication condition. In conjunction with the UPDRS testing, a modified Hoehn and Yahr (H&Y) stage [32] was assigned and a single Pull Test was performed and rated using the standardized scoring criteria [17]. Following completion of the UPDRS, participants performed the FGA.

On the second day, testing was performed in the Motion Capture Core Facility. This laboratory is equipped with an eight-camera motion analysis system (Vicon Motion Systems; Oxford, UK) and two force plates (AMTI; Watertown, Mass, USA). Prior to participants’ entry into the laboratory, a static and dynamic calibration of the system was performed. Individual anthropometric data were recorded. Passive reflective markers were placed on bony landmarks utilizing a standardized gait analysis marker set (Plug-In-Gait, Vicon Motion Systems; Oxford, UK). Following
subject and system preparation, participants were given an explanation of the Pull Test prior to the execution of the test trials [17]. Once the participant gave verbal confirmation that they understood the test, the participant was placed into position. The examiner, using the UPDRS testing description, performed the Pull Test. Participants performed five trials in both the ON and OFF medication condition. For all trials, kinetic and kinematic data were collected at 250 Hz.

Performance of the Pull Test was characterized using select spatial and temporal variables rather than just using the observational criteria as outlined in the UPDRS. To accomplish this, we segregated out 5 potential temporal and spatial contributors to abnormal Pull Test performance. These variables were chosen to specifically examine temporal and spatial constructs that have been previously shown to be affected by PD (reaction time, movement amplitude, and movement speed) [16]. The five kinematic dependent variables were defined as follows.

(i) **Step reaction time**: the time latency (in seconds [sec]) from the initial examiner induced shoulder movement until the time of initial foot movement of the initial stepping limb.

(ii) **Step length**: the distance (in centimeters [cm]) from the static sagital plane position of the heel marker of the initial stepping limb to the sagital plane position of the heel marker at initial contact of the initial stepping limb.

(iii) **Step average velocity**: step length divided by step time (in cm/sec). Step time was defined as the time latency from initial foot movement until the time of foot contact (in sec) of the initial stepping limb.

(iv) **COM displacement**: the sagital plane distance (in cm) from the initial COM position to the COM position at time of foot contact of the initial stepping limb.

(v) **COM average velocity**: COM displacement divided by COM time (in cm/sec). COM time is defined as time latency from initial COM movement until the time of foot contact (in sec) of the initial stepping limb.

For each dependent variable, the average of the first three fully measured trials was used as the representative dependent variable. A fully measured trial consisted of the participant taking at least one step backwards to regain balance following the Pull Test and that all markers remained visible during the trial.

2.4. Data Analysis. All statistical analyses were performed with SPSS 16 for Macintosh (SPSS Inc.). Descriptive statistics were performed for demographic variables. The independent variable used for analysis of our primary hypotheses was medication condition (2 levels: ON and OFF medication). Due to the relatively small sample size and the potential for nonnormally distributed data, in the primary analyses, between medication condition differences were compared using separate nonparametric tests for dependent samples.

To examine our findings in more detail, we performed several post hoc means of analysis. First, between-condition effect sizes were calculated to compare the magnitude of effect of the kinematic variables and the FGA. In addition, we examined the changes of the specific items on the FGA in order to gain insight into the locus of effect of medication on FGA performance. Differences between the ON and OFF medication conditions for each FGA item were compared using separate nonparametric tests for dependent samples and between-condition effect sizes. A determination of whether or not an item was dopamine-responsive was made by examining the statistical significance, the within-medication effect size, and the number of individuals in the sample who improved on an item when ON medication. A conservative approach was applied to this decision in that items were determined to be dopamine-responsive only if 3 criteria were met: (1) there was statistical significance between medication conditions ($P < 0.005$), (2) there was a large effect size ($ES > 0.70$), and (3) the majority of individuals tested demonstrated a performance improvement with dopamine-replacement medication (>7/15).

The experiment wide level of significance was set at $P < 0.05$. However, to control for type I error risk, the overall alpha level for the tests for differences was adjusted using a Bonferroni correction separately within the primary and post hoc analyses (primary analyses: 0.05/6 comparisons, therefore $P < 0.008$ was needed for significance on individual kinematic variables, and the overall FGA; post hoc analyses: 0.05/10, therefore $P < 0.005$ was needed for significance on individual FGA items).

3. Results

Fifteen persons (9 male, 6 female; mean age: 67 ± 13 years) with PD (disease duration: 7.5 ± 5.0 years) participated in this study. Their median (range) Hoehn and Yahr rating and mean (SD) UPDRS (motor subsection) was 2.5 (2–4) and 13.7 (6.8), respectively, while ON medication and 3.0 (2.5–4) and 27.6 (7.0), respectively, while OFF medication. Furthermore, 8 of the 15 participants in this study reported a history of falls.

3.1. Comparison of Reactive Postural Responses during ON and OFF Medication Conditions. Comparison of the reactive postural response variables recorded from the Pull Test revealed no significant difference between ON and OFF medication conditions. In addition, the effect sizes for dopamine replacement for all the postural response variables were small (0.02–0.12) (Table 1, Figures 1 and 2).

3.2. Comparison of Clinical Balance Test Performance during ON and OFF Medication Conditions. Comparison of the index scores for the FGA revealed a significant higher score during the ON medication condition ($P \leq 0.008$). Furthermore, the effect size for dopamine replacement on the FGA score was 1.07 (Table 1, Figure 3). In addition, post hoc examination revealed that dopamine-replacement-medication-induced improvements in FGA scores were focused on a select group of tasks (Table 2).
Table 1: Results of PD group ON and OFF medication (Mean ± SD).

<table>
<thead>
<tr>
<th></th>
<th>Step reaction time (sec)</th>
<th>Step length (cm)</th>
<th>Step avg velocity (cm/sec)</th>
<th>COM displacement (cm)</th>
<th>COM avg velocity (cm/sec)</th>
<th>Pull Test (UPDRS motor subsection item 30)</th>
<th>FGA</th>
</tr>
</thead>
<tbody>
<tr>
<td>ON meds 95% CI</td>
<td>0.77 ± 0.39</td>
<td>25.94 ± 10.33</td>
<td>62.45 ± 17.11</td>
<td>19.05 ± 6.91</td>
<td>19.42 ± 6.59</td>
<td>0.73 ± 0.46</td>
<td>23.67 ± 4.59*</td>
</tr>
<tr>
<td></td>
<td>0.56–0.99</td>
<td>20.22–31.67</td>
<td>52.98–71.93</td>
<td>15.23–22.88</td>
<td>15.77–23.07</td>
<td>0.48–0.99</td>
<td>21.12–26.21</td>
</tr>
<tr>
<td>OFF meds 95% CI</td>
<td>0.75 ± 0.39</td>
<td>25.72 ± 11.61</td>
<td>63.38 ± 24.05</td>
<td>19.66 ± 7.46</td>
<td>20.20 ± 7.01</td>
<td>1.0 ± 0.53</td>
<td>18.80 ± 4.80</td>
</tr>
<tr>
<td></td>
<td>0.53–0.97</td>
<td>19.29–32.15</td>
<td>50.07–76.70</td>
<td>15.53–23.80</td>
<td>16.32–24.09</td>
<td>0.70–1.30</td>
<td>16.14–21.46</td>
</tr>
<tr>
<td>Effect size</td>
<td>0.06</td>
<td>0.02</td>
<td>.05</td>
<td>0.09</td>
<td>0.12</td>
<td>0.56</td>
<td>1.07</td>
</tr>
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</table>

* $p \leq 0.008$.

4. Discussion

Our clinical experience and previous reports in the literature have suggested that dopamine replacement may have a differential effect on reactive postural responses compared with gait-related mobility. Specifically, through its reduction of bradykinesia and rigidity [33, 34], it may improve gait-related mobility. Despite these improvements, laboratory studies of reactive and anticipatory postural tasks suggest that postural coordination is not improved [13, 35]. Therefore, with improved gait-related mobility and deficient postural coordination, some individuals may have an increased risk of falling. This paradox was the basis for this study.

Our results agreed with our hypotheses that dopamine replacement does not have a significant influence on reactive postural responses as measured by the temporal and spatial characteristics of the Pull Test. In addition, as hypothesized, dopamine-replacement medication improved gait-related mobility as measured by the overall FGA score. Further investigation of the results from the FGA indicated that dopamine-replacement medication improved a limited number of items.

Ultimately, fall events in everyday life are a product of postural abilities and the frequency of exposure to postural challenges. The research designs (ON and OFF medication testing as well as the measures utilized) were intended to systematically provide an initial controlled examination of the possibility that dopamine-replacement medications may improve gait-related mobility without commensurate improvements in reactive postural responses. As an initial step in exploring this postural response—mobility paradox, we found that this is indeed the case. Conceivably, if such a differential effect persisted during community mobility, it could lead to increased fall risk and falls in the community through greater exposure to balance challenges and still deficient postural responses. Certainly, this proposition requires further research.

5. A Measured View of the Pull Test

The validity of the Pull Test as a predictor of falls and value in clinical balance examinations has been questioned [18, 36, 37]. Although our results could be seen as support for this view, we do not interpret our findings in this way.
The kinematic characteristics of the Pull Test reported in this study are consistent with the hypokinetic reactive postural responses seen in other studies [14, 27]. Few clinical balance tests examine reactive postural responses as a component of the motor sign of postural instability. In isolation, such information provides a narrow view of potential contributors to fall risk of persons with PD in the community. However, in conjunction with other clinical balance tests, the examination of reactive postural responses may provide clinicians with a better understanding of postural instability and fall risk in persons with PD. In addition, concerns regarding Pull Test reliability may be addressed through the use of the recently proposed Push and Release Test [37] as well as the Balance Evaluation Systems Test (BEST test and a streamlined version (the Mini-BEST)) [29, 38].

6. Implications for Rehabilitation

Through the analysis of the validity indices of clinical balance tests, we previously advocated for a battery of tests [39] and environmentally valid testing [18] in the examination of fall risk in individuals with PD. Our current findings add an additional dimension to this issue. Analysis of reactive postural responses revealed no consistent medication effect. Examination of specific FGA items suggested that tasks with stable sensory integration demands (e.g., walking on solid ground with eyes open) were more likely to be dopamine-responsive. In contrast, the dopamine-nonresponsive items shared the constraint of fluctuating sensory integration demands (e.g., gait with horizontal head turns). While this interpretation is speculative, such findings suggest that clinicians should not blindly accept a composite score or specific biomechanical outcome as an indicator of fall risk or as response to a rehabilitation intervention. Rather, there must be a critical analysis of the individual task performance in order to understand the clinical implications of examination findings and the potential targets for intervention.
Despite the fact that postural instability appears to be a dopamine-resistant motor sign, it does not follow that it is not amenable to change. There are few studies that have examined the efficacy of focused rehabilitation interventions on kinematic and kinetic outcomes [40]. In the few studies that have examined such outcomes, there are suggestions that reactive postural responses or postural sway may improve with focused training of an adequate dosage [41].

### 7. Limitations and Directions for Research

Despite their statistical significance, these results should be interpreted with caution. Future research with larger samples is needed to gain further insight into the beneficial and potentially detrimental effects of dopamine replacement on postural performance and falls. Furthermore, this study included only persons currently taking dopamine-replacement medications, and we did not randomize the order of the ON and OFF medication conditions. While such a cohort may reflect persons who have progressed to a moderate disease severity, persons with mild PD (Hoehn and Yahr stage 1) and severe PD (Hoehn and Yahr stage 5) did not participate in this study. Future research should examine participants with these characteristics as well as persons who have undergone surgical management of their PD (such as deep brain stimulation). Lastly, by design, this study used constrained outcomes, such as the Pull Test and the FGA, as an initial test of the posture and mobility paradox. Future studies of postural performance and falls in persons with PD should attempt to employ validated measures of reactive and anticipatory balance responses, clinical balance abilities, and community ambulatory/fall risk monitoring as outcomes.

### 8. Summary and Clinical Implications

Our findings suggest that dopamine-replacement medications alone may improve gait-related mobility without commensurate improvements in reactive postural responses and therefore could result in iatrogenic increases in fall risk. Rehabilitation providers should be aware of the limitations of dopamine-replacement treatment and implement interventions intended to improve postural responses.

### Conflict of Interests

The authors declare that they have no conflict of interest that could inappropriately influence this work.

### Acknowledgement

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### References


Motor learning has been found to occur in the rehabilitation of individuals with Parkinson's disease (PD). Through repetitive structured practice of motor tasks, individuals show improved performance, confirming that motor learning has probably taken place. Although a number of studies have been completed evaluating motor learning in people with PD, the sample sizes were small and the improvements were variable. The purpose of this meta-analysis was to determine the ability of people with PD to learn motor tasks. Studies which measured movement time in upper extremity reaching tasks and met the inclusion criteria were included in the analysis. Results of the meta-analysis indicated that people with PD and neurologically healthy controls both demonstrated motor learning, characterized by a decrease in movement time during upper extremity movements. Movement time improvements were greater in the control group than in individuals with PD. These results support the findings that the practice of upper extremity reaching tasks is beneficial in reducing movement time in persons with PD and has important implications for rehabilitation.

1. Introduction

Motor learning is defined as a relatively permanent change in the ability to move associated with either practice or experience [1]. In neurologically healthy adults, brain activity changes occur in the basal ganglia during the process of motor learning [2]. From functional MRI studies, the key changes include a reduction of overall brain activation and a shift from cortical to more basal ganglia activity during the consolidation phase of learning [2, 3].

Parkinson's disease (PD) is a neurodegenerative disorder affecting basal ganglia functioning, characterized by four cardinal signs; bradykinesia (slowness of movement), rigidity (stiffness), resting tremor, and postural instability. Bradykinesia is an inherent component of PD and affects both movement initiation and execution [4, 5]. Motor deficits are not the only problem in PD. Due to the dysfunction of the basal ganglia in PD, motor learning may also be impaired.

Acquisition and retention of movement skills are important to researchers and clinicians who are involved in rehabilitation of individuals with PD [2, 6–8]. Nieuwboer et al. (2009) [6] reviewed 11 studies that evaluated acquisition and retention in a broad range of tasks. The studies suggest that overall, acquisition does occur in people with PD, but performance on the task during acquisition is typically impaired relative to controls. Nieuwboer et al.'s [6] review also suggests that long-term retention of new skills is impaired in individuals who have striatal problems, particularly in people with PD.

Although a number of studies have examined acquisition and retention of tasks in PD, the sample sizes have been small and heterogeneous, and the experimental tasks and outcomes used have varied widely. For example, kinematic variables, including distance (or displacement, which is distance with a specific direction), speed (or velocity, which is speed with a direction), and acceleration, have been used
to measure motor learning both in the upper and the lower extremities in individuals with PD [9, 10]. Other movement parameters that have been measured include time, force, accuracy of movement to a target, coordination of more than one joint segment of the limb, sequencing of movement [9], interlimb function [11], and the ability to switch motor tasks [12]. Any of these measurements can provide researchers with valuable information about motor learning abilities in individuals with PD.

Regardless of the design features of each study, practice of the experimental task is integral to any of the research paradigms. While some researchers have suggested that people with PD do improve with practice, but not to the same level or as well as do control subjects [13–15], others have suggested that people with PD were able to benefit from short-term, but not long-term practice [16]. Sequence learning (learning of movements in a set sequence) has been shown to take more time and to be related to the stage of disease [13].

Given the apparent heterogeneity of methodologies and participant samples, it is not surprising that there is disagreement on the extent and duration of skill acquisition in persons with PD. Such disagreement makes it difficult to draw firm conclusions and provide therapeutic recommendations to clinicians. To date, there have been systematic reviews, but no meta-analyses pooling or combining the existing data on acquisition and retention of skills in individuals with PD that may provide insight into the consistent effects of motor task practice.

By focusing only on upper extremity and on movement time during practice of upper extremity reaching tasks, we were able to find a sufficient body of literature to analyze using a meta-analysis paradigm. The purpose of this study, therefore, was to determine how practicing a simple upper extremity motor task affects movement time for the task in people with PD.

2. Methods

2.1. Literature Search. The electronic databases used to find research that evaluated upper extremity motor learning in people with PD were CINAHL, EMBASE, PubMed, MEDLINE, PEDro, Proquest, PsycINFO, the Cochrane Database of Systematic Reviews, and Scopus. The comprehensive search used terms within the following categories: motor learning, Parkinson’s disease, upper extremity, and time/speed/rate. The specific terms within categories are listed in Table 1.

The first four authors worked in pairs. Each pair was randomly assigned to search a set of databases and to select articles for screening. This initial search strategy resulted in 127 articles.

<table>
<thead>
<tr>
<th>Table 1: Search terms used for the meta-analysis.</th>
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<tbody>
<tr>
<td><strong>Practice</strong></td>
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<td>Training</td>
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<td>Sequential learning</td>
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<td>Procedural learning</td>
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<td>Motor skill learning</td>
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<td>Skill learning</td>
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<td>Task performance</td>
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<td>Response</td>
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<td>programming</td>
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<td>Motor function</td>
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<td>Motor function loss</td>
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<td>Motor activity</td>
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Where there was disagreement between members of the pair of reviewers, the fifth and sixth authors (S. J. Spaulding and M. E. Jenkins) were consulted, and a consensus was reached. Inclusion criteria were as follows: articles that were published between the beginning of included databases up to September 2010, articles published in English, studies that examined upper extremity motor learning in individuals with PD, studies that included means and standard deviation or standard error, studies that evaluated motor learning with time as an outcome measure, and studies that had a control group.

Following the methodologies used by Siegert et al. [17], articles in the “grey literature,” such as conference proceedings or research published in Master’s or PhD theses, were excluded to avoid the use of evidence that had not been peer reviewed at the level of a journal article. After the application of the initial inclusion criteria, the authors had determined that 30 articles met all the criteria.

The authors then examined the experimental design of these 30 articles to determine research that provided pre/postmeasurements of movement time prior to and following an intervention designed to elicit motor learning. The final group of articles included five publications published between 1998 and 2009. Within those articles, there were seven independent studies.

2.2. Criteria for Inclusion in Systematic Review. Once the set of 127 articles was retrieved, the first four authors evaluated them. The title, abstract, and full content of all articles were screened against the inclusion criteria, with each article appraised by two of the first four authors. Based on the criteria, articles for inclusion in the meta-analysis were chosen.

2.3. Data Extraction for Meta-Analysis. The first four authors working in pairs extracted the data from the seven independent studies. The following information was obtained for both experimental and control groups in all studies: sample size, pretraining mean, pretraining standard deviation or standard error, posttraining mean, and posttraining standard
deviation. All time point values were documented immediately following the intervention and late (in terms of time after practice) as defined by each individual study. Data were extracted from text or figures, depending on how each article presented the data. If the resultant data were presented in a figure, each author, in the original pair of authors, extracted values, thus two measures were taken from the figure. The final value used was an average of the two authors’ extracted numbers. Three studies reported both immediate and follow-up scores. When more than one follow-up period was measured, the authors chose to use the longest interval between training and followup. For the purposes of this meta-analysis, this period was termed late after training. Platz et al. [4] and Marinelli et al. [18] included two separate studies in their articles. The studies had different numbers of participants and different paradigms; thus, the results were entered into the analysis separately.

2.4. **Meta-Analysis.** A meta-analysis was conducted using the program Comprehensive Meta-Analysis (CMA) [19]. Hedge’s g, a measure of the standardized mean difference, was determined for the pre/postscores in each of the control group and the group of individuals with PD. Hedge’s g accounts for the overestimation of the population-standardized differences [20].

Because it could not be assumed that the people in the studies were highly homogeneous in their characteristics, a random effects model was used and provided a conservative estimate of the differences between the groups in the individual studies [20].

### 3. Results

A total of 58 individuals with PD and 56 participants without PD were included from the seven studies. Descriptive statistics of all the subjects are included in Table 2. Descriptive statistics of the findings extracted from the studies included in this meta-analysis are shown in Table 3. Table 4 outlines the description of the motor learning paradigms in the studies used in the meta-analysis.

Hedge’s g with a 95% confidence interval (CI) for each of the included studies is summarized in Table 5.

As seen in the forest plot representing the results for the control group (Figure 1(a)), the point estimator of the overall effect shows that participants without PD demonstrated improvements in movement time. The point estimator of the overall effect for individuals with PD did show improvements, but the changes were smaller and showed greater variability than did the results of the control group (Figure 1(b)). The interval estimators of the overall effects (95% CI) for each group overlapped. When comparing movement times immediately (early) posttraining to late posttraining, slower times of movement and larger 95% CI were evident for the later posttraining time, for both groups.

### 4. Discussion

Although many studies have reported that motor learning occurs in individuals with PD, not all studies have reported improvements [4]. Among studies that examine the acquisition and retention of motor skills in PD, study sizes have been small, making conclusions less certain [6, 15]. In addition, tasks, duration of practice, and frequency of practice trials are different between studies [6]. This meta-analysis was able to overcome the heterogeneity issue by focusing only on studies of upper extremity movements and studies that analyzed improvements in movement time. Through the application of meta-analytic analysis, we were able to pool results with heterogeneous methods and demonstrate a consistent reduction in movement time as a result of practice of upper extremity reaching tasks.

---

**Table 2: Descriptive statistics of participants with PD in the included studies.**

<table>
<thead>
<tr>
<th>Study</th>
<th>Age mean (SD)</th>
<th>MMSE mean (SD)</th>
<th>Duration of PD in years mean (SD)</th>
<th>Hoen and Yahr stage mean (SD)</th>
<th>UPDRS mean (SD)</th>
<th>Medication status (related to anti-Parkinsonian medication)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Agostino et al. (2004) [21]</td>
<td>64.4 (6.3)</td>
<td>&gt;26</td>
<td>7.6 (3.1)</td>
<td>N/A</td>
<td>15.3 (4)</td>
<td>(motor score)</td>
</tr>
<tr>
<td>Behrman et al. (2000) [22]</td>
<td>74 (7)</td>
<td>28 (1.6)</td>
<td>7 (4)</td>
<td>2.6 (0.5)</td>
<td>N/A</td>
<td>On</td>
</tr>
<tr>
<td>Majsak et al. (2008) [23]</td>
<td>70.4 (3.7)</td>
<td>N/A</td>
<td>7.3 (7.9)</td>
<td>3 (0)</td>
<td>33.7 (7.5)</td>
<td>(motor score)</td>
</tr>
<tr>
<td>Marinelli et al. (2009)a [18]</td>
<td>60 (7.4)</td>
<td>≥27</td>
<td>8.4 (4.5)</td>
<td>2 to 2.5</td>
<td>N/A</td>
<td>On</td>
</tr>
<tr>
<td>Marinelli et al. (2009)b [18]</td>
<td>57.9 (7.3)</td>
<td>≥27</td>
<td>2.1 (3.1)</td>
<td>1 to 2</td>
<td>N/A</td>
<td>Off</td>
</tr>
<tr>
<td>Platz et al. (1998)a [4]</td>
<td>65.9 (8.3)</td>
<td>27.7 (1.6)</td>
<td>7.6 (2.4)</td>
<td>2.5 (0.5)</td>
<td>8.0 (4)</td>
<td>Bradykinesia score2</td>
</tr>
<tr>
<td>Platz et al. (1998)b [4]</td>
<td>62.0 (14.6)</td>
<td>28.8 (1)</td>
<td>4.3 (1.8)</td>
<td>2.0 (.75)</td>
<td>4.0 (3.5)</td>
<td>Bradykinesia score2</td>
</tr>
</tbody>
</table>

1 N/A indicates that the results were not available. SD: standard deviation.

2 [24].

Note: a and b are data from two different paradigms within one publication.

c and d are data from two different experiments within one publication.
The results of the meta-analysis suggest that motor learning in upper extremity function occurs in both neurologically healthy controls and individuals with PD through practice of upper extremity reaching tasks designed to reduce movement time. This effect is present immediately after the training period but also is sustained after a period of time although the late effects are somewhat diminished. The control participants have a mild to moderate increased effect based on their mean effect sizes compared to people with PD. However, the substantial overlap of confidence intervals would suggest that
Table 5: Effect sizes (as measured using Hedge’s g) with upper and lower 95% confidence intervals for the studies included in the meta-analysis and the resultant effect sizes. A negative value of the effect sizes is indicative of a reduction in the movement time.

(a)

<table>
<thead>
<tr>
<th>Authors</th>
<th>Time of testing*</th>
<th>Effect size (Hedge’s g)</th>
<th>95% CI</th>
<th>Effect size (Hedge’s g)</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Agostino et al. (2004)</td>
<td>Immediate</td>
<td>−0.937</td>
<td>−1.668 to −0.582</td>
<td>−0.177</td>
<td>−0.773 to 0.419</td>
</tr>
<tr>
<td>Behrman et al. (2000)</td>
<td>Immediate</td>
<td>−1.233</td>
<td>−1.884 to −0.582</td>
<td>−1.031</td>
<td>−1.663 to −0.426</td>
</tr>
<tr>
<td>Majsak et al. (2008)</td>
<td>Immediate</td>
<td>−0.192</td>
<td>−0.815 to 0.431</td>
<td>−0.361</td>
<td>−1.002 to 0.280</td>
</tr>
<tr>
<td>Marinelli et al. (2009)</td>
<td>Immediate</td>
<td>−0.551</td>
<td>−1.331 to 0.229</td>
<td>−0.727</td>
<td>−1.561 to 0.106</td>
</tr>
<tr>
<td>Marinelli et al. (2009)</td>
<td>Immediate</td>
<td>−0.265</td>
<td>−0.955 to 0.425</td>
<td>−0.071</td>
<td>−0.746 to 0.604</td>
</tr>
<tr>
<td>Platz et al. (1998)</td>
<td>Immediate</td>
<td>−0.667</td>
<td>−1.197 to −0.156</td>
<td>−1.581</td>
<td>−2.400 to −0.863</td>
</tr>
<tr>
<td>Platz et al. (1998)</td>
<td>Immediate</td>
<td>−2.030</td>
<td>−2.873 to −1.186</td>
<td>−0.992</td>
<td>−1.571 to −0.414</td>
</tr>
<tr>
<td>Group immediate effect</td>
<td></td>
<td>−0.814</td>
<td>−1.288 to −0.340</td>
<td>−0.698</td>
<td>−1.070 to −0.325</td>
</tr>
</tbody>
</table>

(b)

<table>
<thead>
<tr>
<th>Authors</th>
<th>Time of testing*</th>
<th>Effect size (Hedge’s g)</th>
<th>95% CI</th>
<th>Effect size (Hedge’s g)</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Agostino et al. (2004)</td>
<td>Late</td>
<td>−2.174</td>
<td>−3.339 to −1.009</td>
<td>−0.256</td>
<td>−0.857 to 0.346</td>
</tr>
<tr>
<td>Behrman et al. (2000)</td>
<td>Late</td>
<td>−1.148</td>
<td>−1.778 to −0.517</td>
<td>−0.973</td>
<td>−1.565 to −0.381</td>
</tr>
<tr>
<td>Majsak et al. (2008)</td>
<td>Late</td>
<td>−0.215</td>
<td>−0.839 to 0.410</td>
<td>−0.781</td>
<td>−1.506 to −0.056</td>
</tr>
<tr>
<td>Group late effect</td>
<td></td>
<td>−1.028</td>
<td>−1.784 to 0.272</td>
<td>−0.665</td>
<td>−1.226 to −0.105</td>
</tr>
<tr>
<td>Overall effect</td>
<td></td>
<td>−0.875</td>
<td>−1.276 to −0.473</td>
<td>−0.688</td>
<td>−0.998 to −0.377</td>
</tr>
</tbody>
</table>

Note: ^a and ^b data were extracted from two different experiments within one publication. ^c and ^d data were extracted from two different training programs within one publication. Effect size was corrected using Hedge’s g.

^a The overall effect is the combination of the group immediate effect and the group late effect.
^b Time of testing is indicated as either immediately following training (immediate) or following an interim period specified by each individual study (late).

Results for control group

<table>
<thead>
<tr>
<th>Group by time point</th>
<th>Study</th>
<th>Time</th>
<th>Hedges’s g and 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immediate</td>
<td>Behram</td>
<td>Immediate</td>
<td>−0.105 to 0.325</td>
</tr>
<tr>
<td>Immediate</td>
<td>Majsk</td>
<td>Immediate</td>
<td>−0.367 to 0.863</td>
</tr>
<tr>
<td>Immediate</td>
<td>Marinelli (a)</td>
<td>Immediate</td>
<td>−0.665 to 0.410</td>
</tr>
<tr>
<td>Immediate</td>
<td>Marinelli (b)</td>
<td>Immediate</td>
<td>−0.156 to 1.186</td>
</tr>
<tr>
<td>Immediate</td>
<td>Platz (a)</td>
<td>Immediate</td>
<td>−0.127 to 0.778</td>
</tr>
<tr>
<td>Immediate</td>
<td>Platz (b)</td>
<td>Immediate</td>
<td>0.256 to 1.565</td>
</tr>
<tr>
<td>Immediate</td>
<td>Agostino</td>
<td>Immediate</td>
<td>−0.973 to 0.056</td>
</tr>
<tr>
<td>Late</td>
<td>Behram</td>
<td>Late</td>
<td>0.056 to 0.381</td>
</tr>
<tr>
<td>Late</td>
<td>Majsk</td>
<td>Late</td>
<td>0.773 to 0.419</td>
</tr>
<tr>
<td>Late</td>
<td>Agostino</td>
<td>Late</td>
<td>−0.071 to 0.746</td>
</tr>
</tbody>
</table>

(b)

Results for individuals with PD

<table>
<thead>
<tr>
<th>Group by time point</th>
<th>Study</th>
<th>Time</th>
<th>Hedges’s g and 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immediate</td>
<td>Behram</td>
<td>Immediate</td>
<td>−0.127 to 0.778</td>
</tr>
<tr>
<td>Immediate</td>
<td>Majsk</td>
<td>Immediate</td>
<td>−0.256 to 1.565</td>
</tr>
<tr>
<td>Immediate</td>
<td>Marinelli (a)</td>
<td>Immediate</td>
<td>−0.156 to 1.186</td>
</tr>
<tr>
<td>Immediate</td>
<td>Marinelli (b)</td>
<td>Immediate</td>
<td>−0.127 to 0.778</td>
</tr>
<tr>
<td>Immediate</td>
<td>Platz (a)</td>
<td>Immediate</td>
<td>0.256 to 1.565</td>
</tr>
<tr>
<td>Immediate</td>
<td>Platz (b)</td>
<td>Immediate</td>
<td>−0.127 to 0.778</td>
</tr>
<tr>
<td>Immediate</td>
<td>Agostino</td>
<td>Immediate</td>
<td>−0.367 to 0.863</td>
</tr>
<tr>
<td>Late</td>
<td>Behram</td>
<td>Late</td>
<td>0.056 to 0.381</td>
</tr>
<tr>
<td>Late</td>
<td>Majsk</td>
<td>Late</td>
<td>0.773 to 0.419</td>
</tr>
<tr>
<td>Late</td>
<td>Agostino</td>
<td>Late</td>
<td>−0.071 to 0.746</td>
</tr>
</tbody>
</table>

Figure 1: Forest plots of all the included studies for the control group (a) and the individuals with PD (b) including the time the results were acquired, Hedge’s g, and 95% confidence interval (CI) for the control group. Each box and corresponding horizontal line represents the overall mean and confidence intervals in the movement time. The area of each box is proportional to the inverse of that study’s variance. The horizontal line represents the 95% CI for each individual study. A diamond is used to depict overall mean effect size (center of the diamond) along with its CI (width of the diamond) [20].
both groups benefit from the practice in which they participated.

Overall, these results are consistent with previous work in small studies that demonstrate skill acquisition and retention in people with PD in a variety of motor tasks. Such studies have demonstrated acquisition and retention of motor skills in varied upper extremity tasks not included in this meta-analysis such as serial reaction time tasks [25–27] and other sequential aiming movements [7, 9, 13]. Furthermore, motor learning studies in people with PD have demonstrated improvement in balance and lower extremity function through practice [10, 28–30].

In addition, motor learning effect, demonstrated by improvement in movement time, was smaller among individuals with PD. This is not particularly surprising, given the role of the basal ganglia in both acquisition of motor task skill and in consolidation of automatic movements [2, 3, 31]. As evidence of the potential alterations of brain activity in persons with PD during task learning, functional MRI studies in individuals with PD have demonstrated that greater areas of the brain are activated during initial learning of a task and particularly during the repetition of a learned movement in PD compared to healthy controls [31].

4.1. Rehabilitation Implications. A number of differences were identified in the experimental methodologies of the studies from which data were extracted to conduct this meta-analysis. There was variability among the duration and frequency of practice as well as the types of tasks. These differences preclude the authors from determining that there is one type of practice that was more effective to improve upper extremity performance. However, one can conclude that practice in general is beneficial and the manipulation of practice parameters is worthy of further study. Interestingly, even in the studies in which the individuals were off dopamine replacement medication [4, 18], there was a decrease in movement time, suggesting that there could potentially be a rehabilitation program that would benefit people with PD, even if medication effectiveness was suboptimal for some reason. Yet, current studies suggest that dopamine replacement medication may have a deleterious effect on motor learning [32].

4.2. Limitations of the Study. A limitation of the present meta-analysis is the small number of studies that the authors were able to include, but to the best of our knowledge, all of the available studies of simple reaching tasks reporting movement time as an outcome were incorporated. There are more studies evaluating practice, but they were heterogeneous in their tasks or in their outcome measures; therefore, they did not meet our inclusion criteria, and the data could not be included in this meta-analysis. Additionally, the sample sizes of the included studies were small, affecting the generalizability of this meta-analysis [33].

4.3. Recommendations for Future Research. Current literature in this area typically examines one single task or movement. Future research might best examine the generalizability of the effects of practice to other tasks and areas of rehabilitation. Conclusions from a broader range of tasks could lead to the use of programs that are directly related to movements needed for daily functioning. Finally, future motor skill acquisition research should further examine the effects of varied practice parameters in more diverse samples of persons with PD.

5. Conclusions

Results from this pooling of data from various studies provide evidence that upper extremity movement time can be improved through the use of practice of reaching tasks in persons with PD, albeit potentially to a lesser extent than is shown in individuals with no neurological problems. The collective interpretation of this meta-analysis indicates that practice of relevant motor tasks targeted at maximizing acquisition and retention improved movement speed.

References


Lack of Short-Term Effectiveness of Rotating Treadmill Training on Turning in People with Mild-to-Moderate Parkinson’s Disease and Healthy Older Adults: A Randomized, Controlled Study

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Since turning is often impaired in Parkinson’s disease (PD) and may lead to falls, it is important to develop targeted treatment strategies for turning. We determined the effects of rotating treadmill training on turning in individuals with PD. This randomized controlled study evaluated 180° in-place turns, functional turning (timed-up-and-go), and gait velocity before and after 15 minutes of rotating treadmill training or stepping in place in 26 people with PD and 27 age-matched controls. A subset of participants with PD (n = 3) completed five consecutive days of rotating treadmill training. Fast as possible gait velocity, timed-up-and-go time, 180° turn duration, and steps to turn 180° were impaired in PD compared to controls (P < 0.05) and did not improve following either intervention (P > 0.05). Preferred pace gait velocity and timing of yaw rotation onset of body segments (head, trunk, pelvis) during 180° turns were not different in PD (P > 0.05) and did not change following either intervention. No improvements in gait or turning occurred after five days of rotating treadmill training, compared to one day. The rotating treadmill is not recommended for short-term rehabilitation of impaired in-place turning in the general PD population.

1. Introduction

Parkinson’s disease (PD) is a progressive neurodegenerative disease resulting in a variety of motor symptoms. Individuals with PD frequently experience difficulty with gait and turning, with more than half reporting difficulty turning [1–3] which may result in falls and serious injuries [4]. Symptoms of PD are treated using various therapeutic approaches; however, there are currently no effective treatment options that specifically target turning difficulty. Turning difficulties, including increased time to turn and increased number of steps to turn, are present even when individuals with PD are on PD medications [5–10].

Stepping in place on the rotating treadmill has been recommended as a possible rehabilitation option for those with PD [11]. After stepping in place on the rotating treadmill, healthy controls and people with PD show a rotational adaptation response known as podokinetic after-rotation [12–14]. The kinematics of podokinetic after-rotation are similar to those seen during normal in-place turning [11]. It has been suggested that the rotating treadmill may improve turns by serving as an external cue to promote the correct motor programs for successful turning [11].

Immediately after stepping in place on a rotating disk for a total of 15 minutes on one day, turning performance was improved in two people with PD on medication who also experienced freezing of gait during turns [15]. Specifically, there were fewer freezing events, reduced time to turn, less variable vastus lateralis muscle activity, and reduced coactivation of bilateral vastus lateralis muscles...
It remains unclear whether improvements seen with rotating treadmill training are specific to people with PD who experience freezing, nor do we know if improvements occur in other aspects of turning. If turning improvements occurred in a more diverse group of individuals with PD, the rotating treadmill would potentially be relevant as a rehabilitation tool. Our aim was to conduct a randomized controlled study examining the effects of rotating treadmill training on in-place turning in a larger, more representative group of individuals with PD and age-matched healthy controls. This study also includes control exercise groups for PD and healthy older adult participants. These control groups stepped in place on the floor for an amount of time equal to the treadmill training performed by the other groups. We hypothesized that turning would improve in individuals with PD following rotating treadmill training, while turning would likely remain unchanged for all healthy older adults and for those with PD who stepped in place on the floor.

2. Methods

2.1. Participants. We recruited 29 participants from the Movement Disorders Center at Washington University School of Medicine who had been diagnosed with idiopathic Parkinson’s disease according to standard criteria [16]. We also recruited 28 older adults without PD. People with PD were recruited if they were taking medication for PD, were ambulatory, did not have deep brain stimulators implanted, had no history or symptoms of other neurological diseases, and had no recent surgeries or injuries affecting walking or turning. Those with PD were tested approximately one hour after their last dose of PD medication. Of the 29 people with PD recruited, 3 did not complete the study due to fatigue. These individuals were excluded from all subsequent analyses. Older adults without PD were recruited if they were ambulatory, had no history or symptoms of neurological diseases, and had no recent surgeries or injuries affecting walking or turning. Of the 28 controls recruited, one did not complete the study due to fatigue and was excluded. Demographics for included participants are shown in Table 1. All participants provided written informed consent prior to participation, and this study was approved by the Washington University School of Medicine Human Research Protection Office.

<table>
<thead>
<tr>
<th></th>
<th>CN 1-day train</th>
<th>CN 1-day step</th>
<th>PD 1-day train</th>
<th>PD 1-day step</th>
<th>PD 5-day train</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total n</strong></td>
<td>14</td>
<td>13</td>
<td>12</td>
<td>14</td>
<td>3</td>
</tr>
<tr>
<td><strong>Age (yrs)</strong></td>
<td>65.3 ± 11.3</td>
<td>70.1 ± 11.4</td>
<td>69.1 ± 9.7</td>
<td>70.0 ± 11.2</td>
<td>69.0 ± 17.0</td>
</tr>
<tr>
<td><strong>Males/females</strong></td>
<td>9/5</td>
<td>5/8</td>
<td>8/4</td>
<td>8/6</td>
<td>2/1</td>
</tr>
<tr>
<td><strong>Disease duration (yrs)</strong></td>
<td>NA</td>
<td>NA</td>
<td>8.5 ± 4.9</td>
<td>6.6 ± 5.5</td>
<td>8.7 ± 5.7</td>
</tr>
<tr>
<td><strong>UPDRS-III</strong></td>
<td>NA</td>
<td>NA</td>
<td>25.8 ± 10.3</td>
<td>26.9 ± 7.4</td>
<td>27.7 ± 20.6</td>
</tr>
<tr>
<td><strong>H &amp; Y stage</strong></td>
<td>NA</td>
<td>NA</td>
<td>2.1 ± 0.4</td>
<td>2.1 ± 0.7</td>
<td>2.0 ± 0.9</td>
</tr>
</tbody>
</table>

Values are means ± SDs.

2.2. Experimental Design. All participants with and without PD completed testing on one day, and a small subset of participants with PD (n = 3) returned for an additional five consecutive days of training and testing. Training and testing sessions were identical for the one-day and five-day portions of the study. Surgical skin pens were used to ensure consistent placement of reflective markers across days. The Movement Disorders Society Unified Parkinson’s Disease Rating Scale motor subscale (MDS-UPDRS-III) was given to all participants prior to testing to assess movement impairments [17].

2.3. Intervention. Participants with and without PD were randomly assigned (computer-based algorithm) to an intervention condition (rotating treadmill (Train) or stepping in place (Step)). Those in the Train condition were asked to step in place on the perimeter of a rotating disk built into the floor (120 cm diameter, Neuro Kinetics, Inc., Pittsburgh, Pa) as it rotated approximately 45°/sec either clockwise or counterclockwise. The direction of treadmill rotation was selected for each participant to train turns in the worse direction (i.e., the direction requiring greater time to turn in place 180°), where clockwise rotation trained left turns and counterclockwise rotation trained right turns. For the five-day training sessions, right turns were trained for all participants. Participants walked on the rotating treadmill for a total of 15 minutes, divided into 5-minute blocks with interspersed 5-minute rest periods [14]. Those in the Step condition experienced a similar amount of physical activity by stepping in place at a self-selected pace on the stationary ground for a total of 15 minutes, divided into 5-minute blocks with interspersed 5-minute rest periods.

2.4. Data Collection and Analysis. Turning and walking were assessed in two separate blocks, once before (PRE) and once after (POST) the assigned intervention. In each testing block, we examined gait, functional turning while walking, and in-place turns of 180°. Gait was assessed using a 4.8 m GAITRite instrumented walkway (CIR Systems, Havertown, Pa) to determine if the interventions had any effects on gait. The GAITRite calculated gait velocity in six walking trials in each block: three at a participant’s preferred pace and three as fast as possible. Functional turning ability was assessed using the timed-up-and-go (TUG) test where participants rise from a chair, walk three meters, turn 180°, walk three meters back...
2.5. Statistical Analyses. Our primary variables of interest were functional turning ability (TUG), 180° in-place turn duration, and normalized rotation onset of the head, trunk, and pelvis relative to turn onset, to quantify timing of body segment rotations during turn initiation. Secondarily, we looked at number of steps to turn 180°. We also examined velocity during preferred pace and fast as possible gait to determine if the interventions, specifically the rotating treadmill, impacted gait. In the Train groups, we trained the worse turn direction, and the other turn direction was untrained. In order to similarly compare turn performance for the Step groups, we designated the worse turn direction and the better turn direction based on turn durations. For statistical comparisons across groups, the trained direction of the Train group was compared with the worse direction of the Step group, and the untrained direction of the Train group was compared with the better direction of the Step group. We were primarily interested in the trained direction, as turns in this direction were expected to be affected by rotating treadmill training. Separate RM-ANOVAs were run (RM factor: Time; between subjects factors: Condition, Group) for our primary variables of interest for the trained/worse directions. We also ran RM-ANOVAs for step number and gait velocity. Only 3 participants with PD completed the 5-day training
3. Results

3.1. 1-Day Training. The PD and CN groups did not differ significantly in age ($P = 0.503$). The PD Train and Step groups had similar ages, MDS-UPDRS-III scores, and disease durations ($P > 0.05$). Similar ages and MDS-UPDRS-III scores were also seen across CN Train and Step groups ($P > 0.05$). There were no significant differences in any variables at baseline for turns in the trained/worse direction or turns in the untrained/better direction ($P > 0.05$). There were also no significant differences between those with left as the trained/worse turn direction and those with right as the trained/worse direction ($P > 0.05$), so data were combined for analysis.

3.1.1. Gait and Functional Turning. GAITRite data for two participants (1PD, 1CN) were lost due to hard drive failure, but all remaining data for these participants was included in analyses. The mean velocity data are shown for PD and controls before and after the assigned intervention in Figure 1. There were no significant effects of Condition ($f(1,47) = 2.57, P = 0.12$) or Group ($f(1,47) = 1.40, P = 0.24$), nor any significant interaction effects ($P > 0.05$) for preferred pace gait velocity (Figure 1(a)). There was a trend towards an effect of Time ($f(1,47) = 3.79, P = 0.06$), with individuals tending to demonstrate higher preferred pace gait velocity POST intervention. For fast as possible gait velocity (Figure 1(b)), there were no significant effects of Time ($f(1,47) = 0.25, P = 0.62$) or Condition ($f(1,47) = 3.28, P = 0.08$), nor any significant interaction effects ($P > 0.05$). There was a significant effect of Group ($f(1,47) = 4.77, P = 0.034$), with PD walking slower than CN.

For TUG where the turn component was in the trained/worse direction (Figure 2(a)), there were no significant effects of Time ($f(1,47) = 0.25, P = 0.62$) or Condition ($f(1,47) = 3.43, P = 0.070$), nor any significant interactions ($P > 0.05$). There was a significant Group effect ($f(1,49) = 4.77, P = 0.034$), with PD walking slower than CN.
5.25, $P = 0.026$), with PD requiring more time to complete the TUG, turning to the trained/worse direction, compared to controls. Results were similar for the untrained/better direction.

3.1.2. Turn Kinematics. For 180° turn duration in the trained/worse direction (Figure 2(b)), there were no significant effects of Time ($f(1,49) = 0.025, P = 0.62$) or Condition ($f(1,49) = 0.99, P = 0.33$), nor any significant interactions ($P > 0.05$). There was a significant Group effect ($f(1,49) = 15.95, P < 0.001$), with PD turning slower than CN. For the untrained/better direction, results were similar.

For steps to turn 180° in the trained/worse direction (Figure 2(c)), there were no significant effects of Time ($f(1,49) = 2.15, P = 0.15$) or Condition ($f(1,49) = 1.33, P = 0.25$), nor any significant interactions ($P > 0.05$). There was a significant Group effect ($f(1,49) = 13.71, P = 0.001$), with PD requiring more steps to turn. Similar results were seen for the untrained/better direction.

For body segment (head, trunk, pelvis) rotation onsets relative to turn onset for turns in the trained/worse direction, there were no significant effects of Time ($f(3,47) = 1.26, P = 0.30$), Condition ($f(3,47) = 0.60, P = 0.62$), or Group ($f(3,47) = 1.48, P = 0.23$), nor any significant interactions ($P > 0.05$). Figure 3 shows representative sample traces from single individuals in the PD-Train (a), CN-Train (b), PD-Step (c), and CN-Step (d) groups. Mean body segment rotation onsets are shown in Figure 4 for the PD and CN groups for the Train (a, b) and Step (c, d) conditions before and after intervention. In all groups, the sequence of rotation onsets of body segments was head first, followed by trunk, and then pelvis. Comparisons for body segment rotation onsets relative to turn onset were similar for the untrained/better direction.

3.2. 5-Day Training. A small subset of the original group of participants returned for 5 consecutive days of rotating treadmill training. All three individuals who returned for five consecutive days of training were able to tolerate the training program. On average, gait velocity, TUG, turn duration, steps to turn, and body segment rotation onsets relative to turn onset were very similar following a single session of training (Day 1 POST), compared to after five sessions of training (Day 5 POST) in either the trained or untrained direction. Table 2 shows baseline data from Day 1 prior to training, as well as from Day 1 and Day 5 after training for the trained direction.

4. Discussion

Difficulty with turning is common in individuals with PD, and the development of therapeutic approaches that target turn deficits might reduce the occurrence of falls and serious injuries in these individuals. As a result, it is important to evaluate potential treatment strategies in individuals with PD who demonstrate a range of turning ability and might benefit from these treatment options.

Contrary to our initial hypotheses, we did not see improvements in turning in those with PD following one day or five consecutive days of rotating treadmill training. For most turning variables, group effects indicated turning was impaired in those with PD ON medication, compared to controls, as has been previously reported [5–10].
Figure 4: Onsets of Body Segment Rotations. Mean yaw rotation onset times of the head (HTO), trunk (TTO), and pelvis (PTO) relative to the turn onset (i.e., first foot rotation) are expressed as a percentage of the first stride of the turn for PD-Train (a), CN-Train (b), PD-Step (c), and CN-Step (d). Error bars are SDs.

Table 2: Five-day rotating treadmill training results for the trained direction.

<table>
<thead>
<tr>
<th></th>
<th>Day 1 PRE</th>
<th>Day 1 POST</th>
<th>Day 5 POST</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fwd gait velocity (cm/sec)</td>
<td>105.1 ± 24.1</td>
<td>109.8 ± 18.3</td>
<td>110.4 ± 24.6</td>
</tr>
<tr>
<td>Fast gait velocity (cm/sec)</td>
<td>149.3 ± 25.5</td>
<td>149.5 ± 28.0</td>
<td>152.5 ± 26.2</td>
</tr>
<tr>
<td>TUG (sec)</td>
<td>12.0 ± 3.3</td>
<td>12.0 ± 3.5</td>
<td>12.1 ± 2.7</td>
</tr>
<tr>
<td>Turn duration (sec)</td>
<td>2.7 ± 0.8</td>
<td>2.6 ± 0.9</td>
<td>2.5 ± 0.8</td>
</tr>
<tr>
<td>Steps to turn</td>
<td>4.6 ± 0.5</td>
<td>4.6 ± 0.6</td>
<td>4.4 ± 0.5</td>
</tr>
<tr>
<td>NHTO (% Gait Cycle)</td>
<td>−30.7 ± 11.4</td>
<td>−24.3 ± 7.6</td>
<td>−23.5 ± 12.9</td>
</tr>
<tr>
<td>NTTO (% Gait Cycle)</td>
<td>−25.1 ± 9.5</td>
<td>−24.7 ± 8.4</td>
<td>−22.5 ± 13.7</td>
</tr>
<tr>
<td>NPTO (% Gait Cycle)</td>
<td>−24.0 ± 10.7</td>
<td>−22.8 ± 8.8</td>
<td>−20.1 ± 13.1</td>
</tr>
</tbody>
</table>

Values are means ± SDs.

Interestingly, the body segment rotation onset patterns we observed were similar between those with PD and controls. All groups initiated turns with the head, followed by the trunk, pelvis, and foot. Controls display this top-down rotation sequence during turns while walking [8, 18–24], as well as in-place turns [25]. In contrast, those with PD have been reported to display more simultaneous rotation of the head, trunk, and pelvis during turning while walking, including a pronounced delay in initiation of head rotation.
of the Freezing of Gait Questionnaire [30]; however, only included 9 individuals with freezing of gait, as defined by and severity freezing during turns. The present study only of gait frequency, as well as gait velocity, stride length, in one study, robot-assisted gait training improved freezing been used to improve locomotion in PD with freezing of gait. In one study, robot-assisted gait training improved freezing of gait frequency, as well as gait velocity, stride length, coordination, and rhythmicity in those with PD with freezing of gait [26]. It is possible that for individuals with more severe PD or with severe freezing, training on the rotating treadmill may help make the appropriate turning motor patterns more automatic. This might in turn facilitate their treadmill may help make the appropriate turning motor patterns more automatic. This might in turn facilitate their impaired task switching [27–29], reducing the frequency and severity freezing during turns. The present study only included 9 individuals with freezing of gait, as defined by reports of freezing at least once per week on item three of the Freezing of Gait Questionnaire [30]; however, only one individual with freezing was randomly assigned to the rotating treadmill training group, so comparisons between those with and without freezing could not be made. The small overall sample size and the fact that only one person with freezing trained on the rotating treadmill are limitations of the study and warrant careful interpretation of the data, as the study may have been underpowered to detect interaction effects.

Another limitation of the study is that the sessions were of relatively low intensity and were few in number. It may be that more intense rotating treadmill training sessions or increased number of sessions may result in detectable changes, as previous traditional treadmill studies report improvements after completion of 10–28 training sessions of 20–30 minutes each [26, 31]. However, there are also reports of acute effects on gait from just one session of traditional treadmill training [32–34]. Another possibility is that the rotating treadmill may be more useful for people with PD when combined with other cueing strategies. Combining traditional treadmill training with auditory and visual cues improved gait speed, maximum distance walked in six minutes, and score on the Freezing of Gait Questionnaire in one study of people with PD [31].

5. Conclusions

Fifteen minutes of rotating treadmill training alone on one day or for five consecutive days did not affect turn performance in PD. As a result, this type of training is unlikely to serve as an effective short-term rehabilitation strategy for many individuals with PD. However, future studies should determine whether rotating treadmill training may improve turning impairments with longer training paradigms or when combined with other external cues, as well as assess its effects on performance of turns while walking in addition to the in-place turning studied here.

Acknowledgments

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References


Research Article

Accuracy of Fall Prediction in Parkinson Disease:
Six-Month and 12-Month Prospective Analyses

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Introduction. We analyzed the ability of four balance assessments to predict falls in people with Parkinson Disease (PD) prospectively over six and 12 months. Materials and Methods. The BESTest, Mini-BESTest, Functional Gait Assessment (FGA), and Berg Balance Scale (BBS) were administered to 80 participants with idiopathic PD at baseline. Falls were then tracked for 12 months. Ability of each test to predict falls at six and 12 months was assessed using ROC curves and likelihood ratios (LR).

Results. Twenty-seven percent of the sample had fallen at six months, and 32% of the sample had fallen at 12 months. At six months, areas under the ROC curve (AUC) for the tests ranged from 0.8 (FGA) to 0.89 (BESTest) with LR+ of 3.4 (FGA) to 5.8 (BESTest). At 12 months, AUCs ranged from 0.68 (BESTest, BBS) to 0.77 (Mini-BESTest) with LR+ of 1.8 (BESTest) to 2.4 (BBS, FGA).

Discussion. The various balance tests were effective in predicting falls at six months. All tests were relatively ineffective at 12 months.

Conclusion. This pilot study suggests that people with PD should be assessed biannually for fall risk.

1. Introduction

Postural instability is a common cause of falls in people with Parkinson disease (PD) [1]. In contrast to community-dwelling adults over age 65, approximately one-third of whom report falling each year [2], up to 70% of individuals with PD fall once annually, while 50% fall twice or more in a one year period [3, 4]. Falls lead to a myriad of complications [5] that can affect not only physical health, but also the psychological health of the individual. Hip fracture and head trauma are two of the most common physical problems incurred by an individual with PD following a fall [6], while the psychological complications include fear of falling [7, 8] and reduced quality of life [9]. Such fall-related complications are associated with substantial economic costs [10, 11] and indicate an urgent need to identify and protect those individuals at the greatest risk.

Despite the relatively high prevalence of falls in the PD population, accurate and useful methods for predicting an impending future fall, especially during the early stages of the disease, remain elusive. Fall history, a well-known fall risk factor among older adults [12], has a limited utility as a solitary predictive indicator. Although a meta-analysis of prospective studies of falling in PD found that 57% of individuals who had a history of falls in the past year fell during a 3-month surveillance period, so did 21% of individuals with no history of falls [13]. Moreover, fall incidence alone does not help to identify underlying contributors to postural instability specific to PD. People with PD, for example, may demonstrate impairments in areas of movement control such...
as sensory integration, keeping their center of mass within their base of support, coordination of anticipatory postural control tasks [8, 14] as well as medication side effects such as dyskinesias [15]. For this reason, standardized balance assessment tools have been recommended to help determine factors contributing to falls so that therapeutic intervention targets can be identified [16, 17].

The utility of a variety of clinical balance tests has been studied. Balance assessments including the Tinetti [18], Berg Balance Scale (BBS) [19], the Timed Up and Go (TUG) [20], the Functional Gait Assessment (FGA) [21], and recently developed Balance Evaluation Systems Test (BESTest) [22] have been shown to have sensitivity and specificity that exceeds a random guess, but they still demonstrate a clinically relevant proportion of false-positive and false-negative predictions [5, 23]. As noted in a previous meta-analysis [13], new prediction methods are needed. Relatively newly developed balance assessments such as the Functional Gait Assessment (FGA) [21], BESTest [22], and Mini-BESTest, a condensed version of the BESTest [24], have yet to be studied and compared prospectively.

Regardless of the balance assessment utilized, there have been efforts to improve the predictive performance on these balance assessments through diagnosis-specific alterations of cutoff scores or collective interpretation of multiple tests [15, 23, 25, 26]. While these methods may improve accuracy, their overall success may be limited by participant’s fall recall bias. To date, we are unaware of any studies that have examined and compared whether the length of prospective follow-up affects the accuracy of fall prediction in persons with PD.

In order to address these gaps in our understanding of fall prediction in persons with PD, the primary objective of this study was to compare the relative accuracy for fall prediction of four common balance assessments at the six-month and 12-month prospective time points. Relative to our primary objective, we hypothesized that these tests would be useful in predicting falls prospectively at both six and 12 months, with better accuracy over the shortest of the two time periods. Our secondary objective was to compare the predictive accuracy and the validity indices of the four balance assessments. Relative to our secondary objective, we hypothesized that tests such as the FGA, BESTest, and Mini-BESTest that incorporate dynamic tasks would demonstrate improved predictive ability compared to the BBS.

2. Methods

2.1. Participants. We recruited participants using contact information gathered from the Washington University School of Medicine’s Movement Disorders Center database and the Volunteers for Health database. Participants were recruited as part of a larger study [27]. Individuals were included if they had a medical diagnosis of idiopathic PD (Hoehn and Yahr (H&Y) Stages I–IV), were over the age of 40 and were community dwellers. Study candidates were excluded if they had atypical parkinsonism or previous surgical management of PD (pallidotomy or deep brain stimulation). Prior to participation, each participant provided written informed consent in accordance with the policies and procedures of Washington University School of Medicine’s Human Research Protection Office.

2.2. Data Collection. Participants were evaluated at baseline utilizing four balance tests (BBS, FGA, BESTest, and Mini-BESTest) as described below under Balance Assessments. Participants were then followed for 12 months, with fall incidence determined through participant’s report at the six-month and 12-month time points. An individual was considered a faller if he or she reported two or more falls over the surveillance period of interest (0–6 months or 0–12 months). An individual was considered a non faller if he or she reported zero or one fall during the surveillance period.

2.3. Balance Assessments. The BBS is a well-established balance measure consisting of 14 items (sit to stand, transfers, forward reach, etc.) used to determine whether or not one may be at risk for falls [28]. The BBS does not evaluate the balance during walking. It has been shown to be reliable when used to assess balance in people with PD [29]. Each item is scored on a scale of zero (indicating impaired balance) to four (indicating no impairment in balance), with a maximum possible score of 56.

The FGA [21] is a 10-item test of dynamic balance in which all components are evaluated while the participant is walking. Items performed by the participant include forward and backward walking as well as walking while turning the head, changing walking speeds, stepping over obstacles, and walking with a narrow base of support. When used to evaluate individuals with PD, this test had high interrater and test-retest reliability [23]. Each item is scored on a scale of zero (indicating loss of balance, increased time to perform task, significantly altered gait pattern) to three (indicating no impairment of gait or balance and completion of the task in a timely manner), with a maximum possible score of 30.

The BESTest [22] is a measure designed to evaluate balance control via 36 items that are divided into six sections (biomechanical constraints, stability limits and verticality, anticipatory postural adjustments, postural responses, sensory orientation, and stability in gait). Items in the BESTest include selected items from the aforementioned assessments (i.e., BBS and FGA) as well as items such as center of mass alignment, hip and ankle strength, sitting verticality and lateral lean, and multidirectional compensatory stepping correction, among others. The BESTest has high interrater and test-retest reliability in PD [23]. Each item is scored on a scale of zero (indicating poor balance or inability to complete task) to three (no impairment in balance), with a maximum score of 108 points.

A shortened version of the BESTest, the Mini-BESTest, was designed “to improve the structure and measurement qualities” of the BESTest [24]. This shorter version can be administered more quickly than the full BESTest, thereby reducing clinician and patient burden. The Mini-BESTest is a 14-item balance evaluation that concentrates on dynamic balance and its components are derived from four of the six BESTest sections. Items are scored on a scale of zero (poor balance) to two (no impairment of balance), with
a maximum possible score of 32 as two of the 14 items receive two separate scores for different aspects of the tasks [30].

2.4. Procedures. All balance assessments were administered in the Locomotor Control Laboratory at Washington University School of Medicine by a trained physical therapist. Baseline assessments of participants began in July and ended in December of 2009. All participants maintained their normal medication regimen so that they were tested in the “on” phase of their medication, one to two hours after medication intake. Demographic information, fall incidence, and Movement Disorder Society Unified Parkinson Disease Rating Scale Motor Subscale III (MDS-UPDRS-III) scores were obtained prior to administration of balance assessments [31, 32]. Regarding fall incidence, participants were followed prospectively and at six months reported how many times they fell in the period from baseline to six months. At 12 months, participants reported how many times they fell in the period between six and 12 months, with number of falls from 0 to 12 months determined by adding the two reports together. Participants chose from the following answers: (1) none, (2) one time, (3) 2–10 times, (4) weekly, or (5) daily. An individual was classified as a faller if he experienced two or more falls in the period of interest (i.e., from baseline to six months or from baseline to 12 months).

The order of balance assessments was as follows: BBS, FGA, and BESTest. Mini-BESTest scores were derived from the BESTest item scores, as all items on the Mini-BESTest are included in the BESTest. Items that were duplicated among the BBS, FGA, and BESTest were performed only once and scored appropriately for each tool. For example, a sit-to-stand transfer task is in the BBS and BESTest; therefore it was only performed once and scored by the rater according to the criteria listed on each tool.

2.5. Data Analysis. In order to test our primary hypothesis, receiver operating characteristic curves (ROCs) were constructed for each balance assessment at each time point (six and 12 months) and the area under the curve (AUC) was determined for each test at each time point. Using previously established cutoff scores [23], we determined the area under the curve (AUC), positive and negative likelihood ratios, and posttest probabilities for each test at each time point [33–35]. The time point that consistently produced the balance assessments with higher AUC and positive LR as well as lower negative LR would be interpreted as the more accurate time point. Once that determination was made, we examined our secondary objective and hypothesis through the use of empirical tests for noninferiority that were used to make pairwise comparisons of the AUC for each test \( (P < 0.05) \) [36]. Point estimators and interval estimators (95% confidence intervals [95% CI]) were calculated for all AUC and likelihood ratio values.

3. Results

Baseline evaluations were completed on 80 participants. Of the original cohort, 51 participants (41% male) completed the six-month evaluation, and 40 participants (40% male) completed the 12-month evaluation (Table 1). At six months, 14 individuals (27%) were considered fallers, while 13 individuals (32%) were considered fallers at 12 months. Regarding reasons for dropout at six months, 15 participants were unable to be contacted or gave no reason for discontinuing, nine experienced a decline in condition or an unrelated medical condition, one had transportation difficulty, one participant experienced family problems, and three participants had incomplete data sets. At 12 months, in addition to those who had dropped out by six months, four participants were unable to be contacted or gave no reason for discontinuing, three experienced a decline in condition or an unrelated medical condition, and four participants had incomplete data sets. Of the 11 individuals that were lost from six to 12 months, seven (three males) were characterized as fallers at six months.

3.1. Comparison of Six- and 12-Month Results. At six months, AUCs for the tests ranged from 0.8 to 0.89, while at 12 months, AUCs ranged from 0.68 to 0.77. At six months (Table 2(a)), the positive likelihood ratios were greater, the negative likelihood ratios were lower, and the posttest probability values were lower (i.e., better) for all for balance tests than at 12 months (Table 2(b)).

3.2. Individual Test Comparison. Based on the apparent greater accuracy of the six-month prediction, the individual tests were compared at the six-month time point to determine which, if any, was superior to the others in terms of predictive ability. All tests provided greater accuracy than a random guess, with AUC point estimators ranging from 0.89 (BESTest) to 0.80 (FGA) and substantially overlapping 95% CIs (Table 2(a), Figure 1). However, noninferiority tests revealed that the AUC of the BESTest was superior to that of all other tests. Noninferiority tests also showed that the FGA was inferior to all other tests (Table 3).

### Table 1: Demographics.

<table>
<thead>
<tr>
<th></th>
<th>6-Month Group</th>
<th>12-Month Group</th>
</tr>
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<tbody>
<tr>
<td>(n = 51)</td>
<td>(n = 40)</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>67.5 ± 8.8</td>
<td>67.3 ± 9.5</td>
</tr>
<tr>
<td>Years with diagnosis</td>
<td>7.7 ± 3.9</td>
<td>7.2 ± 4.1</td>
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<tr>
<td>UPDRS motor score</td>
<td>39.3 ± 13.3</td>
<td>37.8 ± 13.1</td>
</tr>
<tr>
<td>H&amp;Y stages</td>
<td>2.4 ± 0.6</td>
<td>2.3 ± 0.6</td>
</tr>
<tr>
<td>Fallers (pretest probability of falling)</td>
<td>14/15 (0.275)</td>
<td>13/40 (0.325)</td>
</tr>
</tbody>
</table>

4. Discussion

Previous prospective studies of fall prediction have utilized varied lengths of follow-up period [5, 13]. However, to our knowledge, no previous work has directly compared the accuracy of fall prediction at different follow-up intervals. Our data confirmed our primary hypothesis that a shorter follow-up period (six months) consistently produced more accurate predictions than a longer follow-up period.
and the tests for noninferiority indicated that the BEST est provided the highest level of accuracy and, for the first time, provided prospective documentation of its predictive validity. The BESTest’s likelihood ratio modifications to the pretest probability of being a faller provide a specific example of the clinical relevance of these findings. At six months, the pretest probability of being a faller was 27%. Based on the BESTest positive likelihood ratio, an individual who scored below the cutoffs for the BESTest increased their posttest probability of being a faller to 69%. Based on the BESTest negative likelihood ratio, an individual with a score above the cutoff reduced their posttest probability of being a faller to 3%. These modifications to the pretest probability are similar to those observed in other studies of persons with PD [25].

While our results suggested that the BESTest may be the most accurate as a free-standing test to predict falls in the absence of other balance assessments, the administration time of the BESTest is much longer than the other three tests. Although the results of this study support its use when assessing balance and fall risk in individuals with PD, it is not clear whether the slightly improved accuracy of the BESTest as compared to the Mini-BESTest or BBS at six months is enough to merit utilization of the full BESTest in clinical settings where time constraints must be considered.

We found it surprising that the BESTest, Mini-BESTest, and BBS outperformed the FGA when used prospectively over six months. Based on previous research, we hypothesized that more dynamic balance tests such as the BESTest, Mini-BESTest, and FGA would be more likely to accurately predict falls than a less dynamic balance test like the BBS [23, 38]. However, our findings regarding this hypothesis were mixed, with the FGA having the lowest predictive accuracy in this sample. Regardless of the FGA findings, our (12 months). In addition, at the six-month follow-up time point, all of the balance assessments studied provided clinically useful predictive accuracy. Comparisons of the point estimators and statistical tests of noninferiority suggested that the BESTest produced the greatest predictive accuracy. However, it is unclear whether the differences between the BESTest and the other balance measures are sufficiently large to merit use of one test over another in a clinical setting.

### 4.1. When Should Fall-Related Screening Take Place?

The recently published American Academy of Neurology quality of care measures for Parkinson Disease state that persons with PD should be assessed for fall-related issues “at least annually [37].” While these guidelines provide targets for clinicians, they were developed through a consensus building process that involved expert panel input, public comment, and stakeholder input, and therefore lacked research-based support. Our findings of both six- and 12-month predictive accuracy having AUC values greater than 0.50 (the level of a random guess) support this metric. However, if clinicians wish to most accurately assess the risk of falling of a person with PD, our data suggest that they should consider that biannual follow-up of persons with PD regarding falls.

### 4.2. Is One Test Better Than Another?

The validity indices (AUC, positive and negative likelihood ratios) demonstrated that all of the tests studied provided clinically meaningful predictive ability. Substantial overlap of the interval estimators agreed with previous studies that have documented moderate levels of accuracy for the BBS and the FGA [16, 23]. In this sample, the point estimators of the validity indices and the tests for noninferiority indicated that the BESTest (12 months).
Parkinson's Disease

results generally agreed with recent research advocating for ecologically valid balance assessments [16].

4.3. Limitations and Directions for Future Research. While our results suggest that balance assessments may be justified on a biannual basis, these results should be interpreted with some caution. First, our sample size for this pilot study was small and representative of a cohort with only mild-to-moderate PD severity with a smaller percentage of fallers than seen in previous balance assessment validity studies. In addition, a moderate number of participants were lost to follow-up at the six- and 12-month measurement points. Future research should examine larger samples of participants over a broader spectrum of disease severity and perhaps also consider different motor phenotypes within PD.

Second, we utilized previously established cut-off scores for all of the four balance assessments. These cut-off scores still resulted in false-negative and false-positive predictions. Since cut-off scores based on validity indices will likely change depending on the sample being studied, it is important to emphasize that cutoff scores should be utilized with caution and with the appreciation that any and all cut-off scores are simply guidelines and not definitive boundaries that separate fallers from nonfallers.

Third, our method of collecting fall incidence data, when used over a period of six months or more, can lead to an underreporting of falls [39]. As such, we suggest that future studies follow more rigorous procedures for collecting fall incidence data as outlined by Lamb and colleagues [40]. Future studies may also be designed to assess people with PD off anti-Parkinson medication to determine whether falls are more likely during this state.

5. Conclusion

Prospective identification of fall risk for individuals with PD is extremely important in order to demonstrate a need for therapeutic intervention aimed at reducing fall risk. Our comparison of varied duration of follow-up revealed that a six-month follow-up resulted in greater accuracy of fall prediction than a 12-month follow-up. In terms of accuracy of fall prediction during that six-month follow-up period, all tests provided moderate-to-strong accuracy for fall prediction with clinically meaningful alterations in the probability of being a faller. While the BESTest was slightly more accurate than the other tests, no test eliminated false-positive and false-negative predictions.

5.1. Rehabilitation Implications. None of the tests examined possesses acceptable predictive ability in determining who is at risk for falls within the next 12 months, suggesting the need for regular balance evaluations every six months among people with PD. Such a model of preventative evaluation and treatment twice per year is in keeping with other models of healthcare, such as the well-established system of prophylactic dental care in the United States. Such a model would likely be appropriate and beneficial to apply in the rehabilitative care of individuals with PD.

Acknowledgments

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References


Parkinson's Disease


Research Article

Community Walking in People with Parkinson’s Disease

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People with Parkinson’s disease often have walking difficulty, and this is likely to be exacerbated while walking in places in the community, where people are likely to face greater and more varied challenges. This study aims to understand the facilitators and the barriers to walking in the community perceived by people with Parkinson’s disease. This qualitative study involved 5 focus groups (n = 34) of people with Parkinson’s disease and their partners residing in metropolitan and rural regions in Queensland, Australia. Results found that people with PD reported to use internal personal strategies as facilitators to community walking, but identified primarily external factors, particularly the environmental factors as barriers. The adoption of strategies or the use of facilitators allows people with Parkinson’s disease to cope so that participants often did not report disability.

1. Introduction

Community ambulation is compromised in many people living with Parkinson’s disease (PD), which is thought to affect around 2 percent of the population over the age of 65 [1]. Gait changes are a hallmark of PD, and people with PD frequently walk with reduced speed and step length [2, 3], reduced cadence [2–5], and increased gait variability [6]. People with PD may also experience freezing when walking. Walking difficulties are exacerbated when attention is drawn away from walking by performing additional tasks [5–9]. Challenging environments that demand attention may also compromise the ability to walk in people with this debilitating condition.

Community walking is an important enabler to participation in community activities and a range of societal, work, and leisure roles. It has been defined as locomotion in environments outside the home or the residence [10]. This includes the ability to negotiate public and private venues both indoors and outdoors that incorporate a variety of environmental demands [10, 11], which could prove challenging for people with PD.

The physical, social, and attitudinal environments are generally more varied and less predictable in the community than for the home or the laboratory settings. Walking in the community is generally assumed to be a more complex and high-level skill than walking around the home or in the laboratory. Research in older adults suggests that loss of walking function is a gradual process which results in a restriction of the variety of places they go to and the distance they will venture from home [12]. Impairments can accelerate this, and disabled older adults report fewer encounters with and greater avoidance of physical challenges in the environment [13].

People living with PD have walking challenges in addition to the usual ageing process. The impact of these challenges on community walking is not yet understood. A greater understanding of the perceived factors (both internal and external to the person) that positively and negatively impact on the ability of people with PD to walk in the community is needed. Understanding these factors may allow clinicians to design assessment tools more appropriate for measuring community mobility deficits and provide a basis for the development of interventions to improve community mobility and potentially participation in people with PD. The aim of this qualitative study is to understand what specific facilitators and barriers individuals with PD perceive affect their ability to walk successfully in the community.
Table 1: Demographic information of study participants.

<table>
<thead>
<tr>
<th>Participant number</th>
<th>PD/partner</th>
<th>Age (yrs)</th>
<th>Disease duration (yrs)</th>
<th>Freezing of gait</th>
<th>Falls in past 6 mths</th>
<th>Group type</th>
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</table>

Mean age 67 years, range 41–82 years.
Mean disease duration 10 years, range 4–21 years.

2. Methods

A qualitative study design was used to allow data to be gathered directly from people living with PD. Focus groups were used with the aim of encouraging discussion of a variety of experiences and opinions. Data collection ceased when saturation of the data was achieved.

2.1. Participants. People with PD and partners of people with PD were recruited using advertising in local PD Association publications in Queensland, Australia. Participants were eligible for the study if they or their partner had PD or they cared for someone with PD, were able to sign informed consent, and able to attend a focus group in a community setting.

Five focus groups were conducted \( n = 34 \) including three metropolitan groups of people with PD and their partners \( n = 22 \), one metropolitan group of partners only \( n = 6 \), and one rural group \( n = 7 \). A partner group was included as it was felt that partners of people with PD could have a valuable contribution to make to this data collection but that some may be reluctant to honestly express their feelings regarding the ability of their partner if they were present. The group of partners of people with PD was purposively sampled using a database of people willing to participate in research related to PD. Demographic information about the participants is included in Table 1.

2.2. Procedure. Each focus group included the participants, a facilitator, and a scribe who took field notes regarding
group dynamics, nonverbal communication, and interviewing conditions. Groups lasted one to two hours and were audio recorded. Prior to each focus group, participants were given written information outlining the aim of the research, the procedure for the session, and an outline of the 4 key questions (see Table 2) for discussion. They were given the opportunity to ask any questions, provided written informed consent, and completed a short questionnaire of general demographic information.

Key questions were open ended so responses were in participants’ own words. Probing questions were used when needed, but every effort was made to maintain a natural discussion. At the end of each focus group, the facilitator summarized the main points of the discussion and her perceptions. Participants were asked to confirm the accuracy of this summary.

Approval for this study was obtained from the University of Queensland’s Behavioural and Social Sciences Ethical Review Committee (Application #2008001843).

2.3. Analysis. Immediately after each group, the facilitator reflected on the discussion with the aim of putting aside any immediate thoughts or judgments so the next group was approached with minimal preconceptions.

All audio recordings were professionally transcribed verbatim by professionals external to the study. To confirm accuracy, members of the research team checked each transcription twice against the audio file. Two researchers (RL & SB) then performed thematic content analysis of the transcripts, using a process of repeated readings. Initial reading aimed to capture the context of the entire discussion. Further readings aimed to identify themes that were emerging with notes initially made in the margins identifying noteworthy phrases, lines, and paragraphs of the prose. These were analysed, asking first “what does this mean?” and then “how is this the same/different to other segments?” [14]. At this point the two researchers met to discuss the themes each had identified and classify the distinctive features of these themes. Subsequent readings of the transcripts were performed to ensure the accuracy of the themes and to identify sections of discussion consistent and inconsistent with these themes.

At this point the researchers performed an analysis of the existing literature. This ensured that themes were drawn solely from the data without influence of preconceived ideas interpreted from the literature.

3. Results

Eighteen people with PD with a mean age of 67 years (range 41–82 years) and mean disease duration of 10.3 years (range 4–21 years) participated in the study. Freezing was reported by 44% (8) of participants, and 33% (6) reported falls in the prior 6 months (Table 1). Twenty-two partners who had a mean age of 65.4 (range 39–78) were also included.

Three primary themes emerged from the data: (i) people with PD used internal and external facilitators to make walking in the community easier, (ii) they perceived barriers to be primarily external environmental factors, and (iii) due to their effective use of facilitatory strategies, many people with PD did not report community walking disability. These will be outlined in turn.

3.1. Facilitators. Several factors which contribute to the ability of a person to walk in the community were discussed by the groups. These are termed facilitators and included both internal factors driven by the person and external factors mediated by objects or people outside the person with PD. Internal factors were often strategies people adopted to ensure they could continue to optimally walk in the community. These could be spontaneous strategies, used to cope with a particular situation or symptom as it arose, planned in advance to maximise the chance of success, or may have become a normal behaviour now used without compromise.

3.1.1. Internal Facilitators. A common strategy described was consciously attending to walking speed, step length, and toe clearance. This strategy was reported to be used to respond to challenges to walking when they arose. Most people who reported gait changes described using this strategy as either concentrating on their walking or taking extra care with walking.

“But if you walk slower and lift your feet and concentrate that helps” (PD-27).

While thinking of taking long, rhythmical steps was commonly used to aid walking in the community, it was reported that remembering to use this strategy in a community environment may be less automatic than when at home.

“...you’ve got to try and think and remember to do it, like, think and make sure you do it... try and step it out and lift your feet more” (PD-27).

Planning and preparation played a role to ensure walking in the community was successful. Almost everyone reported timing outings to coincide with times of high medication effectiveness (“ON” times). Being prepared for outings, making a plan and keeping to that plan reduced the chance of running late, feeling rushed, and making errors such as forgetting to take medications, and thereby reduced stress. Errands were also carefully organised to ensure the shortest walking distance.

Community walking facilitated by a novel or enjoyable situation was discussed by a number of people with PD and supported by their partners. Specifically, participants described reduced symptoms and less fatigue while travelling on holiday than they generally experienced at home, a change which could last for a number of weeks after their return.

<table>
<thead>
<tr>
<th>Table 2: Key focus group questions.</th>
</tr>
</thead>
<tbody>
<tr>
<td>(1) Why do you walk outside your home?</td>
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<tr>
<td>(2) How is walking in the community different to walking at home?</td>
</tr>
<tr>
<td>(3) What factors make walking in the community easier?</td>
</tr>
<tr>
<td>(4) What factors make walking in the community difficult?</td>
</tr>
</tbody>
</table>
3.2. Barriers. Barriers is the term used to describe factors reported to exacerbate the negative features of their gait such as slow walking speed and, therefore, negatively influence the experience of walking in the community or cause participants to avoid walking in the community. External environmental factors were more frequently perceived to limit community walking than internal personal factors.

3.2.1. External Barriers. Crowded environments were overwhelmingly disliked by most people in four of the focus groups. The exception was the rural group in which only one participant reported any particular difficulty in crowds. Participants described the need to change direction and avoid obstacles when walking in cluttered (e.g., restaurant) or heavily populated environments (e.g., shopping malls) as a trigger for short shuffling steps and more frequent episodes of freezing. Environments that are busy with people, whose actions are unpredictable, were the most frequently reported barrier.

“I find it more difficult when there are a lot of people around, it means you have to take shorter steps, I like taking long steps, I can balance myself better” (PD-6).

Attention-demanding environments such as unfamiliar environments and road crossing were not reported to contribute to any specific gait difficulty, but many participants reported a need to take extra care while walking in such environments. Road crossing was a particular problem for the rural group, which was conducted in a town that had no signalled and very few designated crossings which were inconveniently located forcing people to cross a busy highway without designated pedestrian crossings.

“Just watching for the traffic—you might not be walking as quick as you should be and you’re watching for the traffic. You have to be pretty careful here” (PD-19).

Characteristics of the walking surface such as uneven footpaths, hills, ramps, flat and inclined moving walkways (travelators), and slippery surfaces were reported as a cause of increased fatigue (hills), fear of falling (uneven and slippery surfaces), and more frequent freezing episodes (ramps and travelators). Even the camber of the footpath, designed to allow water to drain, was commonly reported to make walking more difficult.

“My greatest difficulty when I’m walking is going downhill—can’t handle it, I can go uphill flat out, but I can’t handle going downhill. Even with a trolley my feet get stuck on top of a ramp and I can’t get going” (PD-2).

The rural group specifically emphasised this barrier. In this rural town, footpaths are often absent, where present some of the footpaths are tiled and slippery when wet, and the gutters very deep (20–25 cm high) making access from the road to the footpath difficult.

Inclement weather and reduced or fluctuating lighting were reported to increase difficulty of walking and fear of falling. For some participants these were reasons to avoid community walking all together.

“We avoid going out when it’s raining. It makes him want to walk faster and he gets so fast that he shuffles” (Pa-10).

3.2.2. Speed Demands. Only a small number of participants reported difficulty walking as fast as the environment

Optimising pharmaceutical or surgical interventions was a strong facilitator for some people. Optimal medication regimes were related to a more efficient gait pattern and less fatigue making long-distance walking more feasible. A positive response to surgical intervention had allowed one participant “freedom” from a schedule of medication allowing community outings to occur at times convenient for reasons other than medication effectiveness.

“I love it, I love the independence and I love being able to go to the shops and not be dictated by the medication” (PD-14).

3.1.2. External Facilitators. People with PD and their partners reported that partners supported walking in the community by encouraging their partners to go out, by promoting the importance of continuing to walk as able, by providing physical assistance to overcome barriers in the environment, and by supporting the use of attention or cueing strategies. To be effective, cueing strategies needed to be discrete, mutually agreed on, and practiced to avoid using a counterproductive cue.

Using equipment was discussed by only a few participants but included changing to more appropriate footwear and carrying a wheelchair in the car in case a long walking distance or an ineffective dose of medication was encountered.

Only one aspect of the physical environment was described as a facilitator to community walking, but this was reinforced by many participants. Signalled pedestrian crossings reduce attention required to monitor traffic and decide when to safely cross and were thereby reported to facilitate walking in the community. For a number of participants, this had become a habit, now done without compromise.

“… you never try to run a light, you always wait for the lights and you don’t cross any road if there is not a light” (Pa-11).

Going back three years when (my wife) I’d say had full blown Parkinson’s, she was very, very bad. We took an overseas trip and … (my wife) just kept going and going. By the time we got to France I flaked… She still kept going… Something kept her going because as soon as we got home, boom, she got Parkinson’s again, but while we were away it didn’t seem to affect her” (Pa-15).

Characteristics of the walking surface such as uneven footpaths, hills, ramps, flat and inclined moving walkways (travelators), and slippery surfaces were reported as a cause of increased fatigue (hills), fear of falling (uneven and slippery surfaces), and more frequent freezing episodes (ramps and travelators). Even the camber of the footpath, designed to allow water to drain, was commonly reported to make walking more difficult.

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“We avoid going out when it’s raining. It makes him want to walk faster and he gets so fast that he shuffles” (Pa-10).

demanded. This was often associated with an inability to walk quickly enough to cross the road. One partner reported that his wife felt unable to walk quickly enough for him to achieve exercise benefits so she no longer walked with him for exercise.

“I’m not a quick walker, but it’s quicker than she is and I don’t mind walking slower but she feels she is holding me back … that I’m not getting the exercise” (Pa-33).

Walking distance was described as a barrier only in the rural group. Often these participants related greater walking distance to greater fatigue and avoided walking in the community if long distances were encountered.

“because (my partner) can’t walk or stand for a long time, if we can’t get a park close to somewhere where we want to go we just come home” (Pa-18).

3.2.3. Internal Barriers. Participants reported that their response to PD medication was unpredictable and walking when medication was not effective very difficult. For some participants this meant that trips needed to be postponed, modified, or abandoned due to an ineffective dose.

“I’ll say, right, we’re going down to the shops in half an hour—take medication, might get to the shops, medication doesn’t work—(we have to) come home” (Pa-13).

Even with predictable “ON” and “OFF” times, one participant with PD reported that her need to schedule outings for times that medication would be effective gave her a feeling of being "locked to the medication” (PD-14). This on-off phenomenon was also reported as one source of anxiety.

“What if I get weak, what if I can’t move, what if I’ve got to come home straight away?” (Pa-13).

Anxiety was reported to increase symptoms of PD, resulting in walking difficulty such as shortened step length and increased “shuffling” or dragging a leg. Feeling hurried, examined, stigmatised, or judged was also reported to increase anxiety.

“… walking down here this morning I thought I would be late and I started dragging my foot again” (PD-19).

Some participants reported fatigue due to longer than usual walking distance or time. As a result of fatigue, people reported abandoning some outings before they had intended or experiencing fatigue-related weakness and a resultant increase in walking difficulty.

“You get a fatigue coming in. You will notice it in a weaker muscle group—you might pick it up in the calf where you use it a lot. You might pick it up a hamstring or the front of the leg where it just becomes harder” (PD-17).

3.3. Disease without Disability. The final theme that emerged is that while strategies and facilitators are effective at overcoming barriers to community walking, people living with PD may not appreciate or report any actual problems or difficulty but rather modifications they have made to their walking. This suggests that despite the presence of disease and impairment some people with PD are able to use facilitators and strategies to overcome barriers to community walking so effectively that no difficulty or disability is consciously appreciated, even by their partners.

“I find it is not difficult, you just have to be careful in shopping centres with people left right and centre and you have to keep on the straight and narrow and put your foot in the right place” (PD-2).

“You haven’t had a problem really, have you? You just have to think about it” (Pa-22).

It is clear, however, from the barriers outlined above that some people with PD are aware of difficulties they face walking in the community, and some reported very significant walking disability.

“I don’t go out on my own (anymore), I have a carer who takes me out” (PD-27).

Which indicates that for some people with PD barriers become too significant to overcome using strategies and facilitators, and disability becomes appreciable.

4. Discussion

Walking has been reported to be the first activity of daily living that people with PD identify as having difficulty with, followed closely by a number of activities dependent on walking such as travelling and shopping [15]. To our knowledge this is the first paper published with such a broad focus, where the term community walking is used to capture walking in the community for all reasons including but not exclusive to exercise or physical activity, activities of daily living, and leisure activities. Research in other populations has investigated personal and environmental barriers and facilitators to physical activity [16].

The results demonstrate that people living with PD appreciate that the ability to walk in the community is the result of a successful interaction between themselves, including their disease and associated impairments, and the environment (physical and social) in which they walk. Factors reported to negatively influence this relationship were primarily dimensions of the physical environment which previous authors have labelled density (crowding and clutter in the environment), attention, terrain, ambience (weather and lighting), and temporal demands [10]. Not only do these dimensions present challenges for people with walking impairment, but for people living with PD certain dimensions can exacerbate the negative features of gait. For example, having to stop walking and change direction while walking in crowded environments demands
frequent stopping, starting, and changing direction, thereby, not allowing people to walk at their preferred speed. This dimension may be particularly challenging for people who experience freezing of gait as turning and negotiating obstacles are known triggers for freezing [17]. In addition, monitoring the environment for obstacles while walking may divert attention away from walking, something that laboratory testing has demonstrated people living with PD have particular difficulty with [5–9].

The results also suggest that the interaction is further complicated for people living with PD whose impairments are not static but may fluctuate significantly depending on the effect of their medication, anxiety, and fatigue. In one qualitative study of fatigue in people living with PD, all participants agreed that fatigue had a significant and deleterious effect on their daily activities, social and leisure time [18]. Two types of fatigue are problematic for people with PD, peripheral and central fatigue [19]. Peripheral fatigue was discussed here as fatigue related to increased walking distances, and muscle fatigue related to overuse. Central fatigue is poorly understood and not discussed among any of these groups. Possibly people who suffer from central fatigue are less inclined to commit to outings and were, therefore, inadvertently excluded from this study. This may also be true of depression, which was also not mentioned in any of these groups.

This sample also reported factors that facilitated walking in the community. Primarily these facilitators were internal to the person and involved modifying their behaviour or using strategies to overcome barriers and exploit extrinsic facilitators so they may continue to walk in the community. For many this behaviour modification is so successful that, despite the presence of disease, disability or difficulty is not perceived. This phase between disease and disability may be consistent with the phase of preclinical disability experienced during aging [20]. In older adults, preclinical disability is characterised by reports of no difficulty performing a particular task, but rather reports of modification in the method or frequency of performing that task [20]. People who reported having modified how or how often they walked half a mile or climbed ten steps were found to be 3–4 times more likely to develop disability in the subsequent eighteen months [21].

The current study of walking in community environments adds to a recent qualitative study by Jones et al. [22] which focused on understanding challenges and strategies for everyday walking in people with PD. Jones et al. asked people with PD to reflect on the challenges and strategies they used to address the challenges to walking, both indoors and out. Walking whilst doing something else and walking in different environments were two factors identified to increase the challenge of walking. Specifically, participants strongly disliked walking in busy and crowded environments. Participants in that study also described two attention-based strategies that their sample described using to improve their walking: these were consciously monitoring their walking performance and directing attention to correct their gait pattern.

Although some findings are similar, this study differed to the Jones et al. study in a number of ways. The focus of this study was specifically community walking, and as such the community-specific barriers and facilitators are presented in much greater detail, particularly the environmental barriers. Data was collected using focus groups, rather than in-depth interviews which may have yielded greater reflection on the topic, particularly by those participants who reported modifications to their walking without appreciable difficulty or disability. The participants of partners in the groups may have also contributed to this reflection. Finally this study was a stand-alone qualitative study with broad inclusion criteria. As such, people with unstable and unpredictable “on” and “off” phenomenon, dyskinesias, and significant walking disability were included. Participants were on average 10 years after diagnosis with 44% reporting freezing and one-third falling in the past 6 months. The findings reflect the attitudes of those who currently access the community, and as such the results may not be generalisable to all people with PD in all stages of the disease process.

Assessment of community walking has previously been inferred by assessing an individual’s gait speed and endurance in an uncluttered environment [11]. The findings of this study suggest that assessment tasks that incorporate potentially challenging environmental dimensions such as density, attention demands, terrain characteristics, or ambience could provide more specific information about the particular demands for an individual and how they modify their gait to cope. Self-report tools such as the ambulatory self-confidence questionnaire (ASCQ) [23] and the environmental analysis of mobility questionnaire (EAMQ) [24] do address some of these issues; however, their accuracy and utility in the PD population is yet to be examined. Furthermore, self-report and actual ability may not always correlate. Mobility test batteries have been developed to reflect some demands of community mobility [25] but may not include situations that people with PD find challenging or can include tasks that may be inappropriate.

Wearable sensors such as pedometers, gyroscopes, and accelerometers have been used to demonstrate changes in activity in people with PD [26–28]. These and other technologies have the potential to be developed to measure people with PD walking in challenging environments and to possibly monitor their performance when walking in the community.

Therapeutic intervention to manage, prevent, or delay community walking disability is equally complex. The results of this study suggest that for people with PD the primary barriers are external environmental factors. Although advocacy for modifying or planning environments that would be more easily negotiated by people with PD may go some way to improve the ability of people with PD to walk in the community; environmental modification may be less feasible in the community than in a home environment. As such, a more individualised approach to intervention may focus on enhancing likely personal facilitators. This could include educating about barriers, facilitators and sharing successful strategies used by others, in addition to promoting the use of internal strategies such as attention to walking speed and step length, and planning for outings. Evidence for the use of interventions to improve community mobility in people with PD is needed.
5. Conclusion

This study reports the perspectives of people with PD and highlights the effectiveness of personal strategies and facilitators to enable people with PD to continue walking in the community. People with PD often find environmental challenges barriers to walking in the community but do not tend to report disability; rather, they modify their behaviour. Current clinical methods of assessing community mobility which focus on gait speed or distance, thus, may not provide sufficient information to accurately reflect a person’s ability to walk in the community. Furthermore, a deeper understanding of preclinical walking disability, in people with PD, may allow therapists to provide more timely assessment and therapy, thereby, delaying the onset of disability rather than attempting to reverse disability after it presents.

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References


Progressive Resistance Exercise and Parkinson’s Disease: A Review of Potential Mechanisms

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This paper reviews the therapeutically beneficial effects of progressive resistance exercise (PRE) on Parkinson’s disease (PD). First, this paper discusses the rationale for PRE in PD. Within the first section, the review discusses the central mechanisms that underlie bradykinesia and muscle weakness, highlights findings related to the central changes that accompany PRE in healthy individuals, and extends these findings to individuals with PD. It then illustrates the hypothesized positive effects of PRE on nigro-striatal-thalamo-cortical activation and connectivity. Second, it reviews recent findings of the use of PRE in individuals with PD. Finally, knowledge gaps of using PRE on individuals with PD are discussed along with suggestions for future research.

1. Introduction

The standard treatment for Parkinson’s disease (PD) is pharmacologic treatment with levodopa, a precursor to dopamine. However, continued treatment with levodopa is associated with motor side effects such as dyskinesias and motor fluctuations. Until an oral formulation of levodopa without the accompanying motor side effects is formulated, surgical options offer some relief. Typically, surgery is reserved for when the disease and the side effects due to medication are severely disabling. Currently, the most common surgical option is high-frequency deep brain stimulation of the subthalamic nucleus or the internal globus pallidus [1–4]. Despite the substantial clinical benefits of surgery, surgical treatment is not without complications, which occur in up to 50% of individuals with PD who undergo deep brain stimulation [2, 5]. These complications include device/surgery-related infections, cognitive decline, depression, speech difficulties, gait disorders, and postural instability [2, 5]. Therefore, there is merit to exploring treatment options that may be used as adjuncts to pharmacologic and surgical treatments prescribed in PD. One such option is exercise, specifically progressive resistance exercise (PRE).

This review paper will first discuss the rationale for PRE in PD specifically related to bradykinesia and muscle weakness. Then it will review recent findings related to the use of PRE in individuals with PD. Finally, it will identify gaps in knowledge of using PRE in individuals with PD and makes suggestions for future research.

2. Rationale for Progressive Resistance Exercise

This section will set up the basis for PRE as a therapeutic intervention in PD. To do so, we will outline the underlying mechanisms for the motor symptoms that can be treated...
with PRE. We will focus primarily on the central mechanisms that underlie bradykinesia and muscle weakness in PD. Then we will discuss the central changes that accompany PRE and hypothesize how these changes might modify the central mechanisms that underlie bradykinesia and muscle weakness. We will conclude this section with our rationale for the use of PRE in individuals with PD.

2.1. Bradykinesia and Muscle Weakness. Bradykinesia refers to the slowness of a performed movement [6]. Bradykinesia is a primary motor symptom of PD, which is also considered the most functionally debilitating symptom and is a consistent feature of the disease [7]. Muscle weakness, which is a reduction in the amount of force generated by muscle contraction, is often observed in individuals with PD. In fact, several studies have demonstrated that individuals with PD exhibit muscle weakness [8–15]. We have shown that this weakness is exaggerated in the extensor muscles, specifically extensors of the elbow [8, 16]. Additionally, muscle weakness has also been observed across various muscle groups in the trunk [11], upper limbs [14], and lower limbs [9, 10, 13, 14].

In PD, the idea that bradykinesia and weakness are related can be derived from the fact that bradykinesia and muscle weakness might share common underlying mechanisms. Central to the pathophysiology of PD is the known nigral dopaminergic deficit that results in an increase in tonic inhibition of the thalamus and reduction in the excitatory drive to the motor cortex [17]. This, in turn, may result in disruption of the cortical activation of the muscle [18–21] and may manifest as bradykinesia and muscle weakness. Further, muscle power, the product of movement velocity and muscle torque, is reduced in individuals with PD [13]. Also, torque production during isokinetic muscle strength testing in individuals with PD has been shown to vary with movement velocity. Nogaki et al. found that in individuals with PD, no difference was observed in peak torque between the more and the less affected side for slower movements, while for faster movements, the more affected side was significantly weaker than the less affected side [22]. Therefore, reduction in muscle power is indicative of deficits in either strength, movement speed, or both and strengthens the proposed relationship between bradykinesia and muscle weakness.

Given that the muscle is the final target of cortical output during movement and force production, analyzing the electromyographic (EMG) activation patterns can provide insight into hypothesized impairments that underlie bradykinesia and muscle weakness. We have shown that in individuals with PD, EMG activation patterns during ballistic movements and isometric actions are abnormal and reflect impaired activation of the muscle. Muscle activation patterns during ballistic movement in individuals with PD are abnormal in four significant ways. First, muscle activation patterns show increased variability when compared to age- and sex-matched healthy individuals [23, 24]. Second, in contrast to healthy individuals, the first agonist burst duration does not systematically increase with movement distance [23]. Third, the magnitude of the first agonist burst, early in the disease, is similar to that observed in healthy individuals; however, as the diseases progresses, the magnitude of the first agonist burst is modulated less with increasing movement distance [23]. Fourth, multiple agonist bursting is observed during the acceleration phase of movement, and the number of agonist bursts increases with increasing the movement distance [23, 24]. During isometric actions, individuals with PD manifest deficits throughout the task. At the very beginning of the task, they exhibit decreased rate of torque generation and decreased initial phasic agonist EMG activation, which results in prolonged torque rise times and delayed peak torque [16]. In the middle of the task, during steady-state contraction at 25%, 50%, and 75% of maximal voluntary contraction (MVC), the dominant frequency in the EMG spectrogram in individuals with PD stays fairly constant at $\sim 10$ Hz [25]. In healthy individuals, however, the dominant frequency is higher and increases with the increase in isometric torque generation, that is, the dominant frequency shifts from $\sim 18$ to 25 Hz when isometric torque generation increases from 25% to 75% of MVC [25]. At the end of the task, the rate of release of muscle contraction is also prolonged, and torque fall times are increased in individuals with PD [26].

The abnormal EMG activation patterns discussed above can be partly explained in terms of an impairment in the corticospinal activation of the muscle, specifically, impairments in variability, intensity, and frequency of the corticospinal activation of the muscle. Increased variability in the corticospinal activation of the muscle could lead to variability in motor unit recruitment and result in increased EMG variability [27]. This increased variability in motor unit recruitment could impair coordinated relaxation of actively contracting motor units, contributing to prolonged deceleration phases during movement and prolonged relaxation times during isometric torque generation. Reduction in the intensity of the corticospinal activation of the muscle [28] may result in impaired motor unit recruitment and could contribute both to bradykinesia and muscle weakness. For instance, impaired motor unit recruitment during movement could result in reduced angular impulse during the acceleration phase of a movement and contribute to bradykinesia, and impaired motor unit recruitment during isometric torque generation could result in reduced peak torque and contribute to muscle weakness.

Alterations in the frequency of the corticospinal activation of the muscle could also explain some of the abnormal EMG patterns observed in individuals with PD. In healthy subjects the corticospinal activation to the muscle is characterized by three primary frequencies, that is, 10 Hz, 20 Hz, and 40 Hz [29, 30]. The magnetoencephalographic (MEG) power spectrum is dominated by $\sim 20$ Hz oscillations during weak contractions and $\sim 40$ Hz oscillation during strong contractions [29]. Similarly, the mean power in the EMG power spectrum increases from 10 Hz to 25 Hz with increase in percent MVC from 10% to 80% of MVC [31]. In untreated (de novo) individuals with PD relative to age- and sex-matched healthy individuals, resting state cortical activity in the 8–10 Hz band is increased, while activity in the 30–48 Hz band is reduced [32]. Further, in individuals with PD, the EMG power spectrum is dominated by power
in the low-frequency band (\(\sim 10–15\) Hz) [25, 26, 29], and the MEG-EMG coherence is strong in this low-frequency band with the MEG signal leading the EMG signal by \(\sim 15–38\) ms [29]. Thus, one could hypothesize that if the cortical signal to the muscle is dominated by low-frequency oscillations, then this limits the ability to recruit larger, high-frequency motor units, which are required to rapidly generate torque during ballistic movements and generate maximal torque during isometric torque generation. The evidence reviewed in this and the previous two paragraphs suggests that EMG patterns are abnormal in individuals with PD, and one likely explanation for these observed EMG abnormalities is deficits in the variability, intensity, and frequency of the corticospinal activation of the muscle.

Another factor that could contribute to muscle weakness in individuals with PD is reduced muscle mass. Evidence that muscle mass is reduced in PD is provided by Petroni and colleagues [33]. They reported that midarm muscle circumference was below the 10th percentile in 23% of individuals with advanced PD between 65 and 75 years of age [33]. On the other hand, evidence that this is not the case is provided by Markus and colleagues [34]. They found that even though body mass index and skin fold thickness, relative to age- and sex-matched healthy individuals, were reduced in individuals with PD, midarm circumference was not different from healthy individuals. Thus, the authors concluded that increase in body mass index was due to a loss of fat and not due to a loss of muscle mass.

It is important to note that not only does PD cause weakness, but it is highly likely that muscle weakness and functional limitations such as postural instability and gait disturbances lead to reduced physical inactivity as a compensatory mechanism to minimize the likelihood of falls [35]. Therefore, physical inactivity can contribute to muscle weakness and lead to a vicious cycle between muscle weakness and physical inactivity [36].

Even though we cannot discount muscle mass and changes in muscle properties as likely contributors to muscle weakness, it is our stand that the primary contributors to muscle weakness are central in origin and are related to dopaminergic deficits. This is evidenced by the fact that both anti-Parkinsonian medication and deep brain stimulation result in significant improvement in movement speed [24, 37] and significant gains in muscle strength in relatively short amounts of time (not longer than 90 minutes) [16, 38, 39]. Given that the minimum amount of time required to notice appreciable hypertrophy is at least 20 days [40], it is highly unlikely that the immediate strength gains brought about by anti-Parkinsonian medication or deep brain stimulation are caused by gains in muscle mass.

The question that remains is the extent to which bradykinesia and weakness can be compensated for. We have shown that levodopa and/or deep brain stimulation of the subthalamic nucleus improves bradykinesia and/or muscle strength [24, 38, 39]; however, bradykinesia is not normalized [24, 37]. Moreover, surgical interventions carry significant risks, while medication becomes progressively less effective, and the side effects of medication get progressively worse over time. Therefore, until a cure for PD can be identified, there is a compelling need to develop interventions that improve the signs and symptoms of the disease and slow down the rate at which the signs and symptoms of the disease worsen. One such intervention is PRE, which may be a beneficial and cost effective adjunct treatment in managing PD. As such, if PRE is to be beneficial for individuals with PD, it should bring about central changes that potentially alter nigro-striatal-thalamo-cortical activation and connectivity. Since this has not yet been studied in individuals with PD, we will discuss the central changes that accompany PRE in healthy young and elderly individuals and extend these findings to individuals with PD.

2.2. Central Changes That Accompany Progressive Resistance Exercise. The evidence for the central changes that accompany PRE is threefold [41]. First, gains in muscular strength appear before noticeable muscle hypertrophy [41, 42]. After commencing a PRE protocol, strength gains appear as early as 5 days [43], but muscle hypertrophy appears no earlier than 20 days [40]. Therefore, the initial gains in muscle strength cannot be explained by measurable muscle hypertrophy. Instead, a likely explanation for the observed strength gains is the central changes that accompany PRE. Second, cross-education (i.e., improved performance in the untrained limb) is often observed [41]. Munn and colleagues, in their meta-analysis that included 13 studies, concluded that unilateral PRE brings about a 7% increase in strength in the untrained contralateral limb [44]. Given that this cross-education effect is accompanied by increase in muscle surface EMG, but is not accompanied by gains in muscle size, it is likely to be brought about by the central changes that accompany PRE [42, 45]. Third, improvements in performance following PRE are both specific and generalized. The argument for specificity arises from the fact that short-term dynamic strength training results in significantly greater gains in dynamic strength, while isometric strength gains are marginal [46]. While the argument for generalizability arises from the fact that short-term strength training that focuses on increasing isometric strength also improves movement coordination during an untrained task [47]. Thus, both specific and generalizable motor learning effects of PRE provide a third line of evidence for the central changes that accompany PRE.

Further evidence for the central changes that accompany PRE comes from studies employing transcranial magnetic stimulation (TMS), electroencephalography (EEG), functional magnetic resonance imaging (fMRI), and muscle EMG activation patterns. Using TMS, Carroll and colleagues found that for the same level of torque, the amplitude of the motor evoked potential was significantly reduced following a 4-week PRE program [48]. They concluded that resistance training altered the functional properties of the spinal cord circuitry, and fewer motor neurons were recruited for similar levels of pretraining torque. Using EEG, Falvo and colleagues found that the movement-related cortical potentials were significantly attenuated following a 3-week PRE program [49]. They concluded that PRE reduced the neural effort required to move similar levels of pretraining loads. Using fMRI, Liu-Ambrose and colleagues found that in elderly
women, following PRE, percent signal change significantly increased in the left anterior insula and the anterior portion of the left middle temporal gyrus [50]. They concluded that PRE could facilitate functional plasticity in the cortex. Using EMG, several studies have shown that muscle activation patterns change after PRE [42, 49, 51–54]. These muscle activation changes following PRE include an increase in the EMG activation [40, 53, 54], possibly due to increased motor unit recruitment [55–57], increased firing rate [57, 58], and improved synchronization [52, 59]; a reduction in the EMG activation to torque ratio, that is, reduction in EMG activation relative to the amount of torque produced [60]; a reduction in the variability associated with the timing, amplitude, and duration of muscle activity [47]; a reduced agonist-antagonist coactivation [61]. In addition, central changes accompanying PRE have been inferred using the H-reflex to examine motor neuron reflex excitability. Holtermann and colleagues found that the amplitude of the H-reflex increased following a 3-week PRE program in healthy individuals [62]. Further, they found that the H-reflex increase in amplitude was associated with an increased rate of force development. This could provide a neurophysiological basis for PRE improving bradykinesia in PD. The exact mechanisms underlying the observed increase of the H-reflex amplitude are not yet known however. The authors suggested that one possibility is that the reflex excitability of the motor neuron pool may be enhanced following PRE.

It should be noted that some of the neural changes discussed in the preceding paragraphs may be affected by factors such as age, sex, the muscle group trained, and their interactions [63, 64]. For instance, following PRE, upper and lower body strength gains are greater in young than in healthy elderly individuals [63]. Also, upper body strength gains are greater in men than in women; however, lower body strength gains are not different between men and women [63].

In summary, PRE can bring about changes throughout the neural axis. Currently, none of the central changes that accompany PRE discussed previously in this section have been researched in individuals with PD. Even though improvements in neuromuscular function have been observed in individuals with PD, from a physiological perspective, further research is required to elucidate the central changes that accompany PRE that could mitigate the motor and nonmotor symptoms observed in PD.

Brain regions where PRE could potentially alter activity include the motor cortex, the posterior putamen, the internal globus pallidus (Gpi), and the subthalamic nucleus (STN) (Figure 1). Fisher and colleagues recently demonstrated motor corticospinal changes following body-weight-supported treadmill training in individuals with PD [65]. They showed that cortical hyperexcitability, which is consistently observed in individuals with PD, is reversed following body-weight-supported treadmill training [65]. Petzinger and colleagues have also shown an increase in the stimulus-evoked dopamine release within the dorsolateral striatum following intensive treadmill training in 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine- (MPTP-) lesioned mice [66]. Because the dorsolateral striatum is engaged to a high degree during fore- and hind-limb movements during treadmill exercise, they attributed the observed striatal plasticity to use-dependent synaptic plasticity.

Similarly, there may also be use-dependent synaptic plasticity in the putamen, the Gpi, and the STN following PRE. Our lab has conducted a series of studies in which we have shown that nuclei within the basal ganglia scale with the performance of different force producing tasks in both healthy individuals and individuals with PD. Specifically, we have shown that both the globus pallidus and the STN increase percent signal change when generating progressively larger forces in healthy individuals [67]. We have also shown that individuals with PD have a reduced percent signal change in all nuclei of the basal ganglia during an isometric force production task, even early in the disease process when individuals have not yet started their anti-Parkinsonian medication [68]. In addition, blood-oxygen-level-dependent activity in the nuclei of the basal ganglia was correlated to the motor section of the Unified Parkinson's Disease Rating Scale (UPDRS) [69]. The symptom with the highest correlation with basal ganglia activity was bradykinesia. Thus, if PREs were shown to alter the motor section of the UPDRS and bradykinesia, then it is possible that the neuronal activity of the basal ganglia would also be altered by PRE.

Figure 1 illustrates the hypothesized positive effects PRE might have in individuals with PD by possibly altering activity and connectivity in cortical and subcortical regions. It should be noted that these effects of PRE on activity and connectivity in cortical and subcortical regions are purely speculative, as there are no in vivo studies that have examined this relationship. As can be clearly seen from the figure however, the basal ganglia are strategically positioned to influence cortical output and modulate control of movement and force. As such, we suggest that one potential reason for why PRE could be therapeutically beneficial for individuals with PD is that it may alter activity in the cortex and the basal ganglia, and connectivity between and within these regions. Advances in experimental techniques, such as TMS, EEG, fMRI, positron emission tomography (PET), diffusion tensor imaging (DTI), and EMG and reflex analyses, afford the possibility of testing hypotheses related to the effect of PRE on neural activity, neural connectivity, and structural integrity in vivo, in humans. Figure 1 shows the outcomes and tools that can be used to empirically determine the effects of PRE in specific brain regions. To elaborate, changes in cortical excitability can be measured using TMS, while changes in cortical activity and intracortical connectivity can be measured using EEG. Functional MRI can be used to identify blood-oxygenation-level-dependant signal changes in cortical and subcortical regions following PRE. PET can be used to investigate the effect of PRE on dopamine synthesis, transport, and usage. Diffusion tensor imaging can help elucidate hypotheses related to the changes in structure in cortical and subcortical regions, namely, the substantia nigra, the STN, and the thalamus. Reflex and EMG analyses can be used to identify reflex changes, such as change in H-reflex amplitude, and changes in EMG activation patterns to infer central changes following PRE. Prior to embarking on empirical verification of some of the ideas presented in
In conclusion, the rationale for the use of PRE in PD is fourfold. First, as discussed above, individuals with PD exhibit muscle weakness. PRE can significantly increase the torque- and power-generating capacity of the muscle, thus directly affecting muscle weakness. Even though other forms of exercise such as aerobic exercise provide substantial health benefits, they do not improve muscle strength by design. Improvements in muscle strength and power have significant impact on bradykinesia [71] and could also facilitate independence in the community, improve functional mobility, and may reduce the risk of falls [72]. Second, exercise interventions in general have been shown to enhance cortical activity, possibly beneficially altering variability, intensity, and frequency components of the corticospinal activation of the muscle [47–49, 73]. This could significantly impact bradykinesia in individuals with PD [65]. Third, exercise may slow down the rate at which the UPDRS scores increase. The UPDRS is the clinical gold standard for assessing the severity and progression of symptoms in PD and for evaluating novel therapies, with higher scores reflecting more severe disease. Reuter and colleagues have shown that a 14-week, intense, multimodal exercise training program can bring about ∼12 point reduction in the motor UPDRS scores [74]. Additionally, physical activity has been associated with increasing the survival rate of individuals with PD [75].

Finally, there may well be additional benefits for the non-motor symptoms of PD, such as executive function, mood, and quality of life.

3. Progressive Resistance Exercise in PD

Rehabilitation research studies in individuals with PD demonstrate that PRE can have a positive effect on muscle size [76], muscle strength [15, 71, 76–78], muscular endurance [77, 79], and neuromuscular function [71, 76–79]. To date, only one study [76] has quantified changes in muscle size in individuals with PD. Dibble and colleagues observed a 6% increase in muscle volume, measured using volumetric magnetic resonance imaging, after a 12-week eccentric PRE program [76]. Eccentric PRE training involves the use of eccentric muscle activity, that is, the active lengthening of muscles when an external load is imposed; consequently, work is done on the muscle [80]. The rationale used by Dibble and colleagues for using eccentric PRE is that for the same amount of work (i.e., force × distance), high levels of force are generated with minimal oxygen consumption [81].

With regard to muscle strength, several studies have demonstrated significant gains in muscle strength following PRE in PD [15, 71, 76–78]. For instance, improvements in strength were observed by Hirsch and colleagues in a randomized controlled trial that compared a 10-week balance training protocol to a 10-week balance training plus PRE protocol [78]. At the end of 10 weeks, they observed significant improvements in strength in knee extension, knee
flexion, and ankle plantar flexion in the balance plus PRE group. When the strength measures were combined across the knee and ankle, they observed a 52% increase in strength from before to after treatment in the balance plus PRE group. In another randomized placebo-controlled trial, Hass and colleagues demonstrated significant gains in strength and endurance in upper body muscles, following a 12-week PRE program supplemented with creatine monohydrate [77]. Improvement in endurance was observed by Scandalis and colleagues following an 8-week PRE program that was geared toward the lower body [79]. They found improvements in the total number of abdominal crunches that could be performed at one time. They also observed improvements in lower limb performance, which was quantified as a product of repetitions and weight. Next, we will review the evidence that supports positive changes in neuromuscular function that accompany strength gains in individuals with PD following PRE.

From a rehabilitation perspective, it is critical that strength gains bring about corresponding improvements in neuromuscular function, such as gait, stair climbing, timed up and go, and postural stability. To this end, recent studies have shown significant improvement in neuromuscular function following PRE interventions in PD. First, improvements in gait have been reported. Three-dimensional gait analyses following an 8-week PRE program demonstrated that individuals with PD increased their gait velocity, stride length, and head angle relative to the floor during midstride [79]. Similar findings of increased gait velocity were also reported by Dibble and colleagues following a 12-week eccentric PRE intervention [71, 76]. The functional gait outcomes included the six-minute walk, ten-meter walk, timed up and go, and stair ascent and descent times. They observed that individuals with PD significantly improved gait velocity and increased the distance walked in six-minutes, reduced the time taken to walk ten meters, reduced the time taken to complete the timed up and go, and reduced stair descent times. Their findings led them to conclude that progressive resistance eccentric exercise could significantly impact bradykinesia. Second, improvement in postural stability has been reported. Hirsch and colleagues showed that individuals with PD demonstrated an improved ability to maintain balance during destabilizing conditions following a 10-week balance plus PRE intervention [78]. Third, improvement in patient-perceived quality of life has been reported. Even though quality of life is not a direct measure of neuromuscular function, it is reasonable to assume that improved neuromuscular function might contribute to improved quality of life. Dibble and colleagues found that eccentric PRE significantly improved patient-perceived quality of life as measured by the Parkinson’s disease questionnaire (PDQ-39) [71].

In summary, PRE can significantly improve muscle size, muscle strength, muscle endurance, and neuromuscular function and can significantly impact areas often reported to be problematic in individuals with PD, such as bradykinesia, postural instability, and patient-perceived quality of life.

4. Limitations of Current Research and Recommendations for Future Research

The few studies that have examined the effect of PRE in PD are no doubt vital to our continued understanding of the effect of PRE and the pursuit of adjunct treatments for PD; however, they are not without limitations. First, it is not clear how anti-Parkinsonian medications interact with PRE. To ascertain the unique contribution of PRE on strength and functional outcomes in PD, it is essential to examine individuals while off anti-Parkinsonian medications. Also, if changes to the underlying disease process are to be evaluated, this is best done while off medication. Among the studies reviewed, all except for Scandalis and colleagues [79] tested individuals with PD while on medication. Thus, more research is required to investigate the unique effect of PRE on outcomes of strength, neuromuscular function, and the underlying disease process.

Second, the motor UPDRS, which is the clinical gold standard of assessing severity of motor deficits in PD, has rarely been used as an outcome measure while evaluating the effects of PRE. In order to convince neurologists who manage individuals with PD to prescribe exercise as an adjunct therapy, it is vital to demonstrate clinically important change on the motor UPDRS as a result of PRE. Minimal clinically important change on the motor UPDRS is based on the effect of anti-Parkinsonian medication and is defined as a 5-point reduction on the motor UPDRS score [82]. The scores on the motor UPDRS range from 0 to 108, and higher scores indicate more severe motor symptoms. Thus, if exercise can bring about at least a 5-point reduction in the motor UPDRS, one can make a compelling case to include PRE as an adjunct to the standard management of PD. Future research should include the motor UPDRS as an outcome measure while evaluating the effects of PRE. To date, Dibble et al. [71] and Hass et al. [77] have used the motor UPDRS as an outcome measure; however, they both failed to show any clinically relevant change following PRE. This could have been due to the fact that these studies tested individuals with PD while on medication and/or due to the short duration of the PRE intervention.

Third, long-term effects of PRE are yet to be determined. All of the studies conducted to date evaluate the effect of PRE over 8 to 24 weeks. Given that PD is a progressive neurodegenerative disorder and is further affected by the process of aging, which is accompanied by decline in strength and neuromuscular function [83], it is vital that the long-term effects of PRE are thoroughly understood. For instance, continued benefit of PRE over the long-term could reduce the rate at which the disease progresses. This is significant, especially because recent exciting epidemiological research has concluded that moderate to vigorous levels of physical activity in mid- or later life may be associated with a 40% reduction in the future risk of being diagnosed with PD [84]. Additionally, PRE over the long term could reduce the rate at which dosage of medication is increased and possibly delay the onset of dyskinesias, as well as surgical interventions. Thus, it is essential that future studies evaluate the effects of PRE over the long term in PD.
Fourth, even though it is accepted that cognitive impairment is frequently observed in PD [85–90], the effect of PRE on cognitive function in PD is not well researched. The rationale for PRE as a therapeutic intervention for cognitive dysfunction is threefold. First, PRE has been found to improve cognitive function in healthy subjects between the age of 65 and 75. Cassilhas et al. demonstrated improved performance on measures of working memory and attention for those assigned to 24 weeks of PRE [91]. More recently, Liu-Ambrose and colleagues demonstrated beneficial cognitive effects of 52 weeks of PRE in community dwelling elderly women [92]. They showed improvements in attention and conflict resolution. Additionally, in a subsequent study with the same sample, they demonstrated changes in percent signal change in brain areas that correspond to conflict resolution [50]. Second, even though aerobic training provides cognitive benefits, a combination of aerobic and PRE has been evidenced to render the greatest cognitive benefits [93]. Recently, two studies have evaluated the combined effect of PRE and aerobic exercise on executive function in PD [94, 95]. Both studies concluded that PRE combined with aerobic exercise improved executive function. Third, there is a strong biological basis for the cognitive benefits gained from PRE. These include the reduction in serum levels of homocysteine [96] and the increase in serum levels of insulin-like growth factor I [97], following PRE, which are both known to be associated with cognitive function [98, 99]. Thus, there is evidence in the literature to support the beneficial effects of PRE on cognitive function, and future research should address this in individuals with PD.

Fifth, the diverse experimental designs employed in the studies reviewed may be less than ideal. Given the realities of conducting research with a patient population, the studies reviewed provide an excellent basis for large-scale, long-term prospective randomized clinical trials. However, the small sample sizes used (between 6 and 14 per group, with a total sample size not exceeding 20), the lack of rater blinding (only Hass et al.’s was a randomized, double-blinded, placebo-controlled trial [77]; while Hirsch et al.’s was a randomized control trial, the raters were unblinded [78]), and not employing the intent-to-treat principle in statistical analysis lead to biases that could question the validity of some of the conclusions. Thus, future studies should be blinded, randomized clinical trials, which will provide the most robust experimental design to address the gaps in the literature by assessing the short- and long-term effects of PRE in individuals with PD.

Sixth, the optimal PRE prescription for individuals with PD is yet to be established. There are two aspects of treatment optimization. The first aspect is the optimization of PRE parameters, such as the frequency, intensity, duration, and mode of exercise (i.e., strength and power training). The second aspect is the optimization of PRE with regards to the various clinical subtypes of PD. Within the general diagnosis of PD, distinct clinical subtypes have been identified based in part on the age of onset, the predominant motor sign (e.g., tremor dominant, non-tremor-dominant akinetic rigid etc.), and the clinical course of the disease [100]. There is evidence in the literature that suggests that these different PD subtypes may respond differently to interventions and may progress at different rates [101–103]. For example, individuals who begin with significant rest tremor may not respond as well to levodopa and may progress at a slower rate compared to individuals who present with a nontremor-dominant, akinetic-rigid form of the disease. It is likely that the effect of PRE may vary with the clinical subtype of PD. In addition, the effect of PRE on tremor and rigidity is not yet known. Thus, future research should identify the optimal PRE prescription in the context of the different clinical subtypes of individuals with PD and empirically verify hypotheses related to tremor and rigidity as well.

5. Conclusion

In PD, bradykinesia and muscle weakness are primarily due to nigral dopaminergic deficits that alter corticospinal activation. Given the wide array of neural changes that accompany PRE summarized in this paper, the potential to slow the rate of the progression of the symptoms of PD, the improvement in strength and function, and the positive effects on nonmotor symptoms of PD, there is a strong rationale for the use of PRE as an adjunct treatment in PD.

Acknowledgment

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[40] O. R. Seynnes, M. de Boer, and M. V. Narici, “Early skeletal muscle hypertrophy and architectural changes in response


Parkinson's Disease


Review Article

Exercise and Motor Training in People with Parkinson’s Disease: A Systematic Review of Participant Characteristics, Intervention Delivery, Retention Rates, Adherence, and Adverse Events in Clinical Trials

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There is research evidence that exercise and motor training are beneficial for people with Parkinson’s disease (PD), and clinicians seek to implement optimal programs. This paper summarizes important factors about the nature and reporting of randomized controlled trials of exercise and/or motor training for people with PD which are likely to influence the translation of research into clinical practice. Searches identified 53 relevant trials with 90 interventions conducted for an average duration of 8.3 (SD 4.2) weeks. Most interventions were fully supervised (74%) and conducted at a facility (79%). Retention rates were high with 69% of interventions retaining ≥85% of their participants; however adherence was infrequently reported, and 72% of trials did not report adverse events. Overall, the labor-intensive nature of most interventions tested in these trials and the sparse reporting of adherence and adverse events are likely to pose difficulties for therapists attempting to balance benefits and costs when selecting protocols that translate to sustainable clinical practice for people with PD.

1. Introduction

In recent years there have been an increasing number of randomized controlled trials assessing the effects of exercise and/or motor training in people with Parkinson’s disease (PD). Overall, these trials support exercise and motor training as beneficial in improving walking, balance, muscle strength, and the performance of functional tasks in people with mild-to-moderate PD [1–11]. In order for findings from this research to be of general benefit to people with PD, therapists need to be able to translate the protocols used in the research into clinical practice [12].

Evidence-based practice aims to incorporate and apply high-quality clinical research findings in clinical policy and practice [13, 14]. However, this can be a challenging task as health practitioners may find it difficult to assess, interpret, and implement research evidence [13]. While evidence about beneficial outcomes is paramount in therapists’ decisions to implement a particular intervention, there are other factors that affect how the overall impact of the intervention is interpreted and its potential for widespread clinical application [13–17]. For example, therapists need to consider how the characteristics of participants included in a trial may affect their decision regarding the applicability of the trial intervention with their patients [14]. It is likely that the way in which the intervention was applied in terms of its duration, level of supervision, delivery (i.e., individual versus group), and location (e.g., facilities and equipment required) will influence therapists’ decisions to implement that intervention. A research protocol that has been shown to be effective may not be implemented by therapists if they cannot provide adequate supervision over the required time frame or they do
not have access to necessary facilities or equipment. Finally, information regarding retention, adherence, and adverse events is required so that therapists and patients can weigh up the effectiveness of the intervention against its acceptability and any risks associated with implementation [14].

Therefore, in order to examine the information available to guide the translation of research into clinical practice, we searched randomized controlled trials of exercise and/or motor training for people with PD to determine the

(1) disease severity and cognitive status of the included participants,
(2) duration, supervision, delivery, and location of the interventions,
(3) rates of retention, adherence, and adverse events.

2. Methods

2.1. Data Sources and Searches. Randomized controlled trials of exercise and/or motor training for people with PD were identified via database searches of MEDLINE, EMBASE, AMED, PsycINFO, the Cochrane Central Register of Controlled Trials, and CINAHL. The initial search was conducted in 2009, with a subsequent search conducted over 5 days from the 7th of April, 2011. The electronic search strategy used has been previously reported [2]. The Physiotherapy Evidence Database (PEDro; http://www.pedro.org.au/) was also searched, and the reference lists of previously published systematic reviews [4, 5, 8, 9, 18–30] were checked for any trials not identified with the database search.

2.2. Study Selection. Trials included were published randomized (or quasi randomized, i.e., not truly random but intended to produce similar groups) with PD who at least one of the interventions was an ongoing program of exercise and/or motor training. All forms of exercise (e.g., aerobic, strength, and treadmill walking) and motor training (e.g., cueing and movement strategy training) were included. Whole-body vibration was not considered to be exercise or motor training. Trials were excluded if the intervention was multidisciplinary or was primarily occupational therapy.

The eligibility of trials was determined in a two-stage process. Firstly, all trial titles and abstracts were screened independently by two investigators (N. E. Allen and G. D. Suriyarachchi). Trials were excluded if it was clear that they did not meet the inclusion criteria. Secondly, the full article was obtained for the remaining trials and each trial was assessed independently by at least two investigators (N. E. Allen, C. G. Canning or J. Song), using a standardized form containing the details of the inclusion criteria. Care was taken to identify trials that had been reported in more than one journal article. Where this occurred, the multiple articles were counted as one trial and all articles were used to collect data for that trial.

2.3. Data Extraction. A data collection form was developed, tested on five randomly selected trials and then modified accordingly. All investigators were involved in data extraction, and all data was double-checked by an investigator not involved in its initial extraction (N. E. Allen or J. Song). Discrepancies were resolved by discussion.

Information extracted from each trial included a description of participants (including cognitive status), details of the exercise and motor training program and how it was administered, as well as details regarding retention rates, adherence to the intervention, and monitoring and reporting of adverse events. Retention was defined as the number of participants who completed the trial (i.e., undertook the first or only post-intervention assessment excluding further follow-up assessments) expressed as a percentage of the number of participants who began the trial. Adherence was defined as the number of intervention sessions attended by participants expressed as a percentage of the number of intervention sessions prescribed [15].

3. Results

Searching identified 3,539 records, of which 53 trials involving 1,940 participants were found to be eligible for inclusion in the paper (Figure 1) [32]. There were no disagreements between reviewers regarding the inclusion of any articles. The characteristics of the included trials [1, 3, 6, 7, 10, 11, 33–85] are summarised in Table 1.

3.1. Participant Characteristics. Forty (75%) of the reviewed trials included participants with mild-to-moderate PD (i.e., equivalent to Hoehn and Yahr stage I to III [86]). Seven trials (13%) included participants with mild-to-moderately severe PD (i.e., Hoehn and Yahr stage I to IV), while four trials (8%) included only participants with mild PD and two trials (4%) included only participants with moderate PD (Table 1). Most trials stipulated the cognitive status of included participants. Twenty-nine trials (55%) used the Mini-Mental State Examination [87] to screen potential participants’ cognitive abilities, with the minimum score for inclusion varying between 20 and 28 out of the maximum of 30 [1, 3, 6, 7, 10, 11, 34, 36, 39, 41–43, 45, 47–50, 56, 58, 60, 63–65, 69, 71, 76–78, 80, 85]. One trial (2%) [70] specified that participants required at least moderate scores on the Neurobehavioural Cognitive Status Examination [88]. Thirteen trials (25%) made a statement to the effect that included participants had no dementia and/or reasonable cognition [35, 46, 51, 52, 57, 59, 62, 66, 67, 79, 81, 83, 84]. Ten trials (19%) did not give a clear indication of the participants’ cognitive abilities [33, 37, 40, 53, 55, 68, 72, 74, 75, 82].

3.2. Exercise and/or Motor Training Program Characteristics. In the 53 trials, there were 90 intervention groups that involved exercise and/or motor training (including two intervention groups for the cross-over trials where one intervention was a control [11, 42, 47]) (Table 1). Average intervention duration was 8.3 weeks (SD = 4.2, range = 2 to 26 weeks), with 37 trials (70%) conducting an intervention of 10 weeks or less. The total number of hours of intervention was not clearly reported in all studies (see Table 1); however, from the available data, an average of approximately 20 hours (SD
Records identified through database searching \((n = 3,527)\)

Additional records identified through other sources \((n = 12)\)

Records after duplicates removed \((n = 2,639)\)

Titles and abstracts screened \((n = 2,639)\)

Records excluded \((n = 2,538)\)

Full-text articles excluded \((n = 43)\)

19: Not randomized
9: Multidisciplinary or occupational therapy intervention
7: Not exercise or motor training
2: Article not available
2: Protocol or commentary
2: Does not evaluate ongoing effects of intervention
1: Participants did not have Parkinson's disease
1: Assessing a system of intervention

Trials included in review \((n = 53\) trials in 58 articles)
2 trials had 2 articles
2 trials were combined in a 3rd article
1 trial had 3 articles

Figure 1: PRISMA flow diagram [32] showing flow of information through the review.

approximately 11, range = 4 to 65 hours) appears broadly representative of the included trials. Sixty-seven of the 90 intervention groups (74%) involved full supervision of exercise and/or motor training. Participants in 18 (27%) of the fully supervised intervention groups received one-on-one supervision and 20 (30%) received supervision in small groups but the intervention delivery (one-on-one or small group supervision) was unclear in the remaining 29 (43%) intervention groups. Participants in most intervention groups (71; 79%) were required to attend a facility for all or the majority of the intervention sessions.

3.3. Retention, Adherence, and Adverse Events. Retention was generally well reported and was high, with 62 (69%) of the 90 intervention groups retaining at least 85% of participants (Table 1). Seventeen (32%) of the 53 included trials reported that at least one participant dropped out for a reason related to the intervention (Table 2). Difficulties with transport and disinterest/poor adherence were the most common intervention-related reasons for dropouts.

Overall, adherence and adverse events were infrequently reported in the included trials (Table 1). Adherence was reported in some form in 26 (49%) of the included trials. However, 11 (42%) of these trials only reported adherence for those participants who completed the intervention. Most trials (38; 72%) did not report monitoring for adverse events. Across the remaining 15 trials, 11 adverse events occurred (Table 1). Four participants from two separate trials [41, 80] experienced cardiac problems. Two of these participants, one from each group in a trial comparing physical therapy with and without mental practice [80], withdrew from the study. The two participants from the other trial [41] were able to continue safely with treadmill training. Other adverse events reported included a fall [81] and muscle cramps and tiredness [43] in trials involving cued overground walking, knee pain during a dancing program [52], muscle soreness
Table 1: Characteristics of the 53 included trials.

<table>
<thead>
<tr>
<th>First author, year and intervention type</th>
<th>Initial group sizes</th>
<th>Disease severity</th>
<th>Location and delivery of experimental intervention</th>
<th>Duration of intervention (weeks)</th>
<th>Hours of intervention (approx)</th>
<th>Supervision (%)</th>
<th>Retention (%)</th>
<th>Any dropouts related to intervention?</th>
<th>Adherence (%)</th>
<th>Adverse events occurred</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allen 2010, exercise OR control</td>
<td>24</td>
<td>Mild to moderate</td>
<td>Facility, group + home individual</td>
<td>26</td>
<td>65</td>
<td>10%</td>
<td>87.5%</td>
<td>Y</td>
<td>70%</td>
<td>N</td>
</tr>
<tr>
<td>Ashburn 2007, exercise and strategy OR control</td>
<td>70</td>
<td>Moderate</td>
<td>Home, individual</td>
<td>6</td>
<td>33</td>
<td>18%</td>
<td>96%</td>
<td>Y</td>
<td>U (99% of Supervised exercise)</td>
<td>N</td>
</tr>
<tr>
<td>Bergen 2002, aerobic exercise OR control</td>
<td>4</td>
<td>Mild</td>
<td>Facility, delivery unclar</td>
<td>16</td>
<td>32</td>
<td>100%</td>
<td>100%</td>
<td>NA</td>
<td>NR NRM</td>
<td>N</td>
</tr>
<tr>
<td>Blackinton 2002, exercise OR control</td>
<td>U 15 total</td>
<td>Mild to moderate</td>
<td>Facility, group + home individual</td>
<td>U</td>
<td>66%</td>
<td>U (53%)</td>
<td>Y</td>
<td>N</td>
<td>NR NRM</td>
<td>N</td>
</tr>
<tr>
<td>Bloomer 2008, resistance training OR control</td>
<td>8</td>
<td>Mild</td>
<td>Facility, delivery unclar</td>
<td>8</td>
<td>8</td>
<td>100%</td>
<td>75%</td>
<td>N</td>
<td>U N N</td>
<td>N</td>
</tr>
<tr>
<td>Braun 2011, physiotherapy + mental practice OR physiotherapy + relaxation</td>
<td>25</td>
<td>Mild to moderately severe</td>
<td>Facility, individual or group + home, individual</td>
<td>6</td>
<td>6 + home mental practice U (100%)</td>
<td>88%</td>
<td>Y</td>
<td>(87%)†‡</td>
<td>U NRM</td>
<td>N</td>
</tr>
<tr>
<td>Bridgewater 1996 (also as [38]), aerobic and trunk muscle training OR education</td>
<td>13</td>
<td>Mild to moderate</td>
<td>Facility, group</td>
<td>12</td>
<td>16 to 22</td>
<td>100%</td>
<td>100%</td>
<td>95%</td>
<td>NRM</td>
<td>N</td>
</tr>
<tr>
<td>Burini 2006*, aerobic exercise OR Qigong</td>
<td>13</td>
<td>Mild to moderate</td>
<td>Facility, group</td>
<td>7</td>
<td>17</td>
<td>100%</td>
<td>85%</td>
<td>Y</td>
<td>87%</td>
<td>NRM</td>
</tr>
<tr>
<td>Caglar 2005, exercise OR control</td>
<td>15</td>
<td>Mild to moderate</td>
<td>Facility, group + home, individual</td>
<td>9</td>
<td>63</td>
<td>4%</td>
<td>100%</td>
<td>NA</td>
<td>NRM</td>
<td>N</td>
</tr>
<tr>
<td>First author, year and intervention type</td>
<td>Initial group sizes</td>
<td>Disease severity</td>
<td>Location and delivery of experimental intervention</td>
<td>Duration of intervention (weeks)</td>
<td>Hours of intervention (approx)</td>
<td>Supervision (%)</td>
<td>Retention (%)</td>
<td>Any dropouts related to intervention?</td>
<td>Adherence (%)</td>
<td>Adverse events occurred</td>
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</tr>
<tr>
<td>Cakit 2007, treadmill walking OR control</td>
<td>27</td>
<td>Mild to moderate</td>
<td>Facility, delivery unclear</td>
<td>8</td>
<td>8</td>
<td>100%</td>
<td>78%</td>
<td>U</td>
<td>NR</td>
<td>Partial—2 minor cardiac</td>
</tr>
<tr>
<td>Comella 1994*, physiotherapy OR control</td>
<td>U 18 total</td>
<td>Mild to moderate</td>
<td>Facility, delivery unclear</td>
<td>U 4</td>
<td>12</td>
<td>100%</td>
<td>U</td>
<td>U</td>
<td>U</td>
<td>NRM</td>
</tr>
<tr>
<td>de Bruin 2010, walk with music OR control</td>
<td>16</td>
<td>Mild to moderate</td>
<td>Home, individual</td>
<td>13</td>
<td>19.5</td>
<td>0%</td>
<td>69%</td>
<td>Y</td>
<td>100%</td>
<td>Y—I thigh cramping 10%</td>
</tr>
<tr>
<td>Dereli 2010, supervised exercise OR home exercise</td>
<td>16</td>
<td>Mild to moderate</td>
<td>Facility, individual; home, individual</td>
<td>10</td>
<td>22.5</td>
<td>100%</td>
<td>94%</td>
<td>Y</td>
<td>100%</td>
<td>NRM</td>
</tr>
<tr>
<td>Dias 2005, physiotherapy + cues OR physiotherapy</td>
<td>8</td>
<td>Mild to moderate</td>
<td>Facility, delivery unclear</td>
<td>4 to 10</td>
<td>20</td>
<td>100%</td>
<td>100%</td>
<td>NA</td>
<td>NRM</td>
<td>NRM</td>
</tr>
<tr>
<td>Ebersbach 2010, LSVT BIG OR Nordic walking OR home exercise</td>
<td>20</td>
<td>Mild to moderate</td>
<td>Facility, individual; facility, group; home, individual + all did home, individual</td>
<td>4</td>
<td>16 + home X U (100%)</td>
<td>100%</td>
<td>NA</td>
<td>U</td>
<td>95%</td>
<td>U</td>
</tr>
<tr>
<td>Ellis 2005* (also as [44]), physiotherapy OR control</td>
<td>35</td>
<td>Mild to moderate</td>
<td>Facility, group</td>
<td>6</td>
<td>18</td>
<td>100%</td>
<td>91%</td>
<td>N</td>
<td>93%</td>
<td>NRM</td>
</tr>
<tr>
<td>Fisher 2008, treadmill walking OR physiotherapy OR control</td>
<td>10</td>
<td>Mild</td>
<td>Facility, delivery unclear</td>
<td>8</td>
<td>18</td>
<td>100%</td>
<td>100%</td>
<td>NA</td>
<td>NR</td>
<td>N</td>
</tr>
<tr>
<td>First author, year and intervention type</td>
<td>Initial group sizes</td>
<td>Disease severity</td>
<td>Location and delivery of experimental intervention</td>
<td>Duration of intervention (weeks)</td>
<td>Hours of intervention (approx)</td>
<td>Supervision (%)</td>
<td>Retention (%)</td>
<td>Any dropouts related to intervention?</td>
<td>Adherence (%)</td>
<td>Adverse events occurred</td>
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</tr>
<tr>
<td>Frazzitta 2009, Treadmill walking with cues OR physiotherapy with cues</td>
<td>20</td>
<td>Moderate</td>
<td>Facility, individual</td>
<td>4</td>
<td>9.5</td>
<td>100%</td>
<td>100%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Guo 2009, physiotherapy and education OR control</td>
<td>23</td>
<td>Mild to moderate</td>
<td>Facility, group education and individual therapy</td>
<td>8</td>
<td>12 of therapy</td>
<td>100%</td>
<td>91%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hackney 2007, Tango OR exercise</td>
<td>9</td>
<td>Mild to moderate</td>
<td>Facility, group implied</td>
<td>13</td>
<td>20</td>
<td>100%</td>
<td>100%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hackney 2008 (also as [54]), Tai Chi OR control</td>
<td>17</td>
<td>Mild to moderate</td>
<td>Facility, group implied</td>
<td>10 to 13</td>
<td>20</td>
<td>100%</td>
<td>76% Y 100%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hackney 2009 (also as [54]), Waltz/fox trot OR tango OR control</td>
<td>19</td>
<td>Mild to moderate</td>
<td>Facility, group implied</td>
<td>10 to 13</td>
<td>20</td>
<td>100%</td>
<td>89% Y 100%</td>
<td></td>
<td>Partial—1 knee pain</td>
<td></td>
</tr>
<tr>
<td>Hackney 2010, partnered tango OR nonpartnered tango</td>
<td>19</td>
<td>Mild to moderate</td>
<td>Facility, group implied</td>
<td>10</td>
<td>20</td>
<td>100%</td>
<td>79%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hass 2007, resistance training + supplement OR resistance training + placebo</td>
<td>10</td>
<td>Mild to moderate</td>
<td>Facility, delivery unclear</td>
<td>12</td>
<td>12</td>
<td>100%</td>
<td>100%</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* NRM: Not reported in this study.
<table>
<thead>
<tr>
<th>First author, year and intervention type</th>
<th>Initial group sizes</th>
<th>Disease severity</th>
<th>Location and delivery of experimental intervention</th>
<th>Duration of intervention (weeks)</th>
<th>Hours of intervention (approx)</th>
<th>Supervision (%)</th>
<th>Retention (%)</th>
<th>Any dropouts related to intervention?</th>
<th>Adherence (%)</th>
<th>Adverse events occurred</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hirsch 2003</strong>, balance and resistance training OR balance training</td>
<td>9</td>
<td>Mild to moderate</td>
<td>Facility, delivery unclear</td>
<td>10</td>
<td>22.5</td>
<td>100%</td>
<td>67%</td>
<td>Y</td>
<td>89%</td>
<td>Y—1 inguinal hernia</td>
</tr>
<tr>
<td>Keus 2007, physiotherapy OR control</td>
<td>14/13</td>
<td>Mild to moderately severe</td>
<td>Facility, individual</td>
<td>10</td>
<td>11 to 15</td>
<td>100%</td>
<td>100%</td>
<td>NA</td>
<td>63%</td>
<td>N</td>
</tr>
<tr>
<td>Kurtais 2008, treadmill walking OR control</td>
<td>13</td>
<td>Mild to moderate</td>
<td>Facility, delivery unclear + home, individual</td>
<td>6</td>
<td>12 + home X</td>
<td>U (100%)†</td>
<td>92%</td>
<td>Y</td>
<td>NA</td>
<td>N</td>
</tr>
<tr>
<td>Lehman 2005*, walk with verbal cues OR control</td>
<td>5/6</td>
<td>Mild</td>
<td>Facility implied, delivery unclear</td>
<td>2</td>
<td>5</td>
<td>100%</td>
<td>100%</td>
<td>NA</td>
<td>NA</td>
<td>NR NRM</td>
</tr>
<tr>
<td>Mak 2008, cued sit to stand OR OR exercise control</td>
<td>21/18</td>
<td>Mild to moderate</td>
<td>Facility, delivery unclear</td>
<td>4</td>
<td>4</td>
<td>100%</td>
<td>90%</td>
<td>U</td>
<td>NR</td>
<td>NRM</td>
</tr>
<tr>
<td>Marchese 2000, physiotherapy OR physiotherapy with cues</td>
<td>U/20 total</td>
<td>Mild to moderate</td>
<td>Facility, individual + home, individual</td>
<td>U</td>
<td>18 + home X</td>
<td>U (100%)‡</td>
<td>78%</td>
<td>U</td>
<td>NR</td>
<td>NRM</td>
</tr>
<tr>
<td>Miyai 2000*, treadmill walking OR physiotherapy</td>
<td>5</td>
<td>Mild to moderate</td>
<td>Facility, individual</td>
<td>4</td>
<td>6</td>
<td>100%</td>
<td>100%</td>
<td>NA</td>
<td>NA</td>
<td>NRM</td>
</tr>
<tr>
<td>Miyai 2002, treadmill walking OR physiotherapy</td>
<td>12</td>
<td>Mild to moderate</td>
<td>Facility, individual</td>
<td>4</td>
<td>6</td>
<td>100%</td>
<td>92%</td>
<td>N</td>
<td>NR</td>
<td>NRM</td>
</tr>
<tr>
<td><strong>Table 1</strong>: Continued.</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>First author, year and intervention type</td>
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<td>Supervision (%)</td>
<td>Retention (%)</td>
<td>Any dropouts related to intervention?</td>
<td>Adherence (%)</td>
<td>Adverse events occurred</td>
</tr>
<tr>
<td>----------------------------------------</td>
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<td>---------------------------------</td>
<td>---------------</td>
<td>------------------------</td>
</tr>
<tr>
<td>Morris 2009, movement strategies OR exercises</td>
<td>14</td>
<td>Mild to moderate</td>
<td>Facility, individual</td>
<td>2</td>
<td>Up to 12</td>
<td>100%</td>
<td>100%</td>
<td>NA</td>
<td>88% of maximum sessions</td>
<td>NRM</td>
</tr>
<tr>
<td>Müller 1997, behavioural therapy OR nonspecific exercises and information</td>
<td>15</td>
<td>Mild to moderate</td>
<td>Location and delivery unclear</td>
<td>10</td>
<td>30</td>
<td>100%</td>
<td>U</td>
<td>NR</td>
<td>NR</td>
<td>NRM</td>
</tr>
<tr>
<td>Nieuwboer 2007* (also as [61, 73]), cueing training OR control</td>
<td>76</td>
<td>Mild to moderate</td>
<td>Home, individual</td>
<td>3</td>
<td>4.5</td>
<td>100%</td>
<td>99%</td>
<td>N</td>
<td>100%</td>
<td>Partial—no falls wearing activity monitor</td>
</tr>
<tr>
<td>Pacchetti 2000, physiotherapy OR music therapy</td>
<td>16</td>
<td>Mild to moderate</td>
<td>Facility, group</td>
<td>13</td>
<td>19.5</td>
<td>100%</td>
<td>U</td>
<td>NR</td>
<td>NR</td>
<td>NRM</td>
</tr>
<tr>
<td>Palmer 1986, exercise OR seated karate</td>
<td>7</td>
<td>Mild to moderately severe</td>
<td>Facility, group</td>
<td>12</td>
<td>36</td>
<td>100%</td>
<td>100%</td>
<td>NA</td>
<td>NR</td>
<td>NRM</td>
</tr>
<tr>
<td>Pelosin 2010, physiotherapy with FOG strategies OR physiotherapy</td>
<td>9</td>
<td>Mild to moderate</td>
<td>Facility, delivery unclear</td>
<td>4</td>
<td>12</td>
<td>100%</td>
<td>100%</td>
<td>NA</td>
<td>NR</td>
<td>NRM</td>
</tr>
<tr>
<td>Protas 2005, treadmill walking and step training OR control</td>
<td>9</td>
<td>Mild to moderate</td>
<td>Facility, individual</td>
<td>8</td>
<td>24</td>
<td>100%</td>
<td>100%</td>
<td>NA</td>
<td>100%</td>
<td>NRM</td>
</tr>
</tbody>
</table>

*Table 1: Continued.*
<table>
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<th>Supervision (%)</th>
<th>Retention (%)</th>
<th>Any dropouts related to intervention?</th>
<th>Adherence (%)</th>
<th>Adverse events occurred</th>
</tr>
</thead>
<tbody>
<tr>
<td>Qutubuddin 2007, computerized dynamic posturography OR physiotherapy</td>
<td>12</td>
<td>Mild to moderate</td>
<td>Facility, delivery unclear + home, individual</td>
<td>8</td>
<td>18</td>
<td>20%</td>
<td>75%</td>
<td>U</td>
<td>U</td>
<td></td>
</tr>
<tr>
<td>Ridgel 2009, forced cycling OR self-paced cycling</td>
<td>5</td>
<td>Mild to moderate</td>
<td>Facility, delivery unclear</td>
<td>8</td>
<td>24</td>
<td>100%</td>
<td>100%</td>
<td>NA</td>
<td>NR</td>
<td>NRM</td>
</tr>
<tr>
<td>Sage 2009, aerobic exercise OR SAFEx OR control</td>
<td>17</td>
<td>Mild to moderate</td>
<td>Facility, group</td>
<td>10 to 12</td>
<td>18</td>
<td>100%</td>
<td>76%</td>
<td>Y</td>
<td>86.8%†</td>
<td></td>
</tr>
<tr>
<td>Sage 2010, SAFEx OR non-SAFEx</td>
<td>15</td>
<td>Mild to moderate</td>
<td>Facility, group</td>
<td>12</td>
<td>36</td>
<td>100%</td>
<td>100%</td>
<td>NA</td>
<td>100%</td>
<td></td>
</tr>
<tr>
<td>Schenkmann 1998, exercise OR control</td>
<td>27</td>
<td>Mild to moderate</td>
<td>Location unclear, individual</td>
<td>10 to 13</td>
<td>22.5 to 30</td>
<td>100%</td>
<td>85%</td>
<td>U</td>
<td>100%†</td>
<td></td>
</tr>
<tr>
<td>Schmitz-Hubsch 2006, Qigong OR control</td>
<td>32</td>
<td>Mild to moderately severe</td>
<td>Facility group + home individual</td>
<td>24</td>
<td>16 + home X</td>
<td>66%</td>
<td>91%</td>
<td>Y</td>
<td>87.5%</td>
<td></td>
</tr>
<tr>
<td>Smania 2010, balance training OR general exercises</td>
<td>33</td>
<td>Moderate to moderately severe</td>
<td>Facility, individual</td>
<td>7</td>
<td>17.5</td>
<td>100%</td>
<td>85%</td>
<td>Y</td>
<td>NR</td>
<td>NRM</td>
</tr>
<tr>
<td>Stallibrass 2002, Alexander technique OR massage OR control</td>
<td>32</td>
<td>Mild to moderate</td>
<td>Facility, individual</td>
<td>12</td>
<td>16</td>
<td>100%</td>
<td>91%</td>
<td>Y</td>
<td>99%†</td>
<td></td>
</tr>
<tr>
<td></td>
<td>31</td>
<td>Mild to moderate</td>
<td></td>
<td>12</td>
<td>16</td>
<td>93%</td>
<td>100%</td>
<td>97%†</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Table 1: Continued.

<table>
<thead>
<tr>
<th>First author, year and intervention type</th>
<th>Initial group sizes</th>
<th>Disease severity</th>
<th>Location and delivery of experimental intervention</th>
<th>Duration of intervention (weeks)</th>
<th>Hours of intervention (approx)</th>
<th>Supervision (%)</th>
<th>Retention (%)</th>
<th>Any dropouts related to intervention?</th>
<th>Adherence (%)</th>
<th>Adverse events occurred</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tamir 2007, exercise + imagery OR exercise</td>
<td>12</td>
<td>Mild to moderate</td>
<td>Facility, delivery unclear + home, individual</td>
<td>12</td>
<td>24 + home X U (100%)</td>
<td>U</td>
<td>92%</td>
<td>U</td>
<td>NR</td>
<td>Partial—2 cardiac problems</td>
</tr>
<tr>
<td>Thaut 1996, walk with auditory cues OR walk without cues OR control</td>
<td>15</td>
<td>Mild to moderate</td>
<td>Home, individual</td>
<td>3</td>
<td>10.5</td>
<td>U</td>
<td>91%</td>
<td>U</td>
<td>100%</td>
<td></td>
</tr>
<tr>
<td>Toole 2000, exercise OR control</td>
<td>6</td>
<td>Mild to severely</td>
<td>Facility, delivery unclear</td>
<td>10</td>
<td>30</td>
<td>100%</td>
<td>67%</td>
<td>N</td>
<td>NR</td>
<td>NRM</td>
</tr>
<tr>
<td>Toole 2005, treadmill walking with body weight support OR treadmill walking with weights OR treadmill walking</td>
<td>U</td>
<td>Mild to moderately severe</td>
<td>Facility, delivery unclear</td>
<td>6</td>
<td>6</td>
<td>NR</td>
<td>NR</td>
<td>99% overall</td>
<td>NRM</td>
<td></td>
</tr>
<tr>
<td>Yang 2010, downhill treadmill walking OR conventional therapy</td>
<td>16</td>
<td>Mild to moderate</td>
<td>Facility, delivery unclear</td>
<td>4</td>
<td>6</td>
<td>100%</td>
<td>94%</td>
<td>Y</td>
<td>100%†</td>
<td>N</td>
</tr>
<tr>
<td>Yousefi 2009, exercise OR education</td>
<td>12</td>
<td>Mild to moderate</td>
<td>Facility, group</td>
<td>10</td>
<td>40</td>
<td>100%</td>
<td>100%</td>
<td>NA</td>
<td>NR</td>
<td>NRM</td>
</tr>
<tr>
<td></td>
<td>12</td>
<td></td>
<td></td>
<td>10</td>
<td>40</td>
<td>100%</td>
<td>100%</td>
<td></td>
<td>NRM</td>
<td></td>
</tr>
</tbody>
</table>

Supervision: the number of intervention sessions supervised expressed as a percentage of the number of sessions prescribed; retention: the number of participants who completed the trial (i.e., undertook a post-intervention assessment but excluding follow-up) expressed as a percentage of the number of participants who began the trial; adherence: the number of intervention sessions participants attended expressed as a percentage of the number of intervention sessions prescribed; Y: yes; N: no; NA: not applicable; U: unclear—insufficient information to categorize; NR: not reported; NRM: not reported to be monitored; X: exercise; FOG: freezing of gait; SAFEx: sensory attention focused exercise; †cross-over trial; ‡data only for participants who completed the trial; §data only for the facility component of the intervention; ||part 2 of trial only.
Table 2: Dropout reasons when related to the intervention.

<table>
<thead>
<tr>
<th>First author and year</th>
<th>Dropout reason</th>
<th>Number of participants</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allen 2010</td>
<td>Did not want to do the intervention</td>
<td>1</td>
</tr>
<tr>
<td>Ashburn 2007</td>
<td>Falls (but not during intervention)</td>
<td>1</td>
</tr>
<tr>
<td>Blackinton 2002</td>
<td>Safety concerns</td>
<td>1</td>
</tr>
<tr>
<td>Braun 2011</td>
<td>Imagery too confronting</td>
<td>1</td>
</tr>
<tr>
<td>Burini 2006</td>
<td>Poor adherence to exercise; back pain</td>
<td>2</td>
</tr>
<tr>
<td>de Bruin 2010</td>
<td>No access to necessary equipment</td>
<td>1</td>
</tr>
<tr>
<td>Dereli 2010</td>
<td>Did not want to do the intervention</td>
<td>1</td>
</tr>
<tr>
<td>Hackney 2008 (also as [54])</td>
<td>Exercise not intense enough; transport problems</td>
<td>1</td>
</tr>
<tr>
<td>Hackney 2009 (also as [54])</td>
<td>Knee pain; transport problems</td>
<td>1</td>
</tr>
<tr>
<td>Hackney 2010</td>
<td>Travel distance; classes too fatiguing; lack of interest</td>
<td>2</td>
</tr>
<tr>
<td>Hirsch 2003</td>
<td>Inguinal hernia</td>
<td>1</td>
</tr>
<tr>
<td>Kurtais 2008</td>
<td>Poor adherence to exercise</td>
<td>1</td>
</tr>
<tr>
<td>Sage 2009</td>
<td>Time commitment</td>
<td>4</td>
</tr>
<tr>
<td>Schmitz-Hubsch 2006</td>
<td>Uncomfortable in the group; uncomfortable with Qigong</td>
<td>1</td>
</tr>
<tr>
<td>Smania 2010</td>
<td>Uncooperative</td>
<td>4</td>
</tr>
<tr>
<td>Stallibrass 2002</td>
<td>Could not travel</td>
<td>1</td>
</tr>
<tr>
<td>Yang 2010</td>
<td>Low motivation; transport problems</td>
<td>1</td>
</tr>
</tbody>
</table>

and shoulder pain [56] following resistance training, and a hernia [57] subsequent to muscle strength assessment.

4. Discussion

A substantial number of randomized controlled trials of exercise and/or motor training for people with PD have been published. However, the nature and reporting of these trials are likely to provide challenges for therapists aiming to implement the interventions into clinical practice [17]. Most trials involved only cognitively intact participants with mild-to-moderate PD. Trials tended to be of short duration, highly supervised, and conducted at a facility. Furthermore, the reports for many trials were lacking important details, with adherence and adverse events particularly being inadequately reported.

On the whole, trials included in this paper included only participants with mild-to-moderate PD who were without significant cognitive impairment. Including only these types of participants not only makes it easier to conduct trials of exercise and motor training interventions but also aids interpretation of the results. However, cognitive impairment is now recognised as a common problem in PD, with over 80% of people with PD ultimately developing dementia [89]. Further work is needed to determine the effectiveness of exercise and motor training in people with more severe cognitive impairment and/or more advanced disease.

Most of the reviewed trials were of short duration, highly supervised, and facility based (Table 1). Interventions lasted an average of around two months. Seventy-four percent of the intervention groups were fully supervised, with no reported expectation for participants to undertake unsupervised exercise. Furthermore, 79% of intervention groups were mainly conducted at a facility such as a hospital or university. Such brief, highly supervised interventions conducted in controlled environments are likely to improve the adherence of participants to exercise and motor training programs and to ensure that interventions are being performed optimally. In this regard, these trials are useful and important for determining the short-term efficacy of an intervention. However, given that PD is a long-term, neurodegenerative condition, the capacity of therapists and patients to sustain the intervention over the long term needs to be considered. Furthermore, such brief and highly supervised interventions are costly and less likely to give
information about the effectiveness of the intervention when implemented into usual practice [13, 17]. For example, the requirement for participants to travel to a facility was a common reason for withdrawal from the included trials (Table 2). Moreover, the neurodegenerative nature of PD and the limited resources available to healthcare systems mean that such labor-intensive programs are unlikely to be sustained or afforded by most health-care providers. Additionally, as PD is a progressive disease it is important that people with PD are empowered to self-manage their disease to some extent [90, 91]. To this end, trials of more pragmatic and sustainable exercise and motor training interventions, with the potential for direct translation into clinical practice and including cost-effectiveness analysis, are needed.

The likely adherence to an exercise and motor training program is an important factor to consider when prescribing such a program for an individual with PD. Adherence to the intervention was reported in less than half of the included trials, and some reports of adherence are artificially elevated by including only those participants who completed the trial (Table 1). Some trials were able to effectively maximise adherence by providing a flexible timeframe for participants to complete the intervention [46, 51, 52, 74, 76] and so allow participants more options in fitting their exercise and/or motor training program around their daily lives. This pragmatic approach is likely to more closely reflect therapy attendance patterns and is therefore likely to be helpful for therapists considering translating the research into their clinical practice.

Given the importance of adherence to exercise and motor training programs, strategies to promote adherence in people with PD need to be considered. Providing a high level of supervision seems likely to promote adherence in the short term, as it may enhance participants’ commitment to the program. However, a Cochrane review comparing home and centre-based exercise programs for older adults found that, in the long term, participants were more likely to adhere to home-based programs [92]. Furthermore, the reviewers noted a trend toward more sustained improvements in the home-based than in the centre-based programs and suggested that this was attributable to the higher adherence in home-based programs. In the present paper, three of the included trials report high levels of adherence with minimally supervised home-based programs [40, 43, 81]. Common to all three of these trials was a requirement for participants to keep a daily record of what exercise/motor training they had performed. It seems likely that this simple strategy assisted in promoting adherence in these trials. Other strategies with the potential to improve adherence in sustainable, minimally supervised trials, such as participant involvement in goal setting [93, 94], flexibility to allow programs to be modified for individuals [1, 91, 93, 94], and intermittent followup [91, 94], warrant exploration.

The issue of adverse events was inadequately addressed in the trials included in this paper, with only 15 trials reporting monitoring for adverse events. In these 15 trials, 11 adverse events were reported, most of which were minor in nature (Table 1). However, when discussing and planning exercise and motor training options with people with PD, therapists need to be informed not only about the effectiveness of a given intervention but also about the nature and likelihood of any potential adverse events [95]. Similarly poor reporting of adverse events was found in a recent Cochrane review of progressive resistance training for older adults [95]. Notably, the Cochrane review found that adverse events were more likely to be detected in trials that used a clear definition of adverse events than in trials which did not use a definition. In the same way, the use of a definition for adverse events is likely to improve the assessment and reporting of adverse events in trials of exercise and motor training for people with PD.

This paper has examined several factors in the nature and reporting of trials of exercise and/or motor training which are likely to influence the way research is applied by therapists in clinical practice. However, this paper did not address whether or not trial protocols were reported in sufficient detail to allow therapists to emulate the research intervention in the clinic. This detailed reporting of trial interventions is critical in enabling research to be clinically applied [96]. The ability of many journals to provide online material which supplements the published article will aid the provision of such details despite the necessary word count limitations placed on authors.

5. Conclusions

Clinicians seeking to use research to inform their clinical practice rely heavily on the design and reporting of randomized controlled trials to reach their decisions. However, the nature and reporting of trials of exercise and/or motor training for people with PD are likely to provide challenges for therapists aiming to implement the interventions into clinical practice. The short duration, highly supervised and facility-based nature of many of the interventions, coupled with the tendency to include only cognitively-intact participants with mild-to-moderate disease, mean that findings may not generalise when therapists set out to apply them in the long-term management of people with PD. Infrequent reporting of adherence and adverse events compounds this problem and makes cost-benefit balancing more difficult. It is recommended that these issues be taken into account in the design and reporting of future trials.

References


M. van Nimwegen, A. D. Speelman, K. Smulders et al., “Design and baseline characteristics of the ParkFit study, a randomized controlled trial evaluating the effectiveness of a multifaceted behavioral program to increase physical activity in Parkinson patients,” *BMC Neurology*, vol. 10, article 70, 2010.


Research Article

Effectiveness of an Inpatient Movement Disorders Program for Patients with Atypical Parkinsonism

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This paper investigated the effectiveness of an inpatient movement disorders program for patients with atypical parkinsonism, who typically respond poorly to pharmacologic intervention and are challenging to rehabilitate as outpatients. Ninety-one patients with atypical parkinsonism participated in an inpatient movement disorders program. Patients received physical, occupational, and speech therapy for 3 hours/day, 5 to 7 days/week, and pharmacologic adjustments based on daily observation and data. Differences between admission and discharge scores were analyzed for the functional independence measure (FIM), timed up and go test (TUG), two-minute walk test (TMW), Berg balance scale (BBS) and finger tapping test (FT), and all showed significant improvement on discharge (P > .001). Clinically significant improvements in total FIM score were evident in 74% of the patients. Results were similar for ten patients whose medications were not adjusted. Patients with atypical parkinsonism benefit from an inpatient interdisciplinary movement disorders program to improve functional status.

1. Introduction

Atypical parkinsonism is used to describe disorders characterized by parkinsonism—tremor, rigidity, akinesia, and postural instability—but not caused by Parkinson's disease (PD). These disorders often include other prominent features. The term includes progressive supranuclear palsy (PSP), multiple system atrophy (MSA), Lewy body dementia (LBD), corticobasal degeneration (CBD), vascular parkinsonism, drug-induced parkinsonism, and parkinsonism secondary to infection and other causes. PSP is characterized by parkinsonism along with a supranuclear vertical gaze palsy and early onset of balance problems and falls. The hallmark features of MSA include parkinsonism, autonomic instability, and cerebellar and corticospinal deficits. LBD has similar pathology to PD; however, accumulation of Lewy bodies in areas outside the substantia nigra leads to hallucinations, cognitive impairment and dementia prior to the onset of parkinsonism. Features of CBD include asymmetric parkinsonism, apraxia, alien limb phenomenon, aphasia, and sensory deficits. Vascular parkinsonism is due to lacunar infarcts in the basal ganglia and can be distinguished from PD by an abrupt onset or stepwise deterioration and development of parkinsonism and evidence of neurovascular disease. Drug-induced parkinsonism is often due to antipsychotics or antiemetics and usually resolves with cessation of the offending drug [1, 2].

Treatment of PD involves medications that increase dopamine in the basal ganglia. However, there has been less success with pharmacologic treatment in atypical parkinsonism [1, 3–5]. Previous studies have shown physical therapy to be an effective adjunctive treatment in patients with PD [6, 7] but there have only been a handful of case reports and studies investigating the efficacy of nonpharmacologic therapy in atypical parkinsonism patients.
Case reports and studies have shown subjective and objective improvements in gait, balance, and patient safety in patients with PSP [8–12] and in a patient with mixed CBD and PSP [13]. Similar improvements in gait, balance, transfers, and stability were seen in case reports of physical therapy intervention in patients with MSA [14, 15]. Timed up and go, functional reach test, 360-degree turn, and 50 foot timed walk are examples of some of the improved objective measures. Another case report showed improvement in activities of daily life (ADLs) and finger manipulation after repetitive finger exercises in a patient with CBD [16]. A small pilot randomized controlled trial showed significant improvement in MSA patients after receiving individualized outpatient occupational therapy [17].

Regarding intensive inpatient programs, a prior study by Ellis et al. investigated the effectiveness of an inpatient rehabilitation program for people with PD. In the study, medication was adjusted and interdisciplinary rehabilitation program was provided to optimize patients’ functional ability. Significant improvements were noted in all outcome measures. Patients who did not have changes made to their medications also showed significant improvements in total, motor, and cognitive functional independence measure (FIM) scores [18].

The purpose of this study was to investigate the effectiveness of an inpatient movement disorders program in improving functional status for patients with atypical parkinsonism and to determine whether or not these findings were clinically meaningful. We hypothesized that people with atypical parkinsonism would show statistically and clinically significant improvements in functional status after participating in such a program.

2. Methods

2.1. Design and Subjects. A pretest-posttest design was used to determine the effectiveness of a movement disorder program for patients admitted to an inpatient rehabilitation hospital with the diagnosis of atypical parkinsonism. Patients were admitted from home, acute care facilities, skilled nursing facilities, or assisted living between January 2004 and August 2008. They carried diagnoses, determined by a neurologist specializing in movement disorders, which fall under the term “atypical parkinsonism” as described above. They were at least 18 years old and were given a Hoehn and Yahr stage I to V for classification of PD. A total of 91 subjects were admitted to the program. Baseline characteristics are listed in Table 1.

2.2. Outcome Measures. Primary outcomes were FIM total score. Secondary outcomes included FIM motor score, FIM cognitive score, 2-minute walk test (TMW), Timed “up and go” test (TUG) Berg balance score, and finger tapping test (FT).

The FIM is a widely used 18-item assessment of disability among inpatient rehabilitation patients. The FIM measures ability to perform basic life activities, such as self-care, sphincter control, transfers, locomotion, communication, and social cognition. Each item is scored on a scale from 1 to 7, in which 1 is patient requires total assistance to complete the task and 7 is complete independence. The FIM can be divided into 2 sections: motor (13 items) and cognitive (5 items). It has been shown to have good reliability and validity [19].

The TMW is performed by asking subjects to walk as far as they can in 2 minutes. Patients with PD have been shown to cover less distance than age-matched controls [20].

The TUG assesses a patient’s ability to transfer from sitting to standing, ambulate, and make a turn. Patients are timed while rising from a chair, walking 3 m, turning, walking back to the chair, and sitting down. It has been shown to have high interrater reliability for subjects with PD [21]. Subjects were allowed to use an assistive device if necessary for the TMW and the TUG.

The BBS is a 14-item scale assessing balance while sitting, standing, turning, and reaching forward. Items are rated from 0 to 4, with 0 meaning the subject needs assistance or is unable to perform the task and 4 meaning the subject can perform the task safely and independently. It has been shown to be reliable and valid in patients with PD [22, 23]. Minimal detectable change (MCD) has been found to be +/−6 points among patients who have suffered a stroke [24] and +/−5 points in patients with PD [25].

The FT is a timed test useful in assessing the impact of bradykinesia on rapid alternating movements of the upper extremity. Two buttons are attached to a counter 30 cm apart.

<table>
<thead>
<tr>
<th>Table 1: Patient baseline characteristics.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Characteristic</td>
</tr>
<tr>
<td>Age—y, mean (SD) n = 91</td>
</tr>
<tr>
<td>Disease duration—y, mean (SD) n = 91</td>
</tr>
<tr>
<td>Sex no. (%) men/women n = 91</td>
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<tr>
<td>Race no. (%) white n = 91</td>
</tr>
<tr>
<td>Education no. (%) ≤ bachelor’s/ &gt;bachelor’s n = 75</td>
</tr>
<tr>
<td>Hoehn and Yahr stage no. (%) n = 85</td>
</tr>
<tr>
<td>I</td>
</tr>
<tr>
<td>II</td>
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<tr>
<td>III</td>
</tr>
<tr>
<td>IV</td>
</tr>
<tr>
<td>V</td>
</tr>
<tr>
<td>Length of stay—d, mean (SD)</td>
</tr>
<tr>
<td>Diagnosis no. (%) n = 91</td>
</tr>
<tr>
<td>Vascular parkinsonism</td>
</tr>
<tr>
<td>MSA</td>
</tr>
<tr>
<td>PSP</td>
</tr>
<tr>
<td>Medication related</td>
</tr>
<tr>
<td>LBD</td>
</tr>
<tr>
<td>CBD</td>
</tr>
<tr>
<td>Toxin</td>
</tr>
<tr>
<td>Unknown</td>
</tr>
</tbody>
</table>

*MSA: multiple system atrophy, PSP: progressive supranuclear palsy, LBD: Lewy body dementia, and CBD: corticobasal dementia.
Subjects are asked to alternate tapping each button with their left hand for one minute. The sum of the taps is the score for that hand. The test is repeated with the right hand. The FT has been shown to have good validity and reliability and is able to distinguish normal subjects from those with PD [26].

2.3. Intervention. A multidisciplinary team consisting of neurologists specializing in movement disorders and neuro-rehabilitation, physical therapists, occupational therapists, speech-language pathologists, nurses, and case managers provided a comprehensive rehabilitation program for patients admitted to the hospital.

All outcome measures were obtained at admission and discharge, as well as daily measurements of TMW and TUG at the peak and troughs of medication cycles. The same therapists administered interventions and outcome measures. Weekly rounds were conducted to allow the whole team to evaluate the data and discuss the patients’ status. Decisions regarding changes to medications or rehabilitation interventions were made at this time. Subjects’ responses to medication adjustments were discussed further at weekly movement disorder meetings. Adjustments were made to subjects’ therapy and medications during the entire length of stay at the hospital. Medication adjustments included increases or decreases in Parkinson’s disease medications to optimize peak performance. Those medications included carbidopa/levodopa, monoamine oxidase inhibitors, catechol-o-methyltransferase inhibitors and amantadine.

Subjects received individually tailored physical, occupational, and speech therapy for a minimum of 3 hours per day for 5 to 7 days per week. Therapy was provided on an individual and group basis. Interventions included external cueing to improve gait speed, step length and cadence [27–30], cognitive movement strategies during task-based training to improve mobility, balance and transfers [6, 31–33], resistive exercises [34], exercises for joint mobility [35, 36], and speech therapy to improve voice volume and clarity [37, 38]. A more detailed description of the intervention is provided in Table 2.

2.4. Data Analysis. Means, standard deviations, and frequency distributions were calculated for subjects’ baseline characteristics, length of stay, and disposition. The efficacy of the intervention was evaluated by comparing admission and discharge mean scores for each of the outcome measures. Two-tailed paired t tests were conducted with an alpha level set at 0.05. A Bonferroni-adjusted type I error rate (α = 0.007) was applied to all t tests. Results were calculated for patients who received rehabilitation along with PD medication adjustments and for patients who received rehabilitation only. Clinically significant improvement was determined based on a total FIM score change of ≥22, which has been associated with the minimal clinically important difference in people who have suffered a stroke [39]. In this study a change from admission of more than 22 was considered to be clinically meaningful.

3. Results

3.1. Subjects. Ninety-one subjects with atypical parkinsonism underwent rehabilitation therapy. Average age at admission was 76.5 years (SD 0.81), and they had been carrying the diagnosis of parkinsonism for an average of 5.7 years (SD 0.55). Of the 91 subjects with atypical parkinsonism, 25 (27.5%) had vascular parkinsonism, 19 (20.9%) had MSA, 4 (4.4%) had PSP, and the remaining cases were either medication related, due to LBD, CBD, toxin exposure or were unknown. Eighty-five of the subjects were Hoehn and Yahr stages III-V. Six subjects were not evaluated using Hoehn and Yahr (Table 1). The rehabilitation team made changes to 81 subjects’ medications while receiving physical therapy. Ten subjects underwent physical rehabilitation only with no changes to their medications. Length of stay varied from one to six weeks with an average stay of 2.5 weeks.

3.2. Outcomes for All Patients. Statistically significant improvements were made in all outcome measures over the course of the rehabilitation program (Table 3). Total FIM score increased 29.5 points (95% CI = 26.4–32.5). Additionally, motor FIM improved 25.9 points (95% CI = 23.4–28.5) and cognitive FIM improved 3.5 points (95% CI = 2.6–4.4). TUG decreased by 39.4 seconds (95% CI = 20.6–58.2), TMW lengthened by 63.5 feet (95% CI = 44.3–82.9), and Berg balance scale improved 7.5 points (95% CI = 4.3–10.6). Left and right finger tapping improved by 11.5 taps (95% CI = 6.7–16.1) and 10.8 taps (95% CI = 5.8–16.1), respectively.

Previous studies have shown the minimal clinically important difference of total FIM to be 22 [39]. Using this cut-off, sixty-five (74%) patients made clinically meaningful improvements in total FIM.

3.3. Outcomes for Patients Receiving Rehabilitation Only and No Changes to Medication. Statistically significant improvements were made in all but left finger tapping for the 10 patients who received rehabilitation only (Table 4). Analysis showed an improvement of 32.1 (95% CI = 22.8–41.3) for total FIM, 28.6 (95% CI = 19.8–37.3) for motor FIM, and 3.5 (95% CI = 1.7–5.2) for cognitive FIM. TUG decreased by 52 seconds on average (95% CI = 13.1–91.0), TMW length increased by 76 feet (95% CI = 27.4–124.5), and right finger tapping improved by 19.6 taps (95% CI = 3.4–25.7). Left finger tapping increased on average 7.8 taps, but results were not statistically significant (95% CI = −9.7–25.4).

4. Discussion

This study investigated the effectiveness of an interdisciplinary inpatient rehabilitation program for patients with atypical parkinsonism. Our results showed improvements in total FIM, motor FIM, cognitive FIM, TMW, TUG, BBS, and left and right FT. Among patients who received rehabilitation only, without changes to their medication regimens, statistically significant improvement in all but left FT was observed. Clinically meaningful improvement, defined by a change in
Table 2: Description of interventions.

<table>
<thead>
<tr>
<th>Functional training</th>
</tr>
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<tbody>
<tr>
<td>Rolling from supine position to sitting position and from</td>
</tr>
<tr>
<td>sitting position to supine position.</td>
</tr>
<tr>
<td>Transferring from sitting position to standing position,</td>
</tr>
<tr>
<td>from chair to bed, and from chair to toilet.</td>
</tr>
<tr>
<td>Dressing and grooming.</td>
</tr>
<tr>
<td>Balance: reactive and anticipatory within functional</td>
</tr>
<tr>
<td>contexts.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Gait training</th>
</tr>
</thead>
<tbody>
<tr>
<td>Walking with external auditory cues from a metronome to</td>
</tr>
<tr>
<td>optimize gait speed and cadence; increasing cadence by</td>
</tr>
<tr>
<td>10% over baseline and progressing until cadence</td>
</tr>
<tr>
<td>approaches normal or until subject reaches maximum</td>
</tr>
<tr>
<td>capacity.</td>
</tr>
<tr>
<td>Reducing freezing (context specific: doorways,</td>
</tr>
<tr>
<td>thresholds, and narrow spaces) with visual cues in the</td>
</tr>
<tr>
<td>form of lines on the floor from tape or laser beams.</td>
</tr>
<tr>
<td>Reducing freezing (context specific: doorways,</td>
</tr>
<tr>
<td>thresholds, and narrow spaces) with visual cues in the</td>
</tr>
<tr>
<td>form of lines on the floor from tape or laser beams.</td>
</tr>
<tr>
<td>Improving adaptation (various walking surfaces,</td>
</tr>
<tr>
<td>obstacles in the environment, starting and stopping,</td>
</tr>
<tr>
<td>and turning head while walking).</td>
</tr>
<tr>
<td>Curb negotiation and stair climbing.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Range of motion, flexibility, strengthening exercises</th>
</tr>
</thead>
<tbody>
<tr>
<td>Range of motion (increase trunk extension and rotation).</td>
</tr>
<tr>
<td>Stretching (hip flexor, hamstring, and gastrocnemius</td>
</tr>
<tr>
<td>muscles).</td>
</tr>
<tr>
<td>Strengthening (trunk and hip postural muscles and knee</td>
</tr>
<tr>
<td>and ankle extensor muscles).</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Speech exercises</th>
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</thead>
<tbody>
<tr>
<td>Exercises to improve vocal rate control.</td>
</tr>
<tr>
<td>Exercises to improve phonation.</td>
</tr>
</tbody>
</table>

Table 3: All patients.

<table>
<thead>
<tr>
<th>Measure (n)a</th>
<th>Admission mean (SD)</th>
<th>Discharge mean (SD)</th>
<th>Change (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total FIM (88)</td>
<td>41.3 (15.7)</td>
<td>70.8 (21.4)</td>
<td>29.5 (28.4, 32.5)</td>
</tr>
<tr>
<td>Motor FIM (88)</td>
<td>23.6 (11)</td>
<td>49.6 (16.6)</td>
<td>25.9 (23.4, 28.5)</td>
</tr>
<tr>
<td>Cognitive FIM (87)</td>
<td>17.7 (6.1)</td>
<td>21.2 (5.8)</td>
<td>3.5 (2.6, 4.4)</td>
</tr>
<tr>
<td>TUG (60)</td>
<td>81.5 s (89.4)</td>
<td>42.0 s (46.9)</td>
<td>−39.4 s (−20.6, −28.2)</td>
</tr>
<tr>
<td>TMW (60)</td>
<td>138.9 ft (76.9)</td>
<td>202.5 ft (96.9)</td>
<td>63.5 ft (44.2, 82.9)</td>
</tr>
<tr>
<td>BBS (28)</td>
<td>22 (12.2)</td>
<td>29.5 (13.4)</td>
<td>7.5 (4.3, 10.6)</td>
</tr>
<tr>
<td>Left FT (51)</td>
<td>60.2 (23.3)</td>
<td>71.7 (24.8)</td>
<td>11.5 (6.7, 16.1)</td>
</tr>
<tr>
<td>Right FT (50)</td>
<td>68.3 (27)</td>
<td>79.3 (30)</td>
<td>10.9 (5.8, 16.1)</td>
</tr>
</tbody>
</table>


total FIM of greater than 22, was also observed in 74% of patients. These results imply that patients with atypical parkinsonism can show significant improvement in function after receiving intensive inpatient multidisciplinary therapy including rehabilitative and pharmacologic interventions.

Patients with atypical parkinsonism are difficult to manage on an outpatient basis. The complexity of their symptoms, the added cognitive and autonomic deficits, the poor response to most PD pharmacological agents, and the relatively rapid decline in status contribute to the challenges in managing these patients particularly as the disease progresses. This study highlights the benefits of an interdisciplinary rehabilitation program in addition to medication adjustments in an inpatient setting, where patients could be observed over a 24-hour period, 7 days per week by health care professionals with expertise in movement disorders. Objective measures taken daily during peak and troughs of medication cycle allowed an objective, systematic assessment of function. This data was used to guide the decision-making process regarding pharmacological adjustments and the focus of rehabilitation strategies.

Strengths of our study include the large sample size, the variety of disorders, and the advanced disability stages of the patients. Other studies investigating the effectiveness of rehabilitation have been case reports, small pretest-posttest trials with a sample size of 19 or less, and a pilot RCT with a sample size of 17 [6, 8–10, 12–15]. In addition, most of the studies included subjects with PSP, whereas our study sampled across categories of atypical parkinsonism and included primarily vascular parkinsonism and MSA. Our patients were also at higher levels of disability and all were Hoehn and Yahr stages III to V, suggesting that functional gains can be made in these patients with complex symptoms in later stages of the disease.

Limitations of the study include lack of a control group and prescribing rehabilitation while simultaneously changing medications. We are unable to distinguish what effects were due purely to physical rehabilitation. However, our smaller group of 10 patients who received rehabilitation only did show significant improvement, but larger studies should be conducted to address the particular effects of rehabilitation alone. It is also difficult to assess whether the intensive
nature of the program itself had any effect on the subjects’ improvement. The higher frequency of assessments and therapy sessions in an inpatient setting may have continued to the improvements observed. Factors such as treatment intensity, the availability of objective data for treatment decisions and goal setting, and the expertise and frequent communication of the interdisciplinary team were not individually assessed. Further studies comparing specialized interdisciplinary movement disorder rehabilitation programs such as the program described in this study with more traditional standard rehabilitative care would help clarify this question.

Another limitation of our study is the lack of long-term followup data. It is unknown if the gains made during the rehabilitation admission were sustained following discharge. One study of patients with idiopathic PD in Hoehn and Yahr stages II and III who participated in an inpatient exercise training and muscle strengthening program sustained improvements in quality of life at follow-up [40]. Lastly, the gains in the total FIM used to assess clinically meaningful improvement were extrapolated from the stroke literature [39], as this has not been derived in parkinsonian patients.

While our study demonstrated that patients with atypical parkinsonism can benefit from an intensive inpatient rehabilitation program, further studies are needed to look at the long-term gains. In addition, research is needed to assess the efficacy of inpatient rehabilitation programs on atypical parkinsonism patients with earlier stages of disease and their effect on the progression of their disorders.

References


Table 4: Patients receiving rehabilitation only.

<table>
<thead>
<tr>
<th>Measure (n)a</th>
<th>Admission mean (SD)</th>
<th>Discharge mean (SD)</th>
<th>Change (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total FIM (10)</td>
<td>38.3 (13.4)</td>
<td>70.4 (23.4)</td>
<td>32.1 (22.8, 41.3)</td>
</tr>
<tr>
<td>Motor FIM (10)</td>
<td>21.2 (7.8)</td>
<td>49.6 (17.6)</td>
<td>28.6 (19.8, 37.2)</td>
</tr>
<tr>
<td>Cognitive FIM (10)</td>
<td>17.1 (6.1)</td>
<td>20.6 (6.1)</td>
<td>3.5 (1.7, 5.2)</td>
</tr>
<tr>
<td>TUG (10)</td>
<td>83.4 s (61.5)</td>
<td>31.3 s (10.1)</td>
<td>−52.1 s (−13.7, −91.0)</td>
</tr>
<tr>
<td>TMW (9)</td>
<td>114.4 ft (77.6)</td>
<td>190.4 ft (68.4)</td>
<td>76.0 ft (27.4, 124.5)</td>
</tr>
<tr>
<td>Left FT (8)</td>
<td>61.5 (19.8)</td>
<td>69.3 (13.4)</td>
<td>7.8 (−9.7, 25.4)</td>
</tr>
<tr>
<td>Right FT (8)</td>
<td>67.2 (24.8)</td>
<td>86.8 (24.9)</td>
<td>19.6 (3.4, 35.7)</td>
</tr>
</tbody>
</table>


Review Article

A Review of Dual-Task Walking Deficits in People with Parkinson’s Disease: Motor and Cognitive Contributions, Mechanisms, and Clinical Implications

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Gait impairments in Parkinson’s disease (PD) are exacerbated under dual-task conditions requiring the simultaneous performance of cognitive or motor tasks. Dual-task walking deficits impact functional mobility, which often requires walking while performing concurrent tasks such as talking or carrying an object. The consequences of gait impairments in PD are significant and include increased disability, increased fall risk, and reduced quality of life. However, effective therapeutic interventions for dual-task walking deficits are limited. The goals of this narrative review are to describe dual-task walking deficits in people with PD, to discuss motor and cognitive factors that may contribute to these deficits, to review potential mechanisms underlying dual-task deficits, and to discuss the effect of therapeutic interventions on dual-task walking deficits in persons with PD.

1. Introduction

Gait impairments and walking limitations are common among people with Parkinson’s disease (PD). While gait abnormalities are not pronounced in the early stages of PD, their prevalence and severity increase with disease progression. Within 3 years of diagnosis, over 85% of people with clinically probable PD develop gait problems [1]. The potential consequences of gait impairments in PD are significant and include increased disability [2, 3], increased risk for falls, and reduced quality of life. Falls are common among people with PD and can result in fear of falling, injury, and hospitalization [4–10]. The estimated prevalence of falls in PD ranges from 40 to 90% and increases with the duration of follow-up [4, 5, 11–16]. It is estimated that 45–50% of falls in this population occur when walking [5, 17], with balance and walking deficits commonly identified as risk factors for falls [5, 10–12, 14, 18, 19]. Reduced quality of life is also associated with balance and gait abnormalities in PD, including festination and freezing of gait [2, 20–24]. In fact, people with PD consider mobility and walking limitations to be among the worst aspects of the disease [25].

Mobility in daily life frequently requires walking while performing simultaneous cognitive or motor tasks, such as talking with a friend or carrying a cup of coffee. Gait impairments in people with PD are exacerbated under such dual-task conditions. In recent years, dual-task walking research has expanded rapidly. The association of gait impairments with adverse consequences like increased fall risk has motivated research into clinical strategies to assess and treat dual-task walking deficits in PD. Several recent review papers have been published on dual-task posture and gait deficits among older adults and in a general neurologic population [26–29], but none have focused specifically on people with PD. While people with PD demonstrate dual-task deficits in a variety of movements, including postural control tasks [30, 31], upper extremity movements [32, 33], and speech [34], the focus of this paper is dual-task walking. The goals of this review are to describe dual-task walking deficits in people with PD, to discuss motor and cognitive factors that may contribute to these deficits, to review potential mechanisms underlying dual-task deficits, and to discuss the effect of therapeutic interventions on dual-task walking deficits in persons with PD.
2. Dual-Task Walking Deficits in PD

Single-task gait impairments in PD include reduced speed and stride length and increased double limb support time and stride-to-stride variability [35–38]. With progression of PD, gait abnormalities worsen, and festination, freezing, and dystonic or dyskinetic gait patterns can emerge [39]. Gait impairments in PD are exacerbated under dual-task conditions, with further reductions in gait speed and stride length [40–46], decreased symmetry and coordination between left and right steps [47, 48], and increased stride-to-stride variability [45, 49, 50]. This section will review reported dual-task walking deficits in people with PD and will consider factors that influence the magnitude of these deficits.

2.1. Individual, Task, and Environment Framework. Table 1 summarizes dual-task walking studies in people with PD, including relevant individual, task, and environmental characteristics of each study. Comparing dual-task walking deficits across studies is challenging because of variations in methodology. In Table 1, decrements in walking under dual-task conditions are expressed as a percentage of single-task performance, commonly referred to as the dual-task cost (DTC = [dual-task – single-task]/single-task ∗ 100) [51, 52]. The DTC allows a more direct comparison of dual-task deficits across studies and provides a way to assess the relative effects of individual, task, and environmental factors. For example, a study by Plotnik and colleagues measured gait speed DTCs of 17% in people with moderate PD, on medication, when walking approximately 80 m and performing serial-3 subtractions [45]. Lord and colleagues measured gait speed DTCs of 32% in people with moderate PD, off medication, when walking approximately 6.5 m in their home while carrying a tray and counting auditory tones [43]. Dual-task walking deficits can be compared using the DTC even though these studies varied in terms of the participants’ medication status, the concurrent tasks used, and the environment where walking occurred. Because multiple factors differed between studies, it is not clear whether the greater DTCs reported by Lord and colleagues are due to off-medication status, more challenging concurrent tasks, or a more complex home environment. When assessing dual-task deficits in PD, it is important to consider individual characteristics such as the severity of motor and cognitive impairments, the complexity of both walking and concurrent tasks, and the overall challenge presented by the environment.

2.2. Individual Factors. Studies of dual-task walking in PD vary substantially with respect to participant characteristics. Dual-task walking deficits increase with age among healthy adults [29, 60, 61], but people with PD consistently demonstrate greater dual-task walking deficits than healthy, age-matched individuals [42, 44, 50, 54, 59]. For example, O’Shea and colleagues found that people with PD had greater dual-task declines in gait speed than healthy older adults, with gait speed DTCs of −18% to −19% in the PD group compared to −7% in the control group [44]. Most research has examined people with mild-to-moderate disease severity, as measured by the Unified Parkinson Disease Rating Scale (UPDRS) and Hoehn and Yahr scores, although disease severity is associated with dual-task walking deficits [43, 57]. The majority of studies examined the impact of concurrent task performance during the on-medication state, though a small number of studies examined dual-task walking in people with PD in the off-medication state only [43, 59]. Studies that examined the effects of medication demonstrated improvements in dual-task walking performance on-medication compared to off-medication [53, 57]. Some studies specifically examined individuals with PD and freezing [53, 55, 59], motor response fluctuations [45], or a history of falls [62]. For example, research comparing people with PD and freezing to those without freezing demonstrated increased dual-task walking deficits when walking forwards, turning, and walking backwards [53, 55, 59].

2.3. Task Factors. Dual-task studies in PD also vary in terms of walking and concurrent task characteristics. Most examined walking on a level surface at a self-selected speed, but some included more complex walking tasks. For example, some walking tasks involved sit-to-stand transfers and/or turning [43, 46, 53, 54, 57–59], and one study examined backwards walking [55]. Concurrent tasks varied in terms of type (cognitive or motor), domain, and difficulty. Concurrent cognitive tasks included mental tracking, such as attentional tasks [43, 50, 59] or arithmetic calculations [41, 42, 44, 45, 47–50, 55, 56], verbal fluency or conversational tasks [42, 53, 54], and memory tasks [46, 50]. Concurrent motor tasks were used less commonly and included carrying objects [40, 43, 46, 57, 58] or manipulating objects [42, 44]. It is not clear whether motor or cognitive tasks have a greater impact on walking in people with PD. One study found similar impacts of cognitive and motor tasks [44], while other studies showed a greater impact of cognitive tasks [42, 46]. However, the tasks incorporated differed in terms of both type and complexity, limiting the ability to make direct comparisons. Studies that controlled task domain and varied task difficulty suggest that more complex tasks have a greater effect on walking in PD [40, 54, 56].

Typically, no specific instructions are provided regarding which task to prioritize during dual-task conditions. In most cases, participants were either instructed to focus on both tasks or instructions were not specified. However, most studies quantified dual-task changes in walking only and did not measure concurrent task performance, making it difficult to determine if there were between-task trade-offs. DTCs provide a means to assess trade-offs between walking and concurrent task performance [63]. In studies that examined dual-task changes in both walking and the concurrent task, most showed declines in both [44, 50]. Only one study demonstrated concurrent task improvements and walking declines under dual-task conditions [42], consistent with trade-offs between tasks and prioritization of the concurrent task over walking.
Table 1: Summary of studies examining dual-task walking in people with PD. Relevant individual, task, and environmental aspects of each study are included. Dual-task costs for walking and the concurrent task are included where they could be calculated.

<table>
<thead>
<tr>
<th>Study (PD sample)</th>
<th>Age (yrs)</th>
<th>Disease severity</th>
<th>Cog.</th>
<th>Walking task &amp; environment</th>
<th>Concurrent task</th>
<th>Instruct.</th>
<th>Walking DTC</th>
<th>Concurrent task DTC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bond and Morris, 2000 [40] (n = 12)</td>
<td>65 (10)</td>
<td>Webster score 13 (5)</td>
<td>STMS: 30 (4)</td>
<td>Walk 10 m (comfortable pace)</td>
<td>Motor: (1) carry tray; (2) carry tray with empty glasses</td>
<td>No prioritization</td>
<td>Speed: (1) −2%; (2) −11%</td>
<td>Stride length: (1) +1%; (2) −1% DLS: (1) −2%; (2) −2%</td>
</tr>
<tr>
<td>Brown et al., 2009 [41] (n = 10)</td>
<td>67 (7)</td>
<td>UPDRS: 28 (2) H&amp;Y: 2.3 (0.3)</td>
<td>MMSE: ≥26</td>
<td>Walk 10 m (self-selected pace, unobstructed walkway)</td>
<td>Cognitive: serial-3 subtraction (data presented for no music trials)</td>
<td>None provided</td>
<td>Speed: −20%</td>
<td>Stride length: −6% DLS: −12%</td>
</tr>
<tr>
<td>Camicioli et al., 1998 [53] (n = 10)</td>
<td>67 (9)</td>
<td>Off-med On-med</td>
<td>UPDRS: 15 (4) UPDRS: 12 (6)</td>
<td>Walk 4.6 m, turn 180°, walk 4.6 m (self-selected pace)</td>
<td>Cognitive: verbal fluency (recite male names)</td>
<td>Not specified</td>
<td>Steps: −40% Time: −50% Steps: −16% Time: −31%</td>
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<tr>
<td>Campbell et al., 2003 [54] (n = 9)</td>
<td>74 (7)</td>
<td>H&amp;Y: 2.8 (0.8)</td>
<td>Timed Up and Go (3 m; comfortable pace)</td>
<td>Cognitive: (1) repeat phrase; (2) repeat days of the week backwards</td>
<td>Not specified</td>
<td>Steps: (1) +1%; (2) −13% Time: (1) −1% (2) −31%</td>
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<tr>
<td>Galletly and Brauer, 2005 [42] (n = 16)</td>
<td>65 (10)</td>
<td>UPDRS: 14 (6) MMSE: 28 (3)</td>
<td>Walk 10 m (comfortable pace)</td>
<td>Motor: (1) button press Cognitive: (2) serial-3 subtraction; (3) verbal fluency</td>
<td>“Concentrate on both tasks”</td>
<td>Speed: (1) −7%; (2) −21%; (3) −21% Stride length: (1) −4%; (2) −16%; (3) −16% Motor: (1) +16% Cognitive: (2) +31%; (3) +73%</td>
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<tr>
<td>Hackney and Earhart, 2009 [55] (n = 78)</td>
<td>65 (10)</td>
<td>UPDRS: 28 (9)</td>
<td>Walk 5 m (comfortable pace both forward and backward)</td>
<td>Cognitive: mental arithmetic (serial-3, 4, and 6 subtraction)</td>
<td>Not specified</td>
<td>*Speed: −33% *Stride length: −14%</td>
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<tr>
<td>Hausdorff et al., 2003 [49] (n = 10)</td>
<td>Range: 52–82</td>
<td>UPDRS: 14</td>
<td>MMSE: 27</td>
<td>Walk 20 m (normal pace; level ground)</td>
<td>Cognitive: serial-7 subtraction</td>
<td>“Walk while performing subtractions”</td>
<td>Stride time: −10% Stride time variability: −154%</td>
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<tr>
<td>LaPointe et al., 2010 [56] (n = 25)</td>
<td>67</td>
<td>H&amp;Y: 2.4 (7) DRS-2: 136 (7)</td>
<td>Walk 4.3 m</td>
<td>Cognitive: (1) count by 1’s; (2) serial-3 subtraction; (3) recite alpha-numeric sequence</td>
<td>Not specified</td>
<td>**Speed: (1) −2%; (2) −12%; (3) −19% **Stride length: (1) −1%; (2) −6%; (3) −10% DLS: (1) −4%; (2) −9%; (3) −10%</td>
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<tr>
<td>Study (PD sample)</td>
<td>Individual Characteristics</td>
<td>Task and Environmental Characteristics</td>
<td>Results</td>
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<tr>
<td>Lord et al., 2010 [43] (n = 29)</td>
<td>Age (yrs): 71 (7)</td>
<td>Disease severity: UPDRS: 39 (15)</td>
<td>Walking task &amp; environment: Stand from a chair, walk 5–11 m (preferred speed; examined in home &amp; distance varied by home)</td>
<td>Concurrent task: Motor: (1) carry tray with 2 beakers of water Cogn. Cognitive: (2) count auditory tones (3) Motor + Cognitive Instruct: “Concentrate equally on walking and task(s)”</td>
<td>Walking DTC: Speed: (1) −24%; (2) −14%; (3) −32% Concurrent task DTC: —</td>
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<tr>
<td>Lord et al., 2011 [57] (n = 50)</td>
<td>Age (yrs): 69 (7)</td>
<td>Disease severity: Off-med On-med UPDRS: 35 (9) MMSE: 28 (2)</td>
<td>Walking task &amp; environment: Walk 6 m, turn 180°, walk 6 m (examined in home)</td>
<td>Concurrent task: Motor: carrying a tray with 2 cups of water Instruct: “Concentrate on task as a whole”</td>
<td>Walking DTC: Speed: −13% Stride time Variability: −8% Speed: −11% Stride time Variability: −21% Concurrent task DTC: —</td>
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<tr>
<td>O'Shea et al., 2002 [44] (n = 15)</td>
<td>Age (yrs): 68 (7)</td>
<td>Disease severity: Modified Webster Scale: 12 (6) STMS: 30 (3)</td>
<td>Walking task &amp; environment: Walk 10 m (preferred pace)</td>
<td>Concurrent task: Motor: (1) coin transfer Cognitive: (2) serial-3 subtraction Instruct: Not specified</td>
<td>Walking DTC: Speed: (1) −18%; (2) −19% Stride length: (1) −14%; (2) −12% DLS: (1) −3%; (2) −6% Concurrent task DTC: Motor: (1) −17.4% Cognitive: (2) −5%</td>
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<tr>
<td>Plotnik et al., 2011 [45] (n = 30)</td>
<td>Age (yrs): 66 (7)</td>
<td>Disease severity: UPDRS: 35 (10) H&amp;Y: 2.1 (0.6) MMSE: 29 (1)</td>
<td>Walking task &amp; environment: Walk ~80 m in a level, ~20 m corridor (comfortable pace)</td>
<td>Concurrent task: Cognitive: (1) serial-3 subtraction; (2) serial-7 subtraction Instruct: Not specified</td>
<td>Walking DTC: Speed: (1) −17%; (2) −23% Stride length: (1) −11%; (2) −15% Stride time variability: (1) −39%; (2) −51% Concurrent task DTC: —</td>
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<tr>
<td>Rochester et al., 2004 [46] (n = 20)</td>
<td>Age (yrs): 65 (8)</td>
<td>Disease severity: H&amp;Y: 2.7 (0.7) MMSE: 27 (2)</td>
<td>Walking task &amp; environment: Stand from a chair, walk 6.6 (1.5) m, return (preferred speed, examined in home &amp; distance varied by home)</td>
<td>Concurrent task: Motor: (1) carrying tray with 2 cups of water; Cognitive: (2) autobiographical memory task(3) Motor + Cognitive Instruct: Not specified</td>
<td>Walking DTC: Speed: (1) −9%; (2) −21%; (3) −23% Step length: (1) −9%; (2) −16%; (3) −21% Concurrent task DTC: —</td>
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<tr>
<td>Study (PD sample)</td>
<td>Individual Characteristics</td>
<td>Task and Environmental Characteristics</td>
<td>Results</td>
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<td></td>
<td>Age (yrs)</td>
<td>Disease severity</td>
<td>Cog.</td>
<td>Walking task &amp; environment</td>
<td>Concurrent task</td>
<td>Instruct.</td>
<td>Walking DTC</td>
<td>Concurrent task DTC</td>
</tr>
<tr>
<td>Spildooren et al., 2010 [59]</td>
<td>69 (7)</td>
<td>Off-med</td>
<td>MMSE: 28 (1)</td>
<td>Walk 5 m: (1) straight; (2) turn 180°; (3) turn 360°</td>
<td>Cognitive: color identification (auditory attentional task)</td>
<td>No prioritization</td>
<td>Steps: (1) −25%; (2) −16%; (3) −13%</td>
<td>Time: (1) −23%; (2) −13%; (3) −10%</td>
</tr>
<tr>
<td>Freezeers (n = 14)</td>
<td>67 (7)</td>
<td>Off-med</td>
<td>MMSE: 29 (1)</td>
<td>Steps: (1) −7%; (2) +1%; (3) −2%</td>
<td>Time: (1) −9%; (2) −1%; (3) −3%</td>
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<tr>
<td>Non-freezers (n = 14)</td>
<td>71 (8)</td>
<td>UPDRS: 38 (14) H&amp;Y: 2.5 (0.5)</td>
<td>MMSE: 28 (1)</td>
<td>Walk 2 min in a level, 25 m corridor (comfortable pace)</td>
<td>Cognitive: (1) listen to a tape &amp; answer questions; (2) above task + phoneme monitoring; (3) serial-7 subtraction</td>
<td>No prioritization</td>
<td>Speed: (1) −10%; (2) −13%; (3) −19%; Stride time variability: (1) −1%; (2) −6%; (3) −27%</td>
<td>Cognitive: (1) −42%</td>
</tr>
<tr>
<td>Yoge et al., 2005 [50]</td>
<td>72 (7)</td>
<td>UPDRS: 34 (10) H&amp;Y: 2.4 (0.3)</td>
<td>MMSE: 29 (1)</td>
<td>Walk 2 min in a level, 25 m corridor (comfortable pace)</td>
<td>Cognitive: serial-7 subtraction</td>
<td>No prioritization</td>
<td>Gait asymmetry: −43%</td>
<td>—</td>
</tr>
</tbody>
</table>

*: data collapsed across forward & backward walking; **: data collapsed across PD & control groups; Cog.: cognitive status; DLS: double limb support; DRS-2: Dementia Rating Scale-2; DTC: dual-task cost; H&Y: Hoehn & Yahr stage; Instruct.: instructions provided during dual-task conditions; MMSE: Mini-Mental State Examination; MoCA: Montreal Cognitive Assessment; STMS: Short Test of Mental Status; Steps: number of steps required to complete walking task; Time: time required to complete walking task; UPDRS: Unified Parkinson Disease Rating Scale, motor examination.
2.4. Environmental Factors. Studies that systematically manipulate environmental factors to determine the effects on dual-task walking deficits in PD are lacking. Most research was conducted in a clinical or laboratory environment, but some was conducted in participants’ homes [43, 46, 57, 58]. Studies conducted in the home environment may be more representative of mobility challenges in daily life.

In summary, the literature as a whole confirms the presence of significant dual-task walking deficits among persons with PD, despite methodological variations in participant characteristics, task demands, and environmental constraints. The extent of these deficits appears to vary as a function of individual, task, and environmental characteristics, but the relative contribution of each factor is not well understood. Carefully controlled studies are needed to better quantify how these factors impact dual-task walking deficits in people with PD.

3. Motor and Cognitive Factors Contributing to Dual-Task Walking Deficits

3.1. Motor Factors. It is not clear how motor and cognitive symptoms contribute to either single-task or dual-task walking deficits in PD. The motor phenotype of PD is heterogeneous, with cardinal features of rigidity, tremor, and bradykinesia [64]. These symptoms, as well as primary impairments in locomotor control pathways [65], can contribute to both single- and dual-task gait abnormalities. The relative contributions of these factors may vary with disease progression. Cardinal symptoms may contribute more to walking deficits early in the disease, while primary gait impairments might predominate later in the disease.

Single-task walking deficits have been associated with a variety of motor symptoms in PD. For example, increased axial rigidity is associated with poorer performance on single-task measures of balance and functional mobility [66, 67]. In addition, rigidity may contribute to reduced lower extremity joint excursions and a forward flexed posture when walking [39]. Bradykinesia can lead to shortened step length and reduced gait speed during walking [39]. Postural instability, another common motor symptom, may contribute to gait impairments such as increased stride-to-stride variability and double limb support. Several motor factors are associated with dual-task walking deficits in PD. Dual-task gait speed has been associated with disease severity, as measured by Hoehn and Yahr stage [46] and UPDRS motor subscale scores [43]. The severity of PD motor symptoms has also been related to single- and dual-task gait variability both off and on medication [57]. Dual-task walking performance in people with PD has been associated with performance-based measures of balance [46]. Though not a specific motor symptom of PD, some [46], but not all [43, 57], studies have found associations between physical fatigue and dual-task walking deficits in PD. Dual-task walking deficits in PD are also associated with primary gait deficits. Dual-task changes in speed and stride length were associated with performance on single-task mobility tests in people with PD [45]. In addition, dual-task walking deficits were greater in people with PD and freezing of gait compared to those without freezing [53, 55, 59]. Although dual-task walking deficits have been associated with both motor symptom severity and primary gait impairments, the relative contribution of each to dual-task walking deficits has not been well quantified.

3.2. Cognitive Factors. PD is associated with a variety of cognitive impairments, including executive function, attention, memory, language, and visuospatial impairments [68–70], that could contribute to dual-task walking deficits. Cognitive profiles in PD are variable [71] and range from mild deficits in specific cognitive domains to severe dementia affecting multiple domains. It is estimated that 19–30% of people with early, newly-diagnosed PD present with cognitive impairments [72–74], and these impairments worsen with disease progression [69]. The presence of mild cognitive impairment in people with PD is associated with development of dementia within 4 years [75]. The prevalence of dementia in PD is estimated at 26–44% [76, 77], with over 80% of people developing dementia within 20 years of diagnosis [13]. Depression can exacerbate cognitive impairments in PD [78], and the frequency of depression in PD is estimated at 25–33% [79, 80]. Specific cognitive functions, such as set shifting, divided or alternating attention, and response inhibition, may be particularly relevant to dual-task walking [28]. Dual-task walking deficits in PD have been associated with impairments in executive function, set-shifting, and attention [43, 45, 46]. For example, Plotnik and colleagues [45] demonstrated a relationship between set shifting, as measured by the Trail Making Test, and dual-task changes in gait speed and step length. Dual-task changes in gait variability were related to executive function, including set shifting and global cognition [45, 50, 57]. Executive function, measured by the Brixton test, has also been associated with gait speed [46] and gait speed DTCs [43]. Deficits in attention were associated with greater deficits in gait variability [57] and increased gait speed DTCs [43]. Finally, depression has been related to gait speed declines and gait variability increases under dual-task conditions in some studies [46, 57], though associations between dual-task parameters and affect (both depression and anxiety) were not supported by all studies [45].

Cognitive impairments can contribute to dual-task walking deficits in various ways. First, they may limit the ability to compensate for gait impairments using cognitive strategies. People with PD are often taught conscious strategies to improve their gait pattern, such as focusing on walking with longer steps. The type and severity of cognitive impairments may limit the ability to use such strategies to compensate for gait abnormalities. Also, impaired executive function might result in the inappropriate or unsafe prioritization of tasks when walking under dual-task conditions. Bloem and colleagues have proposed that increased fall risk in people with PD may result in part from a “posture second” prioritization strategy, in which concurrent tasks are prioritized above walking [81, 82]. Consistent with this idea, falls in
PD have been associated with reduced performance on a variety of cognitive measures [83, 84]. The prevalence of cognitive impairments in PD and their associations with dual-task walking deficits suggest that they are an important contributing factor. Further research is needed, however, because little is known about how the domains and severity of cognitive impairments affect dual-task walking deficits and their response to therapeutic interventions.

### 4. Potential Mechanisms Underlying Dual-Task Walking Deficits

The mechanisms responsible for interference between walking and concurrent cognitive or motor tasks in people with PD are not clear. Because multiple factors contribute to dual-task walking deficits, it is likely that a number of different mechanisms contribute to these deficits. In addition, characteristics of the concurrent task, such as type, domain, and difficulty, will impact the mechanisms and resources involved in dual-task performance. This section will review both nonspecific mechanisms proposed to explain dual-task interference across populations as well as specific mechanisms that may contribute to dual-task walking deficits in PD.

#### 4.1. Nonspecific Mechanisms

Two general theoretical frameworks have been proposed to explain dual-task interference. Capacity theory conceptualizes the information processing needed for dual-task performance as a flexible but limited resource [27, 85, 86]. Performance of any given task, like walking, requires some portion of this capacity. When two tasks are performed concurrently, competition for limited resources results in dual-task interference and deterioration in performance of one or both tasks [26]. According to this theory, information processing resources such as attention can be flexibly allocated between tasks, with many factors potentially influencing resource allocation [86]. For example, differences in dual-task performance can result from individual differences in overall capacity, and intra-individual variability in dual-task performance can arise from transient variations in effective capacity due to factors like motivation, fatigue, or arousal [86]. Task-related factors also influence resource allocation. For example, a recent meta-analysis demonstrated that dual-task gait speed declines varied as a function of the concurrent cognitive task in healthy young and older adults and a general neurologic population [29].

A second general theory to explain dual-task interference is the bottleneck theory [87]. According to this theory, dual-task performance requires serial or sequential processing of the two concurrent tasks. Dual-task interference results when two tasks compete for the same processing resources. In order to complete one task, processing of the second task is temporarily postponed, resulting in performance decrements in the second task. Dual-task walking studies are limited in their ability to discriminate between these two theories, but these general mechanisms may inform methodological choices and subsequent interpretations.

#### 4.2. PD-Specific Mechanisms

Several mechanisms specific to PD may also contribute to dual-task walking deficits. These mechanisms are not mutually exclusive, but might overlap with one another. Consistent with the capacity theory, a first specific mechanism in people with PD is reduced movement automaticity. Automaticity refers to the ability to perform a skilled movement without conscious or executive control or attention directed toward the movement [88, 89]. The control of standing and walking was previously thought to be automatic, but the role of cognitive and executive functions in postural control is increasingly appreciated [26, 28]. For example, in healthy young and older adults, simple reaction times increased when walking compared to sitting, reflecting greater attentional demands for walking [90, 91]. The basal ganglia are proposed to play a role in the automatic control of movement [65]. In people with PD, basal ganglia dysfunction may lead to reduced movement automaticity and the need for increased reliance on cognitive resources to control movements. During dual-task upper extremity movements, people with PD demonstrated greater levels of activity in premotor and prefrontal cortical areas compared to healthy individuals, as measured by functional magnetic resonance imaging [92]. Similarly, people with PD may rely on greater cognitive control during walking, even under single-task conditions [37, 93]. If reduced movement automaticity contributes to dual-task walking deficits in people with PD, rehabilitation strategies designed to improve the automatic control of walking should improve dual-task walking.

A second mechanism that could contribute to dual-task walking deficits in PD is dopamine-mediated dysfunction of the basal ganglia. Multiple parallel pathways through the basal ganglia subserve different functions, including motor, cognitive, and limbic functions [94–96]. Degeneration of dopaminergic neurons in PD appears to affect both motor and cognitive circuits within the basal ganglia. Pathology of basal ganglia circuits that project to the dorsolateral prefrontal cortex may contribute to the executive function deficits that are prominent in people with PD [97, 98]. For example, specific deficits in set shifting, which are associated with dual-task walking deficits in PD [45], are thought to be mediated by the dorsolateral prefrontal cortex [98]. Dual-task walking deficits are improved by anti-parkinson medications [53, 57], supporting the idea that motor and cognitive impairments are due in part to dopaminergic pathways. However, the impact of anti-parkinson medications may be limited to those impairments mediated by dopamine dysfunction, and many studies demonstrate dual-task walking deficits in people with PD in the on-medication state.

A third mechanism that could contribute to dual-task walking deficits in PD is the presence of nondopaminergic pathology, which may affect both gait and cognition. It is increasingly appreciated that the pathology of PD is not limited to dopamine but includes other neurotransmitter systems, such as serotonin, norepinephrine (noradrenaline), or acetylcholine [71, 99, 100]. Dysfunction in multiple neurotransmitter systems may contribute to gait [101, 102] and cognitive impairments in PD [71]. Thus, non-dopaminergic
pathways may also contribute to dual-task walking deficits in PD. Consistent with this idea, dual-task walking deficits persist even when people with PD are optimally medicated [42, 44, 50, 54, 59].

In summary, research suggests a number of general and specific mechanisms that may contribute to dual-task walking deficits in PD. These mechanisms are not mutually exclusive, and the relative contribution of each may depend on factors like the symptom profile of the individual and the specific task combination performed under dual-task conditions. A better understanding of the mechanisms responsible for dual-task walking deficits in PD can inform novel therapeutic approaches and enhance our ability to identify optimal interventions.

5. Therapeutic Interventions: Impact on Dual-Task Walking Deficits

The effects of various interventions on single-task walking in PD have been well described, but there is less research examining the efficacy of different pharmacological, surgical, or rehabilitative therapies on dual-task walking in this population. Because gait impairments in PD are exacerbated by dual-task conditions, which are common in daily life, it is important to understand how various therapeutic interventions affect dual-task walking.

5.1. Pharmacological Interventions. The reported effects of anti-parkinson medications on walking in PD are variable, even under single-task conditions. Medications improve aspects of single-task walking, including gait speed and stride length, but may not influence others, like stride-to-stride variability [38, 103, 104], festination, and freezing of gait [39, 105, 106]. As noted above, anti-parkinson medications increase speed and decrease variability during dual-task walking in PD [57] and even increase dual-task walking speed in those with freezing [53]. Neither of the above studies examined the effects of medication on concurrent task performance, so it is unclear if medication-related improvements were due to trade-offs between walking and the concurrent task. Medications can have limited or adverse effects on cognitive functions like set shifting [107] and certain types of learning [108, 109] that are critical to dual-task walking. As a result, medications could negatively affect dual-task walking or result in dual-task walking improvements at the expense of concurrent cognitive task performance. The positive effects of anti-parkinson medications on dual-task walking are consistent with a contribution from dopaminergic mechanisms, but persistent deficits in the on-medication state suggest that non-dopaminergic mechanisms may also contribute to dual-task interference.

5.2. Surgical Interventions. The reported effects of surgery on single-task walking are inconsistent. For example, initial improvements in postural control and gait as a result of deep brain stimulation are not sustained beyond 2–9 years [110]. In the short term, subthalamic nucleus stimulation can improve single-task gait speed and stride length, particularly in the off-medication condition [111, 112], but the individual response to subthalamic nucleus stimulation in the on-medication state is variable [113]. To date, no research has examined the effects of deep brain stimulation or ablative surgeries on dual-task walking in people with PD. The limited research on dual-task upper extremity movements is equivocal, with one study showing no effect of subthalamic nucleus stimulation [114] and one showing a decline [115].

5.3. Rehabilitation Interventions. There is considerable research demonstrating training-related improvements in single-task walking in persons with PD [116–122]. However, it is not clear whether dual-task walking deficits can be improved with practice in PD or, alternatively, whether clinicians should teach people with PD to avoid dual-task conditions to improve safety [123]. A variety of rehabilitation strategies to improve dual-task walking in PD have been studied, with most research focusing on external cues, cognitive or attentional strategies, and dual-task gait training.

External visual, auditory, or somatosensory cues improve both single- and dual-task walking in PD [42, 124–129], even among those with de novo PD [130] or cognitive impairment [131]. For example, Rochester and colleagues examined the effects of external rhythmic cues (auditory, visual, and somatosensory) on walking in people with PD [128]. Cueing therapy was provided over nine 30-minute sessions in the home and consisted of training during single- and dual-task walking and during various functional walking tasks. Speed and step length improved during both single- and dual-task cued walking conditions. These improvements transferred to noncued walking and were retained at 6-week follow-up testing. The authors suggest that dual-task walking improvements were likely due to improved walking automaticity. Based on this research, external cueing appears to improve walking under both single- and dual-task conditions in people with PD. However, studies of cue training vary in terms of cueing modality, training duration, tests used for outcomes assessment, and length of follow-up. Further research is needed to determine the parameters of cue training that provide the greatest and most sustained benefits for dual-task walking in PD.

Cognitive or attentional strategies (e.g., focusing attention on walking with long steps) can also improve walking in people with PD [125, 126, 132], but evidence for the efficacy of cognitive strategies to improve dual-task walking is mixed. Dual-task conditions introduce a concurrent task requiring cognitive control. As suggested by the capacity theory of dual-task interference, the need to direct cognitive resources to the concurrent task may limit the ability to use conscious or unconscious cognitive control to improve walking in PD. Some studies indicate that attention can improve dual-task walking [125], while others find that attentional strategies are not effective under dual-task conditions [133].

Recent intervention studies have combined dual-task gait training with cognitive strategies to direct attentional focus and task prioritization. Even people with early PD report the need to monitor and consciously correct walking.
deficits [93]. However, research suggests that people with PD prioritize concurrent tasks over postural tasks under dual-task conditions, thereby decreasing safety and increasing fall risk [82]. A number of intervention studies have examined the effects of dual-task training with various instructions regarding task prioritization. Training with instructions to prioritize walking improved gait velocity and stride length under both single- and dual-task conditions [125, 134], with retention at 30 minutes [134]. Dual-task training with instructions to divide attention equally between walking and the concurrent cognitive task also improved dual-task gait speed and stride length, with retention at 30 minutes [135]. However, the same concurrent task was used for both training and outcomes measurement in this study, so it is not clear if these training-related improvements generalize to other dual-task combinations. Canning and colleagues also examined multitask training with divided attention instructions [136]. In this study, the concurrent tasks used during training differed from those used for outcomes measurement. Training improved gait speed and cadence, with improvements retained at 3-week follow-up. Finally, Brauer and Morris examined the effects of dual-task training using variable-priority instructions, where prioritization is shifted between walking and the concurrent task [137]. Gait speed and step length improved for both the trained dual-task combinations and on novel dual-task walking combinations. Performance on the concurrent tasks did not decline, indicating that dual-task walking improvements were not due to between-task trade-offs. The authors suggest that practice may reduce the attentional demands of walking and increase automaticity, thus enabling individuals with PD to attend to more challenging concurrent tasks. Together, these studies suggest that dual-task gait training is an effective intervention, but the relative impact of different instructional sets requires further research.

One of the limitations in the research on dual-task walking interventions is the lack of consistent and validated measures of dual-task walking performance. Appropriate outcome measures are necessary to determine if a person with PD has dual-task walking deficits and if a given intervention effectively improves these deficits. A variety of tests, including the Stops Walking When Talking test or the Walking and Remembering Test, have been used to assess dual-task walking performance in older adults [138–144]. Few of these measures have been examined in the PD population [54, 81, 145], thus the psychometric properties of these tests in PD are unclear. Future research is needed to determine reliable, valid, and sensitive outcome measures to evaluate dual-task walking performance in people with PD and quantify the response to different interventions.

Research supports the efficacy of rehabilitative interventions, including external cueing, cognitive strategies, and dual-task gait training, to improve dual-task walking deficits in PD. Emerging research is examining additional treatment approaches to improve dual-task walking. For example, treadmill training with virtual reality, designed to incorporate more complex task and environmental conditions, has been shown to improve both single- and dual-task walking in people with PD [146]. Future research is needed to examine optimal treatment parameters for both established and novel dual-task walking interventions, the relative efficacy of different interventions, whether dual-task walking improvements generalize to novel dual-task combinations, and the degree to which improvements in dual-task walking are retained.

6. Summary

This paper has reviewed basic and applied research related to dual-task walking deficits in people with PD. Gait impairments under both single-task and dual-task conditions are prevalent in people with PD and are associated with serious consequences. The severity of dual-task walking deficits appears to vary as a function of individual, task, and environmental characteristics, though the relative impacts of each factor are not well understood. Both motor and cognitive impairments have been associated with dual-task walking deficits in persons with PD. However, because the clinical profile of PD is heterogeneous, further research is needed to elucidate the relative contributions of each of these impairments to dual-task walking deficits. A number of general and specific mechanisms may underlie dual-task walking deficits in PD. The role of each is not clear, but might depend on the dual-task combination performed. These mechanisms inform a number of therapeutic interventions. Rehabilitation interventions, including external cues, cognitive strategies, and dual-task gait training, appear to be effective in reducing dual-task walking deficits in PD. However, a better understanding of the individual, task, and environmental factors that influence dual-task walking deficits is critical to refine existing interventions and identify novel therapeutic approaches.

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References


Research Article

Reliability in One-Repetition Maximum Performance in People with Parkinson’s Disease

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Strength training is an effective modality to improve muscular strength and functional performance in people with Parkinson’s disease (PWP). One-repetition maximum (1-RM) is the gold standard assessment of strength; however, PWP suffer from day-to-day variations in symptom severity and performance characteristics, potentially adversely affecting the reliability of 1-RM performance. Herein, we assessed the reliability of 1-RM in PWP. Forty-six participants completed two sessions of 1-RM testing of knee extension, knee flexion, chest press, and biceps curl at least 72 hours apart. Significantly different differences between testing sessions were identified for knee extension ($P<0.001$), knee flexion ($P=0.042$), and biceps curl ($P=0.001$); however, high reliability (ICC > 0.90) was also identified between sessions. Interestingly, almost third of subjects failed to perform better on the second testing session. These findings suggest that 1-RM testing can be safely performed in PWP and that disease-related daily variability may influence 1-RM performance.

1. Introduction

Parkinson’s disease (PD), a progressive neurological disease which is believed to affect over 1.5 million Americans, results from the degeneration of the dopaminergic neurons in the midbrain and the resulting reduced dopamine availability to the basal ganglia [1, 2]. The cardinal features of PD include rigidity, tremor, bradykinesia, and impaired postural control, and these symptoms are often unpredictable and their severity can fluctuate daily, often termed “day-to-day variability” [3–5]. Further, muscular weakness, identified by Dr. Parkinson as an early symptom of the disease, is also frequently reported by people with Parkinson’s (PWP) [6, 7]. However, inconsistent findings in the literature have obscured the elucidation of the underlying mechanism of the apparent weakness, thus, raising the debate if muscular weakness is intrinsic to the disease or a secondary consequence [8, 9]. Muscular weakness, when present in PWP, presents bilaterally and tends to increase as the velocity of movement increases [9]. While the specific contributory neurophysiological mechanisms remain uncertain, bradykinesia, the inability to energize the appropriate muscles to generate forces at a sufficient rate, is thought to be a major contributing factor [8, 10]. Bradykinesia likely results from basal ganglia pathophysiology leading to impairments in both motor programming and execution [11]. Muscular weakness and bradykinesia impair power production, particularly at lighter loads [8]. These reductions in muscular strength and power have been associated with both reduced functional ambulation and impaired dynamic postural stability in PWP [12–14]. As a result many patients with PD receive physical therapy services to counteract these deficits.

Recent reviews have suggested that strength training may be an effective modality to improve strength and functional performance for PWP [15, 16]. Strength training has frequently been combined with other rehabilitative protocols including cueing strategies, aerobic or cardiovascular training, balance training, stretching exercises, and creatine
supplementation in the development of global rehabilitation programs [17–25]. These programs have led to increased muscular strength [17–20], reduced bradykinesia [21], and improved cognitive functioning [22, 23]. Further, these improvements have transferred to overall increased quality of life [21, 25] and improved functional performance including gait [26], sit to stand [27, 28], sit to walk [29], and overall functional mobility [18]. It is not surprising, therefore, that strength training programs have become more integrated into successful Parkinson rehabilitation programs.

An important first step in initiating a rehabilitation program is the assessment of baseline function by which therapy-based improvements can be judged. When resistance training is a component of the therapeutic protocol, assessment of baseline strength is paramount. Though multiple options exist, including more subjective manual muscle testing, the accepted gold standard of maximal muscle testing is the use of the one-repetition maximum (1-RM) test [30]. The 1-RM is defined as the maximal weight that can be lifted once with correct lifting technique and is generally considered to have good to excellent (ICC > 0.95) reliability in healthy adults [31, 32]. However, therapists and rehabilitation specialists need to be aware of the determinants of 1-RM testing which include both previous weight training experience and familiarization with the test [33–35]. Further challenging the assessment of muscular performance are disease-specific complications including the prevalent motor fluctuations, random changes in symptoms severity, and noted “on/off” daily variability [36–38].

Previous rehabilitation studies in PWP have utilized either one or two sessions of various strength testing protocols to identify the individual’s current strength; however, the reliability of these protocols, specifically maximal strength assessment, has not been assessed in this population [17, 20, 24, 26]. Therefore, the purpose of this study was to investigate the reliability of 1-RM testing in mild-to-moderate PWP across two testing sessions. We hypothesized that 1-RM testing would be generally reliable; however, the disease related day-to-day variability associated with PD would result in individuals differences during the testing.

2. Methods

2.1. Subjects. A total of 46 participants diagnosed with idiopathic PD by a movement disorder neurologist participated in this study (Table 1). Inclusion criteria included a modified Hoehn and Yahr stage 1–3, the ability to ambulate without assistance, and stable response to anti-Parkinson medications. Exclusion criteria included cardiovascular, musculoskeletal, vestibular disorders, or other neurological conditions beyond PD or recent enrollment in an exercise training program. All participants were tested while clinically “on” approximately 1–1.5 hours following the first medication dose of the day and self-reported that their medicines were working maximally at the time of testing. No participants demonstrated any dyskinesia or freezing during the testing sessions. All participants provided written informed consent prior to participating in the study as approved by the University’s Institutional Review Board.

<table>
<thead>
<tr>
<th>Participant characteristics</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>62.6 ± 4.8</td>
</tr>
<tr>
<td>Height (m)</td>
<td>1.72 ± 0.11</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>86.8 ± 13.8</td>
</tr>
<tr>
<td>Disease duration (years)</td>
<td>10.9 ± 9.9</td>
</tr>
<tr>
<td>Hoehn &amp; Yahr score</td>
<td>2.3 ± 0.6</td>
</tr>
<tr>
<td>Hoehn &amp; Yahr 1</td>
<td>2 (4.3%)</td>
</tr>
<tr>
<td>Hoehn &amp; Yahr 1.5</td>
<td>7 (15.2%)</td>
</tr>
<tr>
<td>Hoehn &amp; Yahr 2</td>
<td>14 (30.4%)</td>
</tr>
<tr>
<td>Hoehn &amp; Yahr 2.5</td>
<td>11 (23.9%)</td>
</tr>
<tr>
<td>Hoehn &amp; Yahr 3</td>
<td>12 (26.1%)</td>
</tr>
<tr>
<td>Unified Parkinson Disease Rating Scale (UPDRS)*</td>
<td></td>
</tr>
<tr>
<td>Total score</td>
<td>38.0 ± 6.1</td>
</tr>
<tr>
<td>Motor score</td>
<td>23.8 ± 4.6</td>
</tr>
<tr>
<td>ADL score</td>
<td>12.2 ± 2.2</td>
</tr>
</tbody>
</table>

*UPDRS data was only available on 25 of the 46 subjects.

2.2. Experimental Procedures. Prior to performing the 1-RM testing sessions, all participants underwent two familiarization sessions, between 48–72 hours apart, to orientate themselves with the exercise equipment. During these sessions the appropriate positioning and lifting techniques were instructed and each subject performed two sets of each exercise at a low-to-moderate resistance level. The following week, the 1-RM tests were performed using cable-loaded resistance machines for knee extension (KE), knee flexion (KF) (New York Barbell, Elmira, NY.), chest press (CP), and biceps curl (BC) (Nautilus Corp, Vancouver, WA.). Both the 1-RM testing protocol and the participants body alignment for each tested closely adhered to the recommendations of the National Strength and Conditioning Association [30]. For each exercise, subjects warmed up with a low resistance and performed 10 repetitions. Thereafter, resistance was increased in incremental loads until failure occurred despite verbal encouragement to continue [17]. In order to be classified as a successful attempt, the subject had to move the weight through the complete range of motion in a controlled manner without compensatory movements (e.g., shifting body position). The 1-RM was determined within 5 attempts for all subjects.

In order to reduce the potential confounding effects of fatigue, no individual performed more than two 1-RM tests in a given day and at least 72 hours rest was provided between tests. Specifically, on a given test day the subject would perform one upper body and one lower body assessment. All 46 subjects performed the KE 1-RM tests, followed by 25 subjects performing the BC, 24 subjects performing the CP, and 21 subjects performing the KF.

2.3. Statistical Analysis. The same investigator tested the participants on both days. A paired sample T-test was
performed to compare differences between 1-RM during session 1 and session 2 for each of the four exercises. The mean difference and 95% confidence intervals between the two tests were calculated as session 2 minus session 1, such that a positive number indicates an increase in 1-RM during session 2. A frequency distribution was performed for each exercise to identify which test session most commonly represented the higher value. The intraclass correlation coefficient (ICC) was calculated for each exercise with a two-way random effects analysis of variance. Finally, the standard error of the measurement (SEM) was calculated as $SEM = SD_{baseline} \times \sqrt{(1 - r_{test-retest})}$ [39].

### 3. Results

All subjects completed all 1-RM tests without incident. The paired analysis revealed statistically significant differences in 1-RM performance between the two testing sessions for knee extension, knee flexion, and biceps curl, but not for chest press (Table 2). The intraclass correlation coefficient ranged from 0.91 to 0.97 (Table 2).

Across the four exercises, a total of 116 tests were performed; of these, 11.2% (13 of 116) had identical scores between the two testing sessions. Further, 19.8% (23 of 116) of the evaluations had higher 1-RM values, a mean of 4.6 kg across all 4 exercises, on the first test. Finally, the range of differences between the two testing sessions was 82% of the combined means (54 kg) with one participant increasing their 1-RM by 41% (27 kg) and another subject exhibiting a 41% (27 kg) reduction in 1-RM, both occurred during knee extension exercises, and over half of all participants (51%) had changes of at least 5 kg between test sessions.

### 4. Discussion

Effective and reliable assessment of force production is an integral component in the development of an appropriate physical therapy program. Further, in longitudinal studies it is essential to establish an accurate and reliable baseline performance of strength to compare improvements over time. The purpose of this study was to investigate reliability in 1-RM performance amongst PWP. A primary finding of this study was a significant difference in 1-RM strength between the two sessions for knee extension, knee flexion, and biceps curl exercises in individuals with mild-to-moderate PD despite the subjects performing two orientation sessions in the previous week. However, the tests demonstrated high reliability and the between sessions differences did not exceed the standard error of measurement when collapsed across participants. Interestingly, nearly third of subjects did not increase their 1-RM on the second testing session as would be expected in this inexperienced population. In some cases, the improvements we observed (up to 41% improvement) rival or exceed those reported in many longitudinal training studies [17, 18, 20, 21]. This finding suggests that day-to-day performance variability may play a substantial role in 1-RM strength testing for individuals with mild-to-moderate PD.

Accurate and reliable baseline testing needs to be conducted to correctly prescribe the treatment protocol and elucidate improvements following exercise programs. The results of this study suggest that more than one baseline 1-RM test needs to be performed, although therapists should not assume improved performance with second-day testing. Indeed, over 30% of subjects failed to improve in 1-RM performance on the second testing session and a between-test range of 54 kg was identified during the leg extension exercise. This finding raises two unique concerns to the development and reporting on the effects of strengthening programs for Parkinson's rehabilitation. First, if the initial 1-RM value is low, the exercise prescription based on this value may not be sufficiently challenging to the individual, thus, potentially limiting the effectiveness of the therapy. Secondly, variable performance raises the risk that the true benefit of the intervention may be masked by a single day poor performance in a population known to experience day-to-day performance variability [5, 40, 41]. The results of this study are similar to recent finding of aerobic capacity in PWP [42]. Katzel and colleagues demonstrated generally high test-retest reliability, however a significant between test session, 0.56 mL/mg/min, difference was noted in VO$_2$ peak measurements [42]. Further, almost half of the PWP, failed to improve on the second administration of the maximal test (95% CI of $-3.5$–$4.6$ mL/mg/min) [42]. Taken together, these findings provide important considerations in the development of rehabilitation programs for individuals with mild-to-moderate PD.

The phenomenon of day-to-day variability in PWP has been well established in the literature [5, 40, 41, 43]. The symptoms of Parkinson's, both physical and psychological, are often unpredictable and fluctuate from day to day resulting in substantial alterations in activities of daily living and social activities [40, 44]. This is a separate phenomenon from motor fluctuations, abrupt and unpredictable responses to

### Table 2: One-repetition maximum test results. The session 1-RM values are presented as mean ± standard deviation.

<table>
<thead>
<tr>
<th>Exercise</th>
<th>First session (kg)</th>
<th>Second session (kg)</th>
<th>Mean session difference (kg) (95% CI)</th>
<th>$T$-test results</th>
<th>ICC (95% CI)</th>
<th>SEM (kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Knee extension</td>
<td>63.7 ± 28.1</td>
<td>67.7 ± 29.7</td>
<td>4.0 (1.9–6.2)</td>
<td>$P &lt; 0.001$</td>
<td>.96 (.93–.97)</td>
<td>5.7 kg</td>
</tr>
<tr>
<td>Knee flexion</td>
<td>27.0 ± 12.7</td>
<td>29.4 ± 13.0</td>
<td>2.4 (0.2–4.7)</td>
<td>$P = 0.042$</td>
<td>.91 (.79–.96)</td>
<td>3.8 kg</td>
</tr>
<tr>
<td>Biceps curl</td>
<td>43.9 ± 15.6</td>
<td>46.6 ± 17.6</td>
<td>2.7 (1.2–4.1)</td>
<td>$P = 0.001$</td>
<td>.97 (.92–.98)</td>
<td>2.8 kg</td>
</tr>
<tr>
<td>Chest press</td>
<td>57.8 ± 20.6</td>
<td>60.1 ± 20.8</td>
<td>2.3 (−0.2–4.7)</td>
<td>$P = 0.066$</td>
<td>.95 (.90–.98)</td>
<td>4.3 kg</td>
</tr>
</tbody>
</table>

ICC: Intraclass Correlation Coefficient. SEM: Standard Error of Measurement which was calculated as: $SEM = SD_{baseline} \times \sqrt{(1 - r_{test-retest})}$ [39].
levodopa administration [45]. Further, both hourly and daily variations, potentially due to motor fluctuations or day-to-day variations, in gait rhythm (e.g., velocity, step length, and cadence), have been identified in PWP [46]. The participants in this study were all tested at a consistent time following medication dosage, at their self-described best time of day, and while clinically “on”; so only subtle motor fluctuations could have been a contributing factor to their performance.

The use of 1-RM testing has been examined in a wide range of healthy, aging, and diseased populations [32, 35, 47–54]. In healthy young adults (age 18–30) with strength training experience, the reliability of the 1-RM test is generally considered to be very high (ICC > 0.95) [47, 55]. In healthy older adults, individuals with cardiovascular disease, peripheral obstructive arterial disease, and chronic obstructive pulmonary disease, 1-RM testing is a safe and practical assessment and our results suggest 1-RM testing is also safe amongst the PWP population with comparable reliability [35, 52–54]. Interestingly, Schilling et al. [20] recently found no differences in maximal relative strength testing, reported as maximum strength divided by body weight; however, these tests were separated by 8 weeks, as opposed to 72 hours, and the time between tests may have influenced the relation to our results. The results of the current study suggest that PWP can safely and effectively perform 1-RM testing and, while important differences exist between trials, the overall results are generally reliable.

Generally speaking, the reliability of 1-RM measures may vary depending on the individuals experience with weight training and their familiarity with the specific exercise being tested [32, 33, 47–49, 55]. Although the number of acceptable familiarization sessions has ranged from one to nine, in healthy inexperienced middle-aged to older populations, one to three familiarization sessions are generally considered to be appropriate before assessing maximal strength [32, 34, 35]. Following familiarization with the equipment, most studies on healthy older adults suggest that two to three 1-RM sessions are required as strength values will increase on subsequent trials [33–35]. While the specific mechanism underlying these improvements in 1-RM performance, when present, is not fully understood, it is generally attributed to improved neural efficiency and activation patterns as well as a learning effect represented by improved posture and exercise execution [33, 56]. Appropriate orientation and familiarization to the testing paradigm is likely of particular importance for PWP who are known to reduce overall activity due to social stigmas, loss of confidence in their coordination, and fear of falling [26, 57].

The findings of this study are delimited to this specific protocol, and future studies should address this potential limitation by increasing the number of both familiarization and 1-RM testing sessions to help elucidate the learning effects and the influence of day-to-day variability. Further, additional demographic considerations (e.g., UPDRS scores) and traditional performance variables (e.g., timed get-up and go test) should be explored to identify potential relationships. However, exploratory analysis of our data found no relationship between disease severity as measured by Hoehn and Yahr staging, body weight or initial strength, and the change in performance between testing sessions. While day-to-day variability in PWP is unpredictable, exercise intervention studies should consider a Parkinson’s specific graded symptom checklist on the days of the pre- and posttesting to attempt to control for the variability. Finally, future studies should expand these findings by identifying potential relationships between alterations in strength and performance of activities of daily living.

The 1-RM test is generally considered to be the gold standard for assessing maximal muscular strength in an individual and the results of this study suggest that, when using cable-loaded resistance machines, PWP can successfully and safely perform these tests [30]. Thus, physical therapy interventions can effectively be established and monitored with 1-RM testing in the PD population. Whereas healthy older adults typically demonstrate subtle improvements in 1-RM performance with repeat administration over several days, the results of this study suggest that individuals with mild-to-moderate PD demonstrate inconsistencies in 1-RM test performance.

References

Parkinson's Disease


Comparing the Mini-BESTest with the Berg Balance Scale to Evaluate Balance Disorders in Parkinson’s Disease

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Objective. The purpose of this study was to explore the usefulness of the Mini-BESTest compared to the Berg Balance Scale in evaluating balance in people with PD of varying severity. We evaluated (1) the distribution of patients scores to look for ceiling effects, (2) concurrent validity with severity of disease, and (3) the sensitivity/specificity of separating people with or without postural response deficits.

Subjects. Ninety-seven people with PD were tested for balance deficits using the Berg, Mini-BESTest, Unified Parkinson’s Disease Rating Scale (UPDRS) III and the Hoehn & Yahr (H&Y) disease severity classification. Setting. Clinical research facility at Oregon Health & Science University.

Results. The Mini-BESTest is highly correlated with the Berg ($r = 0.79$, $P < 0.001$), but avoids the ceiling compression effect of the Berg for mild PD (skewness $-2.30$ Berg, $-0.93$ Mini-BESTest). Consequently, the Mini-BESTest is more effective than the Berg for predicting UPDRS Motor score ($P < 0.001$ Mini-BESTest versus $P = 0.86$ Berg), and for discriminating between those with and without postural response deficits as measured by the H&Y (ROC differential $P = 0.06$). Conclusion. The Mini-BESTest is a promising tool for discerning balance deficits in patients with PD, most importantly those with more subtle deficits.

1. Introduction

Postural instability and balance deficits are one of the most debilitating impairments associated with chronic neurological disease, such as Parkinson’s disease (PD) [1]. The most commonly used clinical test of balance severity in people with PD is the Berg Balance Scale (Berg) [2]. The Berg, originally designed for use in the frail elderly, is a 14-item test that focuses on a variety of self-initiated tasks related to everyday function such as sit-to-stand and functional reach forward. The Berg has excellent reliability and is somewhat correlated with severity of PD, as measured with the Unified Parkinson Rating Scale (UPDRS) [3, 4]. However, the Berg has limitations such as documented ceiling effects [5–7] and problems with underutilization and redundancy of categories due to the rating scale [8, 9]. These particular limitations are important considerations when evaluating patients with mild neurological deficits, who are easy to underidentify and therefore less likely to receive rehabilitation.

Such documented limitations of the Berg have led many clinicians to do more than one validated balance assessment in order to identify deficits that may respond to treatment. Recently, a new and more comprehensive clinical balance test, the Balance Evaluation Systems Test (BESTest), has been developed that is essentially a battery of balance and mobility tests, borrowed from other validated tests such as the Berg and Dynamic Gait Index. The BESTest was uniquely designed as a comprehensive clinical tool for evaluating six different balance control systems: biomechanical, stability limits/verticality, anticipatory, reactive, sensory orientation, and stability in gait. Such system-specific assessment is helpful in directing treatment and to ensure that a meaningful deficit is not overlooked. The BESTest has good interrater reliability [10] and good validity in discerning fallers from nonfallers in patients with PD [11].

The BESTest, though comprehensive, valid, and reliable, is lengthy to administer and may not always be practical in a busy clinical setting. Thus, a shorter version of the BESTest, the Mini-BESTest, was developed using
psychometric techniques to reduce item redundancy and simplify scoring [12]. This shorter version has excellent interrater (ICC ≥ 0.91), and test-retest (ICC ≥ 0.88) reliability and similar in length to the Berg [13]. However it is currently unknown how the Mini-BESTest compares with the Berg in detecting balance deficits in the PD population.

The purpose of this study was to explore the usefulness of the Mini-BESTest compared to the Berg in evaluating balance in people with PD of varying severity. Specifically, we evaluated (1) the distribution of patients scores to look for ceiling effects, (2) concurrent validity with severity of disease, and (3) the sensitivity/specificity of separating people who do or do not have postural response deficits.

2. Methods

Ninety-seven participants with idiopathic PD participated in the study. These participants were part of either a larger clinical study examining prospective fall risk or an exercise efficacy study. Therefore, the group here represents a convenience sample of participants with PD, and the data for this paper was taken from their baseline visits.

Inclusion criteria: all people in the study were diagnosed with idiopathic PD by a movement disorders neurologist. People were excluded from the study if they presented with cognitive impairment, prior orthopedic injuries, or impairments that could interfere with mobility such as artificial joints or peripheral neuropathy or prior brain surgery such as a pallidotomy or deep brain stimulation. All participants signed informed consent forms approved by the Oregon Health & Science University Institutional Review Board. All work was conducted in accordance with the declaration of Helsinki (1964).

All participants came in for an assessment of their balance and mobility which included both clinical and instrumented testing. The data presented in this paper is taken from the clinical scales: the Unified Parkinson’s Disease Rating Scale (UPDRS) III Motor section, Hoehn & Yahr (H&Y) disease severity classification, and the Berg and the Mini-BESTest. The testing was performed in the same order for each participant, and rest breaks were given as needed to avoid fatigue. Other balance and gait assessments conducted during testing that were not included in this analysis included gait and sway analysis using wearable inertial sensors. Testing was conducted at the Oregon Clinical Translational Research Institute at Oregon Health & Science University. All participants took their PD medication as normally indicated and were tested in the ON state. All of the participants except for two were currently taking some form of PD medication. The testing was administered by a trained examiner, overseen by a physical therapist. Participant characteristics are outlined in Table 1.

2.1. Clinical Tests

2.1.1. Mini-BESTest. The Mini-BESTest is a 14-item test that focuses on dynamic balance, specifically anticipatory transitions, postural responses, sensory orientation, and dynamic gait [12]. Each item is scored from (0–2); a score of 0 indicates that a person is unable to perform the task while a score of 2 is normal. The best score is the maximum amount of points, being 28.

2.1.2. Berg Balance Scale (Berg) [2]. The Berg is a 14-item test designed to measure the balance of older adults by assessing their performance of specific functional tasks [14]. Each task is scored from (0–4), for a maximum of 56 points. The test indicates that a score of 41–56 is associated with a low fall risk, 21–40 with a medium fall risk, and 0–20 with a high fall risk [14].

2.1.3. Unified Parkinson’s Disease Rating Scale (UPDRS). Disease severity was evaluated using the UPDRS III motor component [15]. This test has a maximum score of 108; each item is scored from 0-not affected through 4-most severely affected.

2.1.4. Hoehn and Yahr (H&Y). Postural response deficits were identified as patients scoring 3 to 4 in the H&Y scale. [16]. A score of 3 and above indicates postural instability as defined by an abnormal stepping response to a backwards pull on the shoulders. The H&Y scale is the most commonly used method for evaluating the severity of PD [17], and the scale ranges from 0 (no symptoms of PD) to 5 (wheelchair bound).

2.2. Statistics. The STATA statistical package was used for both calculations and graphics [18]. We describe the Berg and Mini-BESTest data for the 97 participants, using histograms and a scatter plot displaying the association between the two variables. We used the bootstrap method to assess a P value for the skewness [19]. We also carried out a regression of UPDRS jointly on the two scores for the Berg and Mini-BESTest. This regression provided information on the relative contributions of the Berg and Mini-BESTest for predicting the UPDRS, each adjusted for the other measure using added variable or partial correlation plots that show the extent of information in each test that is not conveyed by the other test [20]. Finally, we considered the relative performance of the Berg and Mini-BESTest in terms of receiver operating characteristic (ROC) curves for classifying people into two groups based on a threshold for the H&Y score, to discriminate between mild PD (H&Y 1-2) versus more severe PD (H&Y 3-4) [21].

<table>
<thead>
<tr>
<th>Variables</th>
<th>Mean</th>
<th>SD</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>UPDRS III</td>
<td>31.6</td>
<td>11.2</td>
<td>12–60</td>
</tr>
<tr>
<td>Hoehn &amp; Yahr</td>
<td>2.3</td>
<td>0.6</td>
<td>1–4</td>
</tr>
<tr>
<td>Age (yr)</td>
<td>65.6</td>
<td>7.1</td>
<td>47–83</td>
</tr>
<tr>
<td>Time since dx (yr)</td>
<td>6.5</td>
<td>5.0</td>
<td>0–23</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>172.6</td>
<td>9.5</td>
<td>152–198</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>79.2</td>
<td>15.6</td>
<td>43–120</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>59</td>
<td>Female</td>
<td>38</td>
</tr>
</tbody>
</table>
3. Results

3.1. Distribution of Scores and Relation between Berg and Mini-BEST est. The distribution of scores among the 97 participants with PD on the Mini-BEST est differed significantly from the Berg (Figure 1). The Mini-BEST est scores were significantly less skewed than the Berg (Berg skewness = −2.3 versus Mini-BEST est skewness = 0.93; $P < 0.001$). Using the bootstrap method, we found that, sampling from a population with the shape of the Mini-BEST est histogram, the chance would be less than 0.001 of obtaining a skewness as extreme as that seen for Berg. The scatter plot in Figure 1(c) shows the relationship between the two measures.

The Mini-BEST est and Berg correlate significantly ($r = 0.79; P < 0.001$). However, people scoring the highest values in the Berg (i.e., 52–56; those with scores in the clinically accepted range as “normal”) had scores representing approximately half of its maximum range in the Mini-BEST est. This suggests that the Mini-BEST est “spreads out” the compression (ceiling effect) at the top end of the Berg.

3.2. Relationship to PD Severity. Both the Mini-BEST est and Berg were moderately correlated with disease severity as measured by the UPDRS. Figures 2(a) and 2(b) display the individual regression lines, indicating that the Berg and the Mini-BEST est each have a significant correlation to the UPDRS ($−0.39$ and $−0.51$, $P > 0.001$, respectively).

Using a multiple regression of the UPDRS on both the Mini-BEST est and the Berg, we determined how much either test compliments the other in the prediction of disease severity. For linear regression prediction of the UPDRS, the Berg did not provide statistically significant information in addition to the Mini-BEST est ($t = 0.18; P = 0.86$). In contrast, the Mini-BEST est provided significant information in addition to the Berg ($t = −3.7; P = 0.001$) to predict severity of disease. The added variable plot in Figure 2(c) shows the extent of information in the Mini-BEST est for predicting UPDRS, beyond that provided by the Berg. This was significant ($P < 0.001$). The added variable plot in Figure 2(d) shows the extent of information in the Berg for predicting UPDRS, beyond that provided by Mini-BEST est. This was not statistically significant ($P = 0.86$).

3.3. Identifying Mild Deficits. We compared the ability of the Berg and Mini-BEST est to differentiate PD patients with and without clinical balance deficits. Participants with
and without clinical balance deficits were classified using H&Y: H&Y 1-2 and H&Y 3-4. A score of H&Y 3 and 4 identifies people with abnormal postural stepping response to the backwards pull test or observable postural instability. Though the mean H&Y score was 2.3, the range was 1-4. Roughly one third (31 of 97) of the participants had a H&Y of 3 or above, indicating postural instability as defined by H&Y. Figures 3(a) and 3(b) compare the distributions of Berg and Mini-BESTest scores for people with H&Y 1-2 versus H&Y 3-4. ROC analysis was done to test the discriminative ability of these different balance tests to differentiate those people with and without abnormal postural responses.

The area under the ROC curves (AUC) differed for the tests; the AUC for the Berg = 0.84 ± 0.04 and the AUC for the Mini-BESTest = 0.91 ± 0.03. The 2-sided P-value for testing equality of the two AUC values was 0.05. A suggested cut-off point for the Mini-BESTest to differentiate those with and without postural response deficits is ≥ 21, yielding (sensitivity, specificity) = (89%, 81%). The nearest point to this for the Berg is ≥ 52, yielding (Sensitivity, Specificity) = (77%, 74%). The points corresponding to these cut-off points are indicated by circles in Figure 3(c).

3.4. Most Difficult Items for People with PD. Individual items from both the Berg and the Mini-BESTest were ranked in order of difficulty for the whole population of people with PD within this study and classified as “difficult” if a person had a score less than perfect on that item (2 = perfect; 1 = some difficulty, or 0 = cannot perform) (Table 2). We found that 72% (10 out of 14) items on the Mini-BESTest presented some difficulty to at least one-third of the group versus only 36% (5 out of 14 items) in the Berg.

4. Discussion

The results from this study suggest that the Mini-BESTest may be more useful than the Berg in evaluating balance disorders in patients with PD, especially in those with mild PD or more subtle balance deficits. Specifically, results showed that (1) although the Mini-BESTest had a high correlation with the Berg, it did not have the same ceiling effects; (2) both the Berg and Mini-BESTest correlated with PD severity but the Mini-BESTest added value to the Berg score; (3) the Mini-BESTest test had better sensitivity/specificity then the Berg to identify people with abnormal postural responses.
Table 2: The Berg and Mini-BESTest individual items ranked from most difficult to least based on the % of participants with PD who did not have normal scores. Difficulty with the test was determined if the participant did not receive a perfect score.

<table>
<thead>
<tr>
<th>Berg test item</th>
<th>Percentage (% with difficulty)</th>
<th>Mini-BESTest item</th>
<th>Percentage (% with difficulty)</th>
<th>System (Mini-BEST)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Turning to look behind</td>
<td>70.1</td>
<td>Rise to toes</td>
<td>86.6</td>
<td>Anticipatory</td>
</tr>
<tr>
<td>Standing with one foot in front</td>
<td>42.3</td>
<td>Single leg</td>
<td>81.4</td>
<td>Anticipatory</td>
</tr>
<tr>
<td>Reaching forward with outstretched arms</td>
<td>40.2</td>
<td>TUG w/Cog</td>
<td>54.6</td>
<td>Gait</td>
</tr>
<tr>
<td>Standing on one foot</td>
<td>39.2</td>
<td>Pivot turn</td>
<td>51.5</td>
<td>Gait</td>
</tr>
<tr>
<td>Turn 360 degrees</td>
<td>30.9</td>
<td>Eyes Closed/foam</td>
<td>46.4</td>
<td>Sensory</td>
</tr>
<tr>
<td>Placing alternate foot on stool</td>
<td>27.8</td>
<td>Obstacle during Gait</td>
<td>46.4</td>
<td>Gait</td>
</tr>
<tr>
<td>Standing to sitting</td>
<td>11.3</td>
<td>Turn head with gait</td>
<td>41.2</td>
<td>Gait</td>
</tr>
<tr>
<td>Retrieving object from the floor</td>
<td>9.3</td>
<td>Incline eyes closed</td>
<td>33</td>
<td>Sensory</td>
</tr>
<tr>
<td>Sitting to standing</td>
<td>5.2</td>
<td>Backwards recovery</td>
<td>29.9</td>
<td>Postural</td>
</tr>
<tr>
<td>Standing with feet together</td>
<td>4.1</td>
<td>Lateral recovery</td>
<td>29.9</td>
<td>Postural</td>
</tr>
<tr>
<td>Transfers</td>
<td>4.1</td>
<td>Change pace gait</td>
<td>13.4</td>
<td>Gait</td>
</tr>
<tr>
<td>Standing with eyes closed</td>
<td>3.1</td>
<td>Forward recovery</td>
<td>13.4</td>
<td>Postural</td>
</tr>
<tr>
<td>Standing unsupported</td>
<td>3.1</td>
<td>Sit to stand</td>
<td>6.2</td>
<td>Anticipatory</td>
</tr>
<tr>
<td>Sitting unsupported</td>
<td>0</td>
<td>Eyes open stance</td>
<td>2.1</td>
<td>Sensory</td>
</tr>
</tbody>
</table>

The high correlation of the Mini-BESTest with the Berg supports concurrent validity since the Berg remains one of the most commonly used clinical scales for balance assessment in people with PD. But importantly, we found very different test score distributions across patients with varied levels of severity. Though neither test had a normal distribution, the Mini-BESTest was significantly less skewed, indicating that there are less ceiling effects as has been shown previously with the Berg [22]. These results are not surprising since the Berg was originally intended for frail elderly and remains an excellent measure of balance deficits for those with more severe PD. The high sensitivity of the Mini-BESTest is important for clinicians who see patients with mild balance deficits who are seeking to identify and treat potentially preventable mobility problems early in the disease progression.

The Berg has been shown to have excellent test-retest reliability [3] and to correlate significantly with disease severity in PD [23], and our results support the relationship with the UPDRS. Both exercise and physical therapy have been shown to improve UPDRS scores. Therapists need measures that reflect improvements with intervention so comparing the Mini-BESTest with the UPDRS establishes concurrent validity of the new test with an established one. The novel information obtained from our study is that while both the Berg and Mini-BESTest correlate with disease severity, the Mini-BESTest adds value not included in the Berg, but the Berg does not add value to the Mini-BESTest. These findings suggest that the Mini-BESTest distinguishes among PD subjects who all get similar, high scores in the Berg, and this information can add to the prediction of disease severity. A previous study demonstrated the Berg to be useful in identifying balance impairments in people with very severe PD (i.e., H&Y 4), but it could not discriminate subgroups of H&Y scores successfully [24]. Here, we found similar results in that the Mini-BESTest was more sensitive than the Berg at discriminating subgroups of PD severity as measured by the H&Y scale. Franchignoni et al. examined the clinimetric properties of the Berg with 57 participants with PD [9]. They found excellent internal consistency, good correlations to other scales of disease severity, and quality of life, all agreeing with previously published work [4]. However, they did find, using a Rasch analysis, that some rating categories were not used and others were underutilized. The authors suggested that improving the rating scale structure would improve the test. The same type of Rasch analysis was performed on the full BESTest to obtain the shortened Mini-BESTest that excludes redundant or underused items [12].

The cut-off point of the Mini-BESTest for identifying patients with PD who had problems with the “Pull test” (i.e., H&Y score of at least 3) was a score of 21. It is interesting that a similar cut-off point for the Mini-BESTest for identifying patients with PD who fall was a score of 20 [13]. Both the Mini-BESTest and the Berg were sensitive (89% and 77%, respectively) and specific (81% and 74%, respectively) in differentiating those with and without postural response deficits. Similarly, the Mini-BESTest was also shown to be sensitive (88%) and specific (78%) in identifying PD patients with a history of falls [13].

It has been suggested that postural instability in PD is multifactorial, therefore, a multitude of tests should be administered by physical therapists [25, 26]. For example, the Berg does not include tests of postural reactions or
dynamic gait, and, therefore, some deficits may be missed. Since the Mini-BESTest is essentially a combination of tests, this may be a reason it successfully identified people with mild balance deficits. As outlined in Table 2, each test item primarily tests one of 4 categories of balance: anticipatory, dynamic gait, reactive control, and sensory orientation. The Berg was not designed with such systems in mind but if a system categorization is assigned to each item, the Berg items primarily evaluate anticipatory and sensory contributions to balance. There are two additional systems that the Mini-BESTest evaluates, dynamic gait, and reactive postural control, this may explain the added variable plot being significant for the Mini-BESTest adding value to the Berg in relating to disease severity. In other words, the Mini-BESTest usefully distinguishes among those persons that are overly range compressed in the Berg. If a clinician is using the Berg for their PD patients, it may be beneficial to augment testing with the Dynamic Gait Index and the Pull test from the UPDRS. Dynamic gait (cognitive task with gait) and reactive postural control (response to perturbation) items were the most difficult items for people with PD, balance systems that are not assessed using the Berg.

Clinicians commonly use single-limb stance for balance assessment. An example of a difference between testing items in the Berg and Mini-BESTest is the assessment of the single-limb stance (item #14 Berg, item #3 Mini-BESTest). In the Berg, the participant chooses either leg, and it is only this side that is assessed. Comparatively, the Mini-BESTest assesses both the left and right leg and records the worst side. In this study, when the Berg was used, assessing only one leg, 39% of the participants had some observable difficulty. When the Mini-BESTest was used, assessing both left and right leg, 81% of the participants had some difficulty. Therefore, clinicians should test standing balance on both sides.

This study was limited to people with PD so it needs to be repeated in patients with other pathologies affecting balance control. One potential limitation is that the order of testing was not randomized so fatigue may have factored into test performance. However, participants were given frequent rest breaks to avoid fatigue.
In conclusion, the Mini-BESTest is a novel, useful, and easy to administer tool for balance assessment. Although the Mini-BESTest had a high correlation with the Berg, it did not have the same ceiling effects. Furthermore, both the Berg and Mini-BESTest correlated with PD severity but the Mini-BESTest added value to the Berg score in predicting disease severity. Finally, the Mini-BESTest test had better sensitivity/specificity than the Berg to identify people with abnormal postural responses. Taken together, these findings suggest that the Mini-BESTest is a promising tool for discerning balance deficits in patients with mild to severe PD.

Acknowledgments

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Research Article

The PIT: SToPP Trial—A Feasibility Randomised Controlled Trial of Home-Based Physiotherapy for People with Parkinson’s Disease Using Video-Based Measures to Preserve Assessor Blinding

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Purpose. To trial four-week’s physiotherapy targeting chair transfers for people with Parkinson’s disease (PwPD) and explore the feasibility of reliance on remote outcome measurement to preserve blinding.

Scope. We recruited 47 PwPD and randomised 24 to a focused home physiotherapy programme (exercise, movement strategies, and cueing) and 23 to a control group. We evaluated transfers (plus mobility, balance, posture, and quality of life) before and after treatment and at followup (weeks 0, 4, 8, and 12) from video produced by, and questionnaires distributed by, treating physiotherapists. Participants fed back via end-of-study questionnaires. Thirty-five participants (74%) completed the trial. Excluding dropouts, 20% of questionnaire data and 9% of video data were missing or unusable; we had to evaluate balance in situ. We noted trends to improvement in transfers, mobility, and balance in the physiotherapy group not noted in the control group. Participant feedback was largely positive and assessor blinding was maintained in every case.

Conclusions. Intense, focused physiotherapy at home appears acceptable and likely to bring positive change in those who can participate. Remote outcome measurement was successful; questionnaire followup and further training in video production would reduce missing data. We advocate a fully powered trial, designed to minimise dropouts and preserve assessor blinding, to evaluate this intervention.

1. Introduction

Chair transfers, a common cause of falls [1, 2], are a key domain of physiotherapy for people with Parkinson’s disease (PwPD) [3–5]. While weak lower limbs and inflexible, unstable trunks extend rising time [6–10], exercise shortens sit-to-stand times and PwPD can relearn motor sequences, facilitating movement through cueing [3, 4, 11–14].

In their 2007 evidence-based analysis of physical therapy in Parkinson’s disease (PD), Keus et al. [3] found supportive evidence for improving the performance of transfers among PwPD in just two studies. The potential to improve transfers among PwPD has been underresearched since Kamsma et al. [11] and Nieuwboer et al. [12] evaluated the use of cognitive movement strategies, the former in a randomised controlled trial (RCT; \( n = 38 \)), the latter in a nonrandomised controlled trial (\( n = 33 \)). Over 12 months, Kamsma et al.’s experimental group (mean age 68 years) practiced a seven-step sequence for safe rising (positioning hands, positioning feet, shifting to the seat edge, repositioning hands, leaning forward, rising into standing, and adopting upright posture), a “logical structure” that offered “maximum opportunity for controlled execution without time constraints.” Participants were found able to learn and demonstrate the strategies and they reported their use in real-life situations, though the effects of training were activity-specific. Nieuwboer et al.’s participants (mean age 66 years) undertook six weeks of home-based physiotherapy aimed...
at reducing specific difficulties during functional activities including rising which was based on cueing, conscious control of movement, biomechanical compensation, and repetition of movement in differing circumstances. The chair rising strategy taught entailed repositioning “the centre of mass in relation to the base of support to compensate for slow trunk flexion and insufficient horizontal momentum.” Chair transfers improved significantly after treatment, when measured against the Parkinson’s Activity Scale (PAS) [13]. More recently, Mak and Hui-Chan [14], recruited 60 PwPD to an RCT comparing rising times after four week’s audio-visual cued task-specific sit-to-stand training, four week’s conventional mobility and strengthening exercise (for the trunk and lower limbs, followed by sit-to-stand training), and no treatment. Rising times shortened after treatment in both the cued group (mean age 63 years) and the exercise group (mean age 66 years), by 25% and 10%, respectively.

In 2006, the National Institute for Health and Clinical Excellence called for further trials to investigate physiotherapy in PD [15]; however, trials overly focused on measuring cost-effectiveness and quality of life might overlook meaningful changes in performance that are the realistic targets of physiotherapy, potentially reducing the chances of PwPD accessing appropriate therapies. Blinding assessors is “one of the methodological safeguards” that ensures a trial’s “internal validity” [16]: inadvertent “unblinding” is an important issue in rehabilitation research. In physiotherapy trials, an assessor’s blinding is jeopardized when a participant says or does something that hints at, or confirms, their group allocation: as face-to-face or telephone contact between assessor and participant is highly likely to break blinding, we investigated remote evaluation of video- and questionnaire-based measures by a blinded assessor.

In a feasibility RCT, we investigated whether focused physiotherapy (cueing, movement strategies, and exercise), increased transfer independence and speed while reducing difficulty and brought secondary changes in gait, balance, posture, and quality of life. Key issues were the programme’s potential for a full-sized trial (we did not power this study to test the significance of differences between groups or over time) and the feasibility and acceptability of methods (including the acceptability of participating in research at home). In keeping with recent physiotherapy studies involving PwPD [17, 18], we opted for a home-based trial, firstly to avoid participant travel being a barrier to anyone’s participation and secondly, as specialists advocate the delivery of physiotherapy at home [4, 12] where “activities are proving problematic” [19].

2. Methods

We recruited PwPD from a clinic and support groups within Hampshire who

(1) had a working diagnosis of PD, stages I to IV [20], fulfilling the UK PDS Brain Bank diagnostic criteria [21]. The staging allowed us to compare grossly the spectrum of PD in the intervention and control groups:

(i) stage I indicating mild unilateral symptoms,
(ii) stage II, bilateral symptoms without balance impairment,
(iii) stage III, postural instability but independently mobile,
(iv) stage IV, severe PD although able to stand and walk with assistance;

(2) self-reported chair transfers as

(a) being excessively slow and/or,
(b) requiring much effort, assistance, or repeated attempts and/or,
(c) associated with a previous fall;

(3) scored at least 8/12 on The Middlesex Elderly Assessment of Mental State [22], a gross screen for cognitive impairment that we have used in previous studies to identify anyone with PD at risk of being unable to give fully informed consent [2, 23] and that is one of the most commonly used assessments by occupational therapists of mental state in PwPD [24];

(4) were willing and able to undertake all aspects of the intervention;

(5) were willing and able to complete the outcome measures (albeit with help from another person in completing questionnaires, if handwriting was problematic).

Southampton and South West Hampshire Ethics Committee approved the project and all participants gave written informed consent to all aspects of the study, including specifically video recording. After responding to an initial invitation to take part, interested parties were visited at home by one of three treating physiotherapists. Having given their consent, a therapist completed the participant’s baseline (week 0) assessment, after which the participant was randomised to either the intervention group (receiving physiotherapy) or the control group (receiving none) through concealed allocation.

2.1. Intervention. The physiotherapy group undertook a four-week-long, evidence-based [3, 11–14], home physiotherapy programme focused on chair transfers, comprising (1) supervised exercise (to enhance hip and knee extensor strength and trunk stability and flexibility), (2) teaching and learning movement strategies for safer and easier standing and sitting, and (3) verbal cueing. The intervention was not novel in content but in its intense, focused delivery. Respecting individuality and professionalism, the protocol dictated only that the physiotherapists provided no more than 12 hours of input focused only on chair transfers (a maximum of one hour, three times per week for four weeks) including only portable equipment (like ankle weights); the therapists decided if, when, and how intensively to use exercise, strategies, and/or cueing based on each participant’s assessment and their clinical experience. The primary objective was to improve the ability to transfer, in terms of
2.2. Assessment. We assessed participants four times, at the same time of day and point during an “on” phase, before and after intervention (weeks 0 and 4) and during followup (weeks 8 and 12). The physiotherapists’ video-recorded five physical performance tests for the blinded assessor to evaluate: PAS; sit-to-stand [14]; Standing Start 180 Degree Turn Test (SS-180) [25]; functional reach (FR) [26]; the Unified PD Rating Scale Posture Item [27]. All five tests have been used previously with PwPD (and three were developed specifically for PwPD), and we followed the published protocols without modification. A single camera, stopwatch, and metre-rule were used across the study but, as a home-based study, the chairs that participant’s rose from during the PAS varied (but each person used their same chair at every assessment point).

The physiotherapists’ also left the participants two questionnaires to complete at home and return in a stamped addressed envelope: PD Self-Assessed Disability Scale (SAS) [28] and 15D instrument of health-related quality of life (HR-QOL) [29]. On SAS, participants indicated on a five-point scale how much effort 25 everyday tasks took: best score 25, worst score 125. On HR-QOL, they indicated on a five-point scale the state of 15 aspects of health: best score 15, worst score 75.

The physiotherapists transferred edited clips of each performance (but nothing superfluous) onto DVD for one independent assessor (blind to group allocation) to evaluate, alongside returned questionnaires and feedback. Independence and effort demonstrated during the PAS Chair Transfer section was rated from zero to eight (worst to best score). Sit-to-stand was stopwatch-timed (during the PAS) from the point when a participant started to move until they attained stable standing. The SS-180 mean turn time was calculated from two turns (one in each direction) to walk towards a target. FR was the mean of three maximal forward reaches in standing. Posture was rated as the degree of stoop noted when participant’s stood for the FR; rated zero to four (best to worst score). Sound was turned off during evaluation to prevent inadvertent unblinding but restored afterwards on a sample to quality check that the therapists had used standard instructions during data collection. During piloting, we found it unacceptable to evaluate FR from video, as the numbers on the metre-rule were (1) too small to read in the wide image necessary to rate posture and quality-check test conduct and (2) obscured by the reaching arm. So during the RCT physiotherapists rated FR in situ.

In their final week of involvement, we gave participants an anonymous feedback form (including space to comment) posing the following questions about the acceptability of home-based research, the randomisation, intervention, and assessments.

Did you find it difficult to fit taking part in the study into your routine?

Was it difficult to find enough space for video recording at home?

How do you feel about not being in the group that had physiotherapy?

Did you find physiotherapy helpful (and why)?

Do you think you had too little, enough, or too much physiotherapy (and why)?

Did you feel comfortable with video recording?

Were the tests quick enough to complete?

Were the questionnaires boring or difficult to complete or difficult to post back?

3. Results

We recruited 47 PwPD (median age 74 years; median years since diagnosis seven), including 45 who found transfers excessively slow, 39 who found transfers an excessive effort, and 17 who had fallen transferring; 13 participants (28%) reported all three indicators. Participant median Hoehn and Yahr stage was III and half the participants had fallen repeatedly in the previous year. The control group (n = 23) and treatment group (n = 24) were similar in characteristics and baseline performances (Table 1).

Thirty-five participants (74%) completed: four (9%) dropped out by week 4, five (11%) by week 8, and 12 (26%) by week 12. Of the final 12 drop-outs, eight (67%) were from the treatment group, through illness. Dropouts were representative of the whole sample age (median 73 years) and years since diagnosis (median 8) but 11/12 (92%) were at Hoehn and Yahr stage III or IV (in comparison with 79% of the whole sample).

Over the intervention period (weeks 0 to 4), as outlined in Table 2, the physiotherapy group median PAS score tended to improve (from 4 to 6) while that of the controls tended to worsen (from 6 to 4). The tendency to improvement in the physiotherapy group continued throughout followup (median score reaching 7 by week 12) while the control median returned to baseline. Median sit-to-stand times tended to shorten from weeks 0 to 4 (by 14%, from 2.2 s to 1.9 s, in both groups) and to continue shortening to week 12 (reaching 1.5 s in the physiotherapy group and 1.7 s in the controls, reductions of 32% and 23% from baseline, resp.). The physiotherapy group median SAS score tended to improve slightly by week 4 (by one point, from 50 to 49) while that of the controls tended to worsen (by 7 points, from 52 to 59); median scores tended to worsen in both groups by week 12 (the physiotherapy group deteriorating from baseline by 2 points, the controls by 12 points).

Over the intervention period, the physiotherapy group median SS-180 time tended to shorten (by 17%, from 5.3 s to 4.4 s) while that of the controls tended to lengthen (by 5%, from 3.7 s to 3.9 s). Throughout followup, the tendency to improvement in the physiotherapy group continued (median reaching 3.8 s by week 12, a reduction of 28% from baseline) while controls turn time remained longer than at baseline. The physiotherapy group median FR tended to improve slightly by week 4 (15%, from 19.2 cm to 22.0 cm) while that
Table 1: Participant characteristics at baseline (n = 47).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Value</th>
<th>Control group (n = 23)</th>
<th>Treatment group (n = 24)</th>
<th>All (n = 47)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>Median (IQR), range</td>
<td>74 (70–78), 58–86</td>
<td>75 (69–77), 64–82</td>
<td>74 (69–77), 58–86</td>
</tr>
<tr>
<td>Gender</td>
<td>Men (n)</td>
<td>18 (78%)</td>
<td>17 (71%)</td>
<td>35 (74%)</td>
</tr>
<tr>
<td>Years since diagnosis</td>
<td>Median (IQR), range</td>
<td>7 (4–12), 1–19</td>
<td>8 (4–11), 1–30</td>
<td>7 (4–12), 1–30</td>
</tr>
<tr>
<td>Hoehn and yahr (grade)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>1</td>
<td>0</td>
<td>1 (2%)</td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>5</td>
<td>4</td>
<td>9 (19%)</td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>10</td>
<td>12</td>
<td>22 (47%)</td>
<td></td>
</tr>
<tr>
<td>IV</td>
<td>7</td>
<td>8</td>
<td>15 (32%)</td>
<td></td>
</tr>
<tr>
<td>UPDRS</td>
<td>Median (IQR), range</td>
<td>30 (18–45), 9–52</td>
<td>26 (21–38), 10–60</td>
<td>28 (20–41), 9–60</td>
</tr>
<tr>
<td>12-month fall history</td>
<td>No falls (n)</td>
<td>7</td>
<td>4</td>
<td>11 (23%)</td>
</tr>
<tr>
<td></td>
<td>Single fall (n)</td>
<td>6</td>
<td>6</td>
<td>12 (26%)</td>
</tr>
<tr>
<td></td>
<td>Repeated falls (n)</td>
<td>10</td>
<td>14</td>
<td>24 (51%)</td>
</tr>
</tbody>
</table>

Indication for physiotherapy

- Transfers excessively slowly: n (%) 23 (100) 22 (92) 45 (96)
- Transfers a considerable effort: n (%) 20 (87) 19 (79) 39 (83)
- History of falls transferring: n (%) 10 (43) 7 (29) 17 (36)

Primary outcome measures

- PAS chair transfer score: Median (IQR), range 5 (4–6), 0–8 4 (4–6), 2–8 4 (4–6), 0–8
- Sit-to-stand time (s): Median (IQR), range 2.2 (1.6–3.7), 0.8–11.1 2.1 (1.5–3.2), 0.8–7.2 2.2 (1.5–3.2), 0.8–11.1
- SAS score: Median (IQR), range 54 (41–70), 37–104 50 (43–63), 36–90 51 (41–65), 36–104

Secondary outcome measures

- SS-180 turn time (s): Median (IQR), range 3.8 (3.4–6.8), 1.8–45.6 5.5 (3.8–8.4), 2.2–43.5 5.3 (3.5–7.4), 1.8–45.6
- FR (cm): Median (IQR), range 21 (17–25), 10–33 18 (16–21), 9–32 20 (16–23), 9–33
- UPDRS posture (score): Median (IQR), range 1 (1–2), 0–3 1 (1–2), 0–3 1 (1–2), 0–4
- HR-QOL score: Median (IQR), range 30 (26–32), 21–44 30 (26–37), 16–47 30 (27–35), 16–47

IQR = interquartile range; range = minimum to maximum.

Table 2: Changes in outcomes (weeks 0–12, by group) in participants who completed a measure on at least three occasions; values presented are medians (interquartile range).

<table>
<thead>
<tr>
<th>Primary outcomes</th>
<th>Group</th>
<th>Week 0</th>
<th>Week 4</th>
<th>Week 8</th>
<th>Week 12</th>
</tr>
</thead>
<tbody>
<tr>
<td>PAS chair transfer score</td>
<td>Control (n = 18)</td>
<td>6 (4–7)</td>
<td>4 (4–6)</td>
<td>6 (4–7)</td>
<td>6 (3–7)</td>
</tr>
<tr>
<td></td>
<td>Physiotherapy (n = 19)</td>
<td>4 (4–6)</td>
<td>6 (4–7)</td>
<td>7 (5–8)</td>
<td>7 (4–8)</td>
</tr>
<tr>
<td>Sit-to-stand time (s)</td>
<td>Control (n = 20)</td>
<td>2.2 (1.4–3.2)</td>
<td>1.9 (1.3–2.8)</td>
<td>2.0 (1.4–2.2)</td>
<td>1.7 (1.3–2.2)</td>
</tr>
<tr>
<td></td>
<td>Physiotherapy (n = 18)</td>
<td>2.2 (1.6–3.1)</td>
<td>1.9 (1.4–2.0)</td>
<td>1.7 (1.0–2.4)</td>
<td>1.5 (1.2–2.0)</td>
</tr>
<tr>
<td>SAS (score)</td>
<td>Control (n = 18)</td>
<td>52 (40–64)</td>
<td>59 (45–71)</td>
<td>60 (48–66)</td>
<td>64 (50–77)</td>
</tr>
<tr>
<td></td>
<td>Physiotherapy (n = 16)</td>
<td>50 (43–59)</td>
<td>49 (43–67)</td>
<td>58 (50–66)</td>
<td>52 (43–60)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Secondary outcomes</th>
<th>Group</th>
<th>Week 0</th>
<th>Week 4</th>
<th>Week 8</th>
<th>Week 12</th>
</tr>
</thead>
<tbody>
<tr>
<td>SS-180 turn time (s)</td>
<td>Control (n = 16)</td>
<td>3.7 (3.1–6.8)</td>
<td>3.9 (3.1–7.0)</td>
<td>4.1 (2.7–9.6)</td>
<td>3.9 (2.8–5.9)</td>
</tr>
<tr>
<td></td>
<td>Physiotherapy (n = 16)</td>
<td>5.3 (3.9–6.7)</td>
<td>4.4 (3.4–6.4)</td>
<td>3.7 (3.4–4.8)</td>
<td>3.8 (3.1–6.1)</td>
</tr>
<tr>
<td>FR (cm)</td>
<td>Control (n = 16)</td>
<td>20.9 (15.7–25.2)</td>
<td>21.0 (15.0–24.3)</td>
<td>21.7 (13.6–25.8)</td>
<td>19.7 (17.4–27.7)</td>
</tr>
<tr>
<td></td>
<td>Physiotherapy (n = 13)</td>
<td>19.2 (17.5–21.9)</td>
<td>22.0 (20.0–25.0)</td>
<td>22.8 (20.3–25.8)</td>
<td>25.5 (19.6–30.2)</td>
</tr>
<tr>
<td>UPDRS posture (score)</td>
<td>Control (n = 19)</td>
<td>1 (1–2)</td>
<td>1 (1–2)</td>
<td>1 (1–2)</td>
<td>1 (1–2)</td>
</tr>
<tr>
<td></td>
<td>Physiotherapy (n = 19)</td>
<td>1 (1–2)</td>
<td>1 (1–2)</td>
<td>1 (1–2)</td>
<td>1 (1–2)</td>
</tr>
<tr>
<td>HR-QOL score</td>
<td>Control (n = 14)</td>
<td>29 (26–31)</td>
<td>30 (25–33)</td>
<td>29 (25–33)</td>
<td>31 (24–34)</td>
</tr>
<tr>
<td></td>
<td>Physiotherapy (n = 14)</td>
<td>29 (26–36)</td>
<td>30 (28–36)</td>
<td>32 (28–38)</td>
<td>29 (27–34)</td>
</tr>
</tbody>
</table>

of the controls changed minimally (0.5%, from 20.9 cm to 21.0 cm); the tendency to improvement in the physiotherapy group continued (median reaching 25.5 cm by week 12, a 33% increase from baseline) while the control’s worsened (to median 19.7 cm, a 6% decrease from baseline). We detected little change in posture or quality of life in either group. On the UPDRS posture item, both groups were rated a median 1 (IQR 1–2) at every assessment point. The median HR-QOL score of both groups worsened by one point (from 29 to 30) by week 4; at week 12 the physiotherapy group median had
returned to baseline while that of the control group was two points worse.

Thirty-nine participants (83%) returned anonymous feedback forms at the end of the study, 20 from the physiotherapy group and 19 controls. Few participants found difficulty fitting in the study or finding space for the video-based assessments (3/35 in each case). Of 17 controls, seven expressed disappointment about not being in the treatment group (“I would have liked to see if it could help my condition”), while ten were ambivalent, for example, “someone had to be in this group and I was one of them.” Two of the treatment group (10%) found the intervention unhelpful but 18 (90%) found it helpful, reporting they had

(1) learned new skills or exercises (“Despite long-term Parkinson’s I still learned new ways”),
(2) found movement or exercise easier (“Easy to follow instruction, made easier by being in my home; I put them into practice during my daily round; they have become part of my routine”),
(3) gained useful advice and support from a good therapist (“Guidance managing my disability”).

Eight (40%) felt they had insufficient therapy time, as one hour was an inadequate representation (“She never saw me at my worst”) or they needed encouragement (“Physiotherapy prompts me into being regular with my own efforts”) and “the more the better” (“It works well at the time and more would have been an advantage”).

It works well at the time and the more the better (“I did not feel bored or disinterested”). Most felt comfortable being video-recorded (35/36) and found assessment acceptably quick (33/35). Few found the questionnaires difficult to complete (2/35) or return (1/39) or found them boring (2/36). Participants wrote few comments; although overwhelmingly positive, one participant felt “filming was unrepresentative; she never saw me totally unable to move or having to crawl on the floor.”

Reliance on video and questionnaires preserved assessor blinding fully; the assessor learned no-one’s group allocation as there were no distinguishing features in 600-plus silent video clips.

Of a potential 1316 measurements (seven outcomes measured for 47 participants four times), 131 (10%) were missing as participants had dropped-out (Table 3); of the remaining measurements, 185/1185 (16%) were missing or unusable. FR was the only test someone declined to attempt, and a documentation error (later rectified) invalidated 14% of potential FR data. Of the tests evaluated from video, the SS-180 had most missing/unusable data, 15% after excluding dropouts: records were discounted if the protocol had been followed incorrectly (e.g., the participant turned in the same direction on both trials), if editing invalidated the clip (e.g., ending before the turn was complete) or if the recording was inadequately lit. Timed sit-to-stand, PAS, and posture score had percentages of unusable data below 10%, after excluding dropouts.

4. Discussion

This study revealed a trend to improved transfers, mobility, and balance among PwPD after physiotherapy. It would be feasible to deliver this focused programme quickly and easily in the home. Over a quarter of participants had multiple difficulties with transfer speed, effort, and stability, all of which physiotherapists can address, yet Keus et al. [30] found transfers to be a physiotherapy priority in just 14% of cases, behind gait (74%), posture (49%), and balance (37%). While controls deteriorated, our intervention group tended to continue to improve over followup (sit-to-stand time decreased 14% by week 4 and 32% by week 12), which suggests continual refinement of newly learned strategies. As the need is evident and intervention possible, as suggested by these results and others [1–14], transfer training (preferably at home, where people can deploy strategies learned) should be integral to physiotherapy for PwPD. Illness, fatigue, and a lack of perceived benefit are commonly reasons why PwPD discontinue exercise regimes [31]. Illness among our treatment group accounted for most dropouts (as was the case when Nieuwboer et al. [12] lost 15% of their recruits to a home-based physiotherapy trial over 12 weeks), and some participants reported extreme fatigue after physiotherapy: this intervention warrants selective application.

The importance of physiotherapists’ expertise and relationships with patients in the quality and outcome of treatment is well recognised [30, 32]. From feedback, our sample appeared pro-physiotherapy (they learned new skills and ways of managing their condition) and pro-research (they understood their role within the study). Although several controls were disappointed, none dropped out following randomisation. Experienced clinicians in physiotherapy trials enhance the participant experience and data collection.

Among our video-based evaluations, drop-outs accounted for two-thirds of the missing data; technical difficulties with video production errors (such as filming in too dark a setting or in too confined or cluttered a space or editing the clip prepared for the blinded assessor too harshly) and protocol/documentation errors (such as having the person performing the SS-180 turn twice in the same rather than the opposite direction or recording the FR as habitually done during clinical practice rather than in the standard way used in the study) accounted for the rest. The layout, light levels, and contents of an individual’s home are their choice and researchers cannot expect the ideal conditions for data collection that they might expect in a purpose-built movement laboratory; although they can prepare the area used for video-recording to a certain extent, it is not reasonable to impose whole-scale modifications. It can be difficult to know at the time of recording that a clip will be too poorly illuminated for the assessor when they see it later. Similarly, a participant may move out of the camera’s scope in an unexpected way that only comes to light when editing the clip. The more complex the test, the more likely it is that a proportion will be obscured or lost. On balance, we believe that losing a proportion of data recorded in the home is outweighed by the benefits of the inclusivity that home-based research offers to the people who wish to participate. Specific
training and monitoring of therapists would improve these aspects of data collection. This feasibility study revealed that while experienced clinicians make good researchers, they are unlikely to have been trained in all the necessary research skills beforehand and they are also likely to have developed ways of conducting and recording tests in their professional practice that differ from the study protocols. Again, on balance, we believe that the benefit of employing experienced clinicians outweighs the costs involved in employing and training them in research skills which may be entirely new.

FR was the only test declined for fear of falling (by one individual on three occasions) and was the only assessment not feasible in the home, in this study. After dropouts, the major causes of missing/unusable questionnaire data were unreturned questionnaires (13% were missing) and incomplete questionnaires (omitted answers invalidated 9% of otherwise complete HR-QOL questionnaires). Feedback did not indicate problems but prompts or collection (both with cost and ethical implications) would have increased returns. Haapaniemi et al. [29], who received 15% of their HR-QOL questionnaires incomplete, used regression analysis to predict missing data, an option we would advocate.

Our assessment battery, which took approximately 20 minutes to complete in the home, measured the difficulty, slowness, and dependence associated with transfers. Speed improved by week 4 in both our groups, associated with an improvement in PAS score in the treatment group and deterioration among the controls. Others have demonstrated changes in transfer strategy after training while speed remains unchanged [33] and have stressed that function and stability are more important than speed [4]. We could recommend both the PAS score and sit-to-stand time as primary outcome measures in future, as the demand on participants is low and evaluation from video was associated with relatively little missing data. In light of the numbers of unreturned and incomplete questionnaires, and its breadth, we would not advocate the SAS in a similar way.

While it may be impossible to blind a trial participant as to whether they have actively taken part in a physiotherapy intervention [34], it should be possible to keep the assessor blind. Even when it is possible to blind the assessor, this is not always done or reported. In the present study, using silent video and questionnaires preserved total assessor blinding and was associated with other advantages over face-to-face or telephone contact. Working without distraction from edited clips reduced the time (and money) spent travelling to, and engaging with, participants by the experienced assessor. Video facilitates reliability testing, team review, illustration of findings, and quality control. Participants found the assessments acceptable, and (with the exception of FR) the assessments were feasible using standard equipment. Evaluation of video by a blinded assessor has been used successfully in fields such as gastric surgery [35] and pain control [36]; here we have demonstrated its feasibility in movement analysis. Video should only be used with explicit consent ensuring precautions are taken to (a) avoid recording anyone else’s image or conversation and (b) maintain the subject’s safety [37]: a tripod-mounted, battery-powered camera is safer than one which occupies the recorder’s hands and presents a trip hazard.

We make the following recommendations for a future RCT. Employ experienced clinicians, teach them the required research skills, and monitor fidelity to the recording protocol throughout the trial. When calculating a sample size, consider that our 19 controls scored a mean 5.11 (1.97) on the PAS Chair Transfer at baseline, which decreased a mean 0.32 (1.29) to a mean 4.79 (1.47) at week 4; the intervention group (n = 20) scored a mean 4.55 (1.39) at baseline, which increased a mean 0.90 (1.80) to a mean 5.45 (1.61) at week 4. Over-recruit by 25% to compensate for dropouts. Offer controls some intervention, in light of the multiple transfer difficulties of PwPD and our controls’ feedback. Use more sensitive measures of posture (such as tragus-to-wall distance) and quality of life than we trialled.

<table>
<thead>
<tr>
<th>Measure type</th>
<th>Number of potential measurements</th>
<th>Number of data missing</th>
<th>Number of data unusable</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Participant drop-out</td>
<td>Test declined, omitted, or not returned</td>
</tr>
<tr>
<td>In situ—real time</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FR</td>
<td>188</td>
<td>19 (10%)</td>
<td>18 (10%)</td>
</tr>
<tr>
<td>Video based</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PAS</td>
<td>188</td>
<td>19 (10%)</td>
<td>9 (5%)</td>
</tr>
<tr>
<td>Transfer time</td>
<td>188</td>
<td>19 (10%)</td>
<td>9 (5%)</td>
</tr>
<tr>
<td>SS-180 time</td>
<td>188</td>
<td>19 (10%)</td>
<td>10 (5%)</td>
</tr>
<tr>
<td>Posture</td>
<td>188</td>
<td>19 (10%)</td>
<td>9 (5%)</td>
</tr>
<tr>
<td>Postal questionnaires</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SAS</td>
<td>188</td>
<td>18 (10%)</td>
<td>24 (13%)</td>
</tr>
<tr>
<td>HR-QOL</td>
<td>188</td>
<td>18 (10%)</td>
<td>25 (13%)</td>
</tr>
<tr>
<td>Total</td>
<td>1316</td>
<td>131 (10%)</td>
<td>104 (8%)</td>
</tr>
</tbody>
</table>
As specifically supervised exercise was a component of the intervention in this trial, we did not ask participants to report any unsupervised exercise they may have undertaken; we suggest that researcher’s consider recording the latter in a full RCT. While the performances evaluated in this study were analysed by one blinded assessor, they were recorded by the unblinded trial physiotherapists: while the recordings allowed us to quality check test conduct, employing an independent recorder to collect and prepare clips for the assessor might reduce potential bias even further.

5. Conclusion

If the measures are suitable, an intense, focused physiotherapy programme delivered at home by experienced physiotherapists is likely to bring about positive change in those who can participate. We recommend a fully powered trial (over-recruiting to offset dropouts and offering the controls an incentive to remain) using remote outcome measurement (especially silent video assessment), as far as possible, to preserve blinding: missing/unsuitable data can be reduced by comprehensive training in video recording/editing and following up/collating questionnaires or replacing missing answers using statistical methods. The key implication of this feasibility trial is that a sample of PwPD older than in the earlier studies discussed, appeared to derive benefit from a programme that was shorter than most of the earlier studies and one that practicing clinicians could roll out without additional training or equipment.

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References


Research Article

Gait Difficulty, Postural Instability, and Muscle Weakness Are Associated with Fear of Falling in People with Parkinson’s Disease

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The present study aimed to examine the contribution of gait impairment, postural stability and muscle weakness to the level of fear of falling in people with Parkinson’s disease (PD). Fifty-seven community-dwelling individuals with PD completed the study. Fear of falling was assessed by the Activities-specific Balance Confidence (ABC) scale. Postural stability and gait difficulty were determined by the posture and gait subscores of the Unified Parkinson’s Disease Rating Scale (UPDRS-PG). A Cybex dynamometer was used to measure isokinetic knee muscle strength. Individuals with PD achieved a mean ABC score of 73.6 ± 19.3. In the multiple regression analysis, after accounting for basic demographics, fall history and disease severity, the UPDRS-PG score remained independently associated with the ABC score, accounting for 13.4% of the variance (P < 0.001). The addition of knee muscle strength significantly improved the prediction model and accounted for an additional 7.3% of the variance in the ABC score (P < 0.05). This is the first study to demonstrate that the UPDRS-PG score and knee muscle strength are important and independent determinants of the level of fear of falling in individuals with PD. Improving balance, gait stability and knee muscle strength could be crucial in promoting balance confidence in the appropriately targeted PD population.

1. Introduction

Fear of falling (FoF) is a common and potentially serious problem in people with Parkinson’s disease (PD). Previous studies have consistently reported that community-dwelling individuals with PD have a greater FoF than age-matched healthy subjects [1–4]. The level of FoF is further increased in those who have had a fall history [5]. In a prospective study, we found that FoF is also a significant risk factor for predicting future falls [4]. While some level of FoF has a protective role against falls, irrational FoF, either too much or too little, may increase fall risk. Delbaere et al. [6] have recently addressed this complex psychological factor in a large cohort of older population and revealed that discrepancies between psychological and physiological risk factors in those who had excessive or unduly low level of FoF. However, only those with excessive FoF had a higher risk of injurious falls. Repeated falls may lead to avoidance of activity, physical deconditioning, and increased institutionalization. Therefore, interventions aiming to enhance balance confidence have the potential to reduce fall risk in appropriately targeted individuals with PD.

To design effective treatment intervention, it is crucial to understand the factors that determine FoF. In people with PD, FoF was found to be associated with postural sway in standing and posture and gait impairment as measured by the unified PD rating scale (UPDRS) [1], one-leg stance time, timed-up-and-go time, 6-minute walk distance, and the UPDRS motor score [7]. Jacobs et al. [2] reported that the combination of the pull test, the gait item of the UPDRS, and one-leg-stance time was better than single items in predicting FoF. However, the regression model used in their study did not include factors that could contribute to the prediction of FoF, such as demographic data, disease severity, and fall history. In addition, the association between muscle strength and FoF has not been examined. We recently found that recurrent PD fallers had more lower extremity muscle weakness than PD nonfallers and single fallers [5]. Deficits
in muscle power were found to associate with slower gait velocity and increase fall risk in individuals with PD [8]. It is, therefore, important to determine the contribution of muscle strength in predicting FoF. The present study aimed to examine the factors that determine FoF in people with PD. Specifically, we examined balance and gait instability as well as muscle strength, as these are significant fall risk factors in people with PD [3, 9].

2. Methods

A convenience sample of 57 individuals with PD completed the study. PD participants were recruited from movement disorders clinics in Hong Kong and the Hong Kong Parkinson’s Disease Association, which is a patient self-help group. All patients were diagnosed by neurologists according to the United Kingdom PD Society Brain Bank Criteria [10]. All subjects were recruited on a volunteer basis. Informed consent was obtained from each participant in accordance with the 1964 Declaration of Helsinki, and all experimental work was carried out with the approval of the university ethics committee. To be included in this study, subjects were required to be between 40 and 85 years of age, medically stable, able to walk 6 metres at least three times with and without an assistive device, and able to understand simple commands (minimental state examination score ≥24 [11]). Subjects were excluded if they had neurological conditions other than idiopathic PD, exhibited postural hypotension, visual disturbance, or vestibular dysfunction affecting balance, or had significant cardiovascular or musculoskeletal disorders limiting locomotion or balance. All individuals with PD were tested within 2 hours after medication, that is, during the “on” phase of the medication cycle (Table 1).

3. Procedure

All evaluations were carried out at the Hong Kong Polytechnic University gait and motion research laboratory. Demographic data including age, body mass, height, and medications were recorded. We measured disease severity by the Hoehn and Yahr staging scale (HY) [12] and the motor component of the UPDRS [13, 14]. FoF was estimated by the activities-specific balance confidence (ABC) scale [15]. The knee muscle strength of participants was measured by a Cybex Norm dynamometer. Information on the number of fall events over the past 12 months was obtained by patient interview. Participants were classified as fallers if they suffered at least one fall in the past 12 months. A fall is defined as “an event during which a subject comes to rest on the ground or at some lower level, not as the result of a major intrinsic event for example, syncope, stroke and seizure, or an overwhelming hazard” [16].

Fear of falling was measured by the validated Chinese version of the ABC scale [17]. Participants were asked to rate their self-perceived balance confidence level from 0 (no confidence at all) to 100 (full confidence) for completing 16 activities of daily living. The mean score was calculated for each subject, with a minimum score of 0 to a maximum of 100. A lower ABC score indicates greater FoF.

The unified PD rating scale motor examination (UPDRS-III) is a valid tool used to assess the level of motor impairment and disability in individuals with PD [13, 14]. It consists of 14 items which assess PD-specific impairments. Each item scores from 0 to 4, with 0 indicating absence of impairment and 4 indicating severe impairment. In this study, the sum of items 27–30 (i.e., rising from a chair, posture, gait, and postural stability (UPDRS-PG) was used to document the postural instability and gait difficulty of PD participants [1].

Knee muscle strength was quantitatively assessed by a Cybex Norm isokinetic dynamometer (Lumex, Inc., Ronkonkoma, NY, USA). The more affected lower extremity, which was determined by a higher unilateral UPDRS-III score, was assessed. Participants were seated with their lower leg at 90° of knee flexion, and a strap and a footplate were attached to their lower leg and feet, respectively. Participants were stabilized by trunk and thigh straps during the test. The investigator then measured an anatomical zero when the knee was passively moved to full extension. Participants were instructed to perform isokinetic concentric and eccentric contraction of the knee flexors and extensors from 100° to 70° of flexion at an angular speed of 90°/s. The order of the 4 testing conditions was randomized. Participants were allowed to practice each type of contraction at their submaximal effort 2 times, which was followed by the test trial when 3 maximum concentric or eccentric contractions were performed. Participants were given a 3-minute rest between each mode of contraction. The average value of the peak torque (Nm) among the 3 test trials was obtained, and the sum of mean concentric and eccentric knee muscle strength

<table>
<thead>
<tr>
<th>Table 1: Subject characteristics.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>People with PD</strong> (N = 57)</td>
</tr>
<tr>
<td><strong>Demographics</strong></td>
</tr>
<tr>
<td>Age (years)</td>
</tr>
<tr>
<td>Height (cm)</td>
</tr>
<tr>
<td>Weight (kg)</td>
</tr>
<tr>
<td>Female gender, n (%)</td>
</tr>
<tr>
<td>Fallers, n (%)</td>
</tr>
<tr>
<td><strong>Parkinson’s disease characteristics</strong></td>
</tr>
<tr>
<td>Years since diagnosis of Parkinson’s disease (years)</td>
</tr>
<tr>
<td>Hoehn and Yahr stage (0–5)</td>
</tr>
<tr>
<td>UPDRS—motor score III (0–108)</td>
</tr>
<tr>
<td>UPDRS-PG (0–16)</td>
</tr>
<tr>
<td>Knee muscle strength (Nm)</td>
</tr>
<tr>
<td>ABC score (0–100)</td>
</tr>
</tbody>
</table>

Data shown are means (standard deviations), median (interquartile range). ABC: activities-specific balance confidence, UPDRS: unified Parkinson’s disease rating scale, UPDRS-PG: unified Parkinson’s disease rating scale (items 27–30).
was used for further analysis. Overall, these strength testing procedures lasted for 20 minutes.

4. Statistical Analysis

All statistical analyses were performed using SPSS 17.0, and a significance level of 0.05 (2-tailed) was set for all statistical tests. The Shapiro Wilk statistic was used to check data normality. Descriptive analysis was performed for the demographic data and variables of interest. Bivariate correlation analyses were performed. Pearson product moment correlation was performed to establish the relationship between the ABC score and knee muscle strength, as the data were normally distributed. For the UPDRS-PG score, which is an ordinal data, the relationship with the ABC score was determined by Spearman’s rho. A hierarchical multiple linear regression model (enter strategy) was used to determine the contribution of the UPDRS-PG score and knee muscle strength to the ABC score after accounting for other potential contributing factors (e.g., demographic data, fall history, and disease severity measured by the HY staging score). Age, duration of PD, fall history, and the HY staging scores were first entered into the regression model followed by the UPDRS-PG scores and knee muscle strength.

5. Results

The mean ABC score for individuals with PD was 73.5 ± 19.3. Individuals with PD had a median HY score of 2.5 ± 1.0, indicating mild-to-moderate disease severity. The median UPDRS-PG score was 4.0 ± 2.0, implying mild gait and postural instability. The mean knee muscle strength was 34.4 ± 13.3 Nm. Correlation analysis showed that the ABC score was positively correlated with knee muscle strength (r = 0.301, P = 0.029) and inversely correlated with the UPDRS-PG score (r = −0.661, P < 0.001). These findings indicate that a higher level of FoF was associated with greater knee muscle weakness and increased gait instability and postural difficulty. The results of the regression model show that after adjusting for basic demographics, fall history, and disease severity, the UPDRS-PG score remained independently associated with the FoF level, accounting for 13.4% of the variance (Model 2, Table 2). The addition of knee muscle strength significantly improved the model prediction by 7.3% (Model 3, Table 2). A total of 47.9% of the variance in the ABC score was predicted by the final regression model (F6,56 = 6.895, P < 0.001). Among all the variables, the UPDRS-PG score was the most important determinant of the ABC score, as reflected by the magnitude of the regression coefficient (β = −0.531).

6. Discussion

Our PD participants had a mean ABC score of 73.6 ± 19.3, indicating that they had moderate level of FoF. This finding is consistent with the published data [1, 2, 4, 5, 7]. The negative association between FoF and the UPDRS-PG score concurs with previous findings. Excessive FoF was shown to be negatively correlated with the UPDRS-PG score [1, 7], centre of pressure sway during standing [1], and Berg’s balance score, tandem Romberg, and timed up and go time [18] in individuals with PD. Our finding extends that reported by Jacobs et al. [2] that postural instability and gait impairment as measured by the UPDRS-PG score is an important determinant of FoF, after accounting for demographic data, fall history, and disease severity in individuals with PD. The UPDRS-PG score alone accounts for 13.4% of the variance of the ABC score. The UPDRS-PG score quantifies participants’ standing upright posture, response to retropulsion, sit-to-stand transfer, and gait stability. Stooped posture in people with PD was found to be destabilizing [19] and capable of predicting future falls [9]. In addition, people with PD are known to be slow and inflexible in response to external perturbation, especially to a backward pull [20–22]. Walking and rising from a chair have often been reported to be fall-related activities [23, 24]. For example, 24%–46% of individuals with PD were reported to have fallen during walking and turning and 15% of individuals with PD fell during transferring from sitting to standing [5, 23, 24]. Greater postural instability and gait difficulty in individuals with PD will lead to less perceived self-confidence in performing balance activities, hence an increased level of FoF.

Previous studies reported that people with PD had reduction in knee and ankle muscle strength [25–27], which was correlated with sit-to-stand performance [28] and gait velocity [26]. Our study is the first to report that knee muscle strength, which accounted for 7.3% of the variance of the ABC score after accounting for demographic data and the UPDRS-PG score, is another important determinant of FoF. In a recent study, we reported that recurrent PD fallers had significantly more reduced lower extremity muscle strength than single fallers [5]. These recurrent fallers also perceived that “muscle gives way” was associated with their falls. Knee muscle strength is crucial for maintaining stability in an upright position. Weakness in this muscle group could give the patients the perception that their “muscles give way” while in the standing position and lead to a lack of confidence in performing standing or walking activities. Lower extremity muscle strength was independently associated with reduced bone mass in individuals with PD [27]. Furthermore, knee extensors muscle strength of the more affected side was a significant fall predictor [9]. When combined with excessive FoF, muscle weakness may restrict individuals' activities, lead to further muscle weakness and accelerated loss of bone mass, and increase the risk of fall-related fracture.

To prevent falls in people with PD, treatment interventions should enhance both physical function and balance confidence. A recent systematic review reported that in older adults, exercise was the most commonly used intervention to improve balance confidence [29]. The exercise interventions include strength, balance, and gait training. Combined cognitive behavioral education (i.e., identification of fall risk factors, discussion of coping strategies for falling, and assertiveness training) and exercise training were found to be effective in enhancing balance confidence and reducing the risk of falls in older people [30]. Based on the significant association between FoF and postural and gait impairment
and knee muscle weakness, clinicians may consider incorporating muscle strengthening programmes, as well as improving patients’ postural and gait stability, in their fall prevention programs. We believe that the promotion of balance confidence can prevent the vicious cycle of activity restriction, physical deconditioning, further decline in self-perceived balance confidence, and future falls. Further interventional study is needed to prove this postulation.

We acknowledge that our study has certain limitations. To be included in the study, participants needed to be able to walk freely to undertake the gait assessments. Our findings, therefore, are not generalisable to individuals with PD with significant gait impairments. Our assessments were also restricted to “on phase” periods. It is possible that conducting assessments during the “off” phase of treatment would increase their sensitivity. In addition, FoF is associated with many factors. However, we could not include many predicting variables in the regression analysis due to our small sample size. Our model was able to predict 47.9% of the variance of the ABC score. Other physical factors such as freezing of gait and cognitive psychological factors such as cognitive impairment, anxiety, and depression could contribute to the level of FoF. Finally, this is a cross-sectional study. We could not establish a causal relationship between postural impairment, gait difficulties, muscle weakness, and FoF. Further research should address the temporal relationship between postural and gait impairment as well as muscle weakness and FoF.

To conclude, postural instability, gait difficulty, and knee muscle weakness are important determinants of the level of FoF. The clinical implication of our study is that the balance confidence of people with PD may be enhanced through promoting muscle strength, balance, and gait stability, thereby preventing activity restriction and physical deconditioning and reducing fall risk. Further intervention study is needed to prove this postulation.

Acknowledgment

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References


Clinical Study

A Manipulation of Visual Feedback during Gait Training in Parkinson’s Disease

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Visual cues are known to improve gait in Parkinson's disease (PD); however, the contribution of optic flow continues to be disputed. This study manipulated transverse line cues during two gait training interventions (6 weeks). PD subjects (N = 42) were assigned to one of three groups: treadmill (TG), overground (OG), or control group (CG). Participants walked across lines placed on either treadmills or 16-meter carpets, respectively. The treadmill (TG) offered a reduced dynamic flow from the environment, while lines presented on the ground (OG) emphasized optic flow related to the participant's own displacement. Both interventions significantly improved (and maintained through retention period) step length, thus improving walking velocity. Only the OG improved in the TUG test, while only the TG showed hints of improving (and maintaining) motor symptoms. Since gait improvements were found in both training groups, we conclude that by reducing optic flow, gait benefits associated with visual cueing training can still be achieved.

1. Introduction

Individuals with Parkinson’s disease (PD) have been shown to walk with a stooped posture, limited arm swing, slow velocity, and small shuffling steps that can often lead to falls [1]. Sensory cueing strategies such as auditory, tactile, and visual cues have often been used to help walking in PD. Stein and Glickstein [2] suggested that of all these modalities, visual cues are most effective in improving PD gait. It is not clear, however, whether improvements might be the result of improved use of optic flow, greater attention directed towards walking, or cortically driven planning of discrete steps that bypass the basal ganglia.

Optic flow is a prominent theory that is often put forward to explain the benefits associated with using transverse lines. This theory suggests that transverse lines improve walking due to the stripes accentuating the flow of the surrounding environment as one moves through space [3, 4]. This notion of optic flow has been strongly supported by Azulay et al. [5] that believe the lines emphasized optic flow which improved gait velocity and stride length in PD participants. Optic flow has been previously manipulated through either virtual reality or a projected tunnel screen [6, 7], and in each case, manipulation was presented by changing the surrounding environment. An interesting method of manipulating visual information from the surrounding environment is to have people walk on a treadmill. Biomechanically, the differences that exist between treadmill and overground walking are negligible [8]. Interestingly, however, walking on a treadmill allows a reduction of typical optic flow that would normally be associated with every day walking. Song and Hidler [8] and Frankel-Toledo et al. [9] acknowledge that subjects on a treadmill do not receive the same optic flow as they do when walking overground. Bello et al. [10] proposed that gait improvements in PD treadmill walking are caused by the subject’s ability to strategically use the distance from the front of the treadmill as a static visual cue. Contrarily, a study by Azulay et al. [5] used stroboscopic lighting to suppress optic flow by transforming stripes on the floor to static cues, resulting rather in a deterioration of gait in PD patients. This contradicting evidence indicates that little is known as to how much, if any, optical flow is
needed to improve gait in PD. Thus, comparing overground and treadmill training with identical visual cues provides a unique opportunity to evaluate how optic flow might contribute to gait improvements.

Fundamental to these gait deficits is the inability to produce a normalized step length [11]. Many popular visually guided cues have been shown to improve step length including the inverted walking stick, projected laser beam [12, 13], and parallel lines [14]. It has been well established that transverse lines an inch wide or more have been best shown to facilitate locomotion [15]. Jiang and Norman [16] found that transverse lines assisted in the initiation of gait in PD individuals. However, most studies that implement transverse lines have often only conducted single sessions [16–18]. Morris et al. [17] showed that a single cueing session was effective in regulating stride length in PD and that a training effect emerged leading to improvements two hours after visual cues were removed. However, the potential for long-term cue training to lead to even longer lasting benefits to gait has yet to be studied. Interestingly, the only case study (with an n = 1) using transverse lines as a long-term cueing intervention revealed potential benefits [19]. Thus, more research must explore transverse lines as a long-term cueing therapy for Parkinson’s disease.

Unfortunately, most of the above studies failed to administer a retention assessment; hence, any persisting long-term improvements to gait have yet to be determined. Also, an assessment of gait transference to a more functional test such as the timed up and go (TUG) has not been used, as well as potential symptomatic improvements (UPDRS motor scores). Through the administration of these tests, we can achieve greater insight into the underlying mechanism of improvement with the use of transverse line cues during gait.

One method of manipulating the provision of transverse lines is to modify the context in which they are provided for training. For example, integrating transverse line cues on a treadmill is novel, as it provides step cues but within a more static background. In contrast, transverse lines provided over the length of a carpet would move past any individual relative to the rest of the surrounding environment. Thus, our study compared two different methods of providing transverse line cues: (1) traditional overground gait training (with transverse lines) and (2) treadmill training. Our primary outcome measure was step length, while additional measures included UPDRS motor scores, lower limb strength gains, TUG times, and other spatiotemporal aspects of gait. All variables were assessed at baseline (pretest), after a 6 week rehabilitation phase (posttest), and 6 weeks later (retention test).

2. Methods

2.1. Subjects. The study included a total of 42 participants that were assigned to one of three PD groups: treadmill (TG), overground (OG), or control (CG). All participants (recruited through a database from the Sun Life Movement Disorders Research and Rehabilitation Centre, Wilfrid Laurier University, Canada) were diagnosed with Parkinson’s disease and then randomized and matched for overall, as well as PD specific demographics (based on a prescreening assessment).

Each participant tested was confirmed to have clinically typical PD from at least one movement disorders neurologist. All PD patients were responsive to anti-Parkinsonian medication and were in an optimally medicated or “on” medication state at the time of all training and testing sessions.

Participants were excluded from the study if they had a past history of neurological conditions other than PD or orthopaedic or visual disturbances that severely impaired walking ability. Also, participants were removed if they were unable to independently walk down an 8 meter GAITRite carpet for a total of 10 trials. Each participant was informed of the requirements of the study and signed institutionally approved consent forms, according to the declaration of Helsinki (BMJ 1991; 302: 1194).

2.2. Materials. Data was collected in two different rooms, a gymnasium and a laboratory measuring approximately 20 m × 10 m and 9.5 m × 6 m, respectively. Gait data was collected in the gymnasium on a GAITRite carpet (GAITRite, CIR System, Inc., Clifton, NJ, USA) which measured 8 m long × 0.92 m wide and contained sensors that provided footfall information to an attached computer. The 30-second chair stand and TUG test were conducted in the laboratory. Materials needed for the two tests included a straight back chair, a taped line 3 meters away from the chair, and a stopwatch. Two Biodex Gait Trainer 2 treadmills were used for the treadmill group, and three 16-meter black landscaping carpets were used for the overground group. Transverse lines were created using white athletic tape.

2.3. Protocol

2.3.1. UPDRS Severity Score. All participants’ motor symptoms were assessed by a blinded movement disorders specialist using the UPDRS Section 3.

2.3.2. Timed Up and Go (TUG). TUG test required participants to sit in a chair and when told “go”, participants were asked “to stand up, walk to the taped line, turn around, and sit back in the chair as quickly and safely as possible.” Two trials were performed and time was recorded using a stopwatch. The purpose of the TUG was to assess functional mobility of PD participants and track gait changes over time [20].

2.3.3. 30-Second Chair Stand. The 30-second chair stand required all participants to be seated in a chair and when told “go” to rise to a full stand position and sit back down again. This was repeated as many times as possible in a span of 30 seconds. Two trials were performed, and the total number of stands was recorded. This measure was used to identify any lower limb strength gains that may result from the intervention.
2.3.4. GAITRite Walking. All participants were requested to walk down an 8-meter GAITRite carpet “at a normal casual walking speed” for a total of 5 trials. If participants needed further explanation, they were asked to walk down the carpet as though they were “walking down the street.” Participants started 1 meter before the carpet and told to walk 2 steps beyond the end of the carpet to ensure gait initiation and termination were not processed in data collection. Footfall information was collected to an attached computer, and the following gait measures were obtained: gait velocity (cm/s), cadence (steps/min), mean step length (cm), double support time (s), step time (s), step-to-step variability, step-time variability, and double support variability.

2.3.5. Training Protocol. Participants completed gait training 3 times a week for 6 weeks (18 sessions in total). Each gait session spanned 30 minutes with a mandatory 2-minute break every 8 minutes. However, participants were allowed additional rest if necessary but were required to walk a total of 24 minutes for the gait session to be considered complete. All participants were “on” medication at the time of pre-, post-, and retention testing and during training. All training sessions were conducted at the same scheduled time. Spotters were provided for all participants to ensure safety. In both training groups, visual cues were provided (on ground or treadmill) with the use of white lines (see description below). To standardize the step length required during training, we selected a separation between lines that was a minimum of 8% greater than the initial step length of any of the groups. Thus, based on previous research [12] and also this 8% requirement, the white lines were separated by 70 cm. This ensured that from one consecutive heel strike to the next, participants in both the overground and treadmill group trained with an equivalent distance between cue steps. Furthermore, in order to control for training velocity, stepping was monitored using a timer over the distance covered for the overground group, while velocity could be set manually for the treadmill group. In both cases, training velocity was based on each individuals predetermined self-paced velocity.

(a) Overground Group. Overground gait training required participants to walk down equally spaced transverse lines, presented on a 16-meter carpet. The cues were white lines of tape equally distributed at a standardized length on the black background carpet. Participants trained at the same walking speed that was measured at pretest (GAITRite analysis). This was achieved by requiring participants to completely clear the carpet within a specified amount of time. Participants were asked to walk across the lines, turn, and continue back. A spotter would also assist in tracking time to ensure participants completed the trial in the allotted time.

(b) Treadmill Group. Treadmill gait training required participants to walk on a treadmill presented with equally distributed standardized transverse white lines. All participants walked at the speed determined at pre-test. This speed was inputted by the student investigator prior to commencement of training.

A posttest was administered six weeks after the pretest, followed by a six week retention test. During the retention period, participants were told to exercise no more than usual.

2.4. Statistical Analysis. Long-term effects compared measurements across time placing pre-, post-, and retention-test values in the same analysis of variance. The dependent variables analyzed were TUG times, 30-second chair stand, UPDRS III score, and all GAITRite measures. Step length and step time data were further analyzed according to more affected versus less affected lower limb. More affected lower limb was defined by summing left and right scores for question 27 and 28 of the UPDRS III (leg agility and leg tremor, resp.) and taking the greater score. However, after finding no differences, left and right limb data was automatically pooled by the statistical analysis software. Also, first and last walking trials of all GAITRite measures were taken out of the analysis to avoid any learning and fatigue effects. Analysis was carried out by STATISTICA 8.0 using a group (treadmill, overground, control) by time (pretest, posttest, and retention test) ANOVA. An alpha level of 0.05 was used in all analyses. A Tukey’s honest significant difference (HSD) post hoc was further employed to determine from where the significant differences were driven.

3. Results

3.1. Baseline Comparisons. Baseline characteristics can be seen in Table 1. Although the OG group appears to be slightly older than TG and CG, one-way ANOVA’s were conducted comparing all three groups for severity using the UPDRS Section 3 height, initial velocity, step length, and TUG times resulting in no significant differences ($P = 0.81$, $P = 0.97$, $P = 0.32$, $P = 0.20$, $P = 0.16$, resp.).

3.2. Outcome Measures (For summary see Table 2). Step length showed an overall group by time interaction ($F_{(4,72)} = 4.5338$, $P < 0.003$), post hoc analysis confirmed that both intervention group improved and maintained (after the retention period), whereas the control group showed no changes over time (Figure 1). Gait velocity also showed an overall group by time interaction ($F_{(4,72)} = 3.7605$, $P < 0.008$), with the interaction being driven by a velocity

<table>
<thead>
<tr>
<th>Group</th>
<th>Age-M (yrs)</th>
<th>Height-M (cm)</th>
<th>UPDRS-M (score)</th>
<th>Gender</th>
</tr>
</thead>
<tbody>
<tr>
<td>PD TG</td>
<td>63.86 (8.41)</td>
<td>170.97 (10.29)</td>
<td>23.68 (10.1)</td>
<td>8 male, 6 female</td>
</tr>
<tr>
<td>PD OG</td>
<td>73.93 (6.53)</td>
<td>170.72 (10.22)</td>
<td>22.07 (8.0)</td>
<td>12 male, 2 female</td>
</tr>
<tr>
<td>PD CG</td>
<td>67.43 (9.26)</td>
<td>170.15 (6.83)</td>
<td>24.21 (9.5)</td>
<td>11 male, 3 female</td>
</tr>
</tbody>
</table>

Note: M denotes mean, standard deviations found in brackets.
Table 2: Mean (± standard deviation) of outcome measures from pre-, post-, and retention test.

<table>
<thead>
<tr>
<th>Measure</th>
<th>Test</th>
<th>PD control</th>
<th>PD treadmill group</th>
<th>PD overground group</th>
<th>ANOVA Pre-, Post-, and Retention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Step length (cm)</td>
<td>Pretest</td>
<td>57.7 (12.3)</td>
<td>63.9 (10.6)</td>
<td>57.6 (26.3)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Posttest</td>
<td>59.3 (12.7)</td>
<td>69.4 (9.9)</td>
<td>62.3 (8.3)</td>
<td>*P = 0.003</td>
</tr>
<tr>
<td></td>
<td>Retention test</td>
<td>58.8 (14.0)</td>
<td>69.9 (12.4)</td>
<td>64.2 (10.3)</td>
<td></td>
</tr>
<tr>
<td>Velocity (cm/sec)</td>
<td>Pretest</td>
<td>109.0 (27.7)</td>
<td>119.2 (15.6)</td>
<td>108.5 (4.2)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Posttest</td>
<td>109.6 (27.1)</td>
<td>128.3 (16.5)</td>
<td>112.2 (18.1)</td>
<td>*P = 0.008</td>
</tr>
<tr>
<td></td>
<td>Retention test</td>
<td>104.3 (32.8)</td>
<td>129.1 (18.0)</td>
<td>118.9 (19.0)</td>
<td></td>
</tr>
<tr>
<td>TUG time (seconds)</td>
<td>Pretest</td>
<td>9.0 (3.0)</td>
<td>7.7 (2.0)</td>
<td>9.9 (4.2)</td>
<td>*P = 0.046</td>
</tr>
<tr>
<td></td>
<td>Posttest</td>
<td>9.1 (3.3)</td>
<td>6.3 (2.0)</td>
<td>8.4 (3.7)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Retention test</td>
<td>9.1 (3.7)</td>
<td>6.5 (2.5)</td>
<td>10.2 (5.8)</td>
<td></td>
</tr>
<tr>
<td>UPDRS score</td>
<td>Pretest</td>
<td>24.6 (9.7)</td>
<td>23.6 (10.5)</td>
<td>22.1 (8.0)</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>Posttest</td>
<td>26.7 (8.8)</td>
<td>23.0 (8.0)</td>
<td>25.5 (7.0)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Retention test</td>
<td>26.8 (8.8)</td>
<td>22.6 (8.0)</td>
<td>27.8 (9.1)</td>
<td></td>
</tr>
</tbody>
</table>

NS: denotes a nonsignificant interaction.
**: denotes significantly different from pretest (P < .05).
3 patients removed from the current analysis.

Figure 1: Step length significantly improves in TG and OG after six weeks (posttest) and is maintained after 12 weeks (retention test).

improvement in both training groups but not the control group. Figure 2 displays an overall ~10 cm/s increase in both TG and OG, while the CG decreased in gait speed; however, post hoc analysis revealed this change in velocity was not significant. There was no change seen in cadence and 30-second chair stand in all groups, across all three testing periods (P > 0.05). Examination of the TUG test revealed a significant group by time interaction (F(2,39) = 4.0477, P < 0.05), suggesting that only the OG had decreased TUG times after the six week intervention. However, while still a significant interaction (F(4,78) = 2.5564, P < 0.05), after three participants (two in TG, one in CG) were excluded from the analysis due to medical conditions at the retention period, improvements in TUG time for the OG returned to baseline values after time of retention (Figure 3). The UPDRS severity scores were analyzed and approached a significant interaction (P = 0.06) (Figure 4). The TG showed a trend to decrease symptom severity from pre- to posttest, and improvements were maintained over the retention period. Contrarily, the CG and OG showed a modest symptom severity increase (i.e., symptoms worsened) from pre- to posttest, which was also maintained after the retention test. All other spatial and timing gait parameters showed no change.

4. Discussion

While many studies have demonstrated the positive benefits associated with visually cued walking in PD, little to no studies have evaluated long term benefits of visually cued gait training. Here we present (according to “level of evidence” and “grading of evidence guidelines”) a Silver BIIa evidence study to evaluate the influence of long-term visual cue training. A primary objective of the current study was to isolate visual cues in a static versus dynamic context in order to understand the extent to which optic flow contributes
to gait improvements in PD. The two gait interventions were conducted in nearly identical fashions, with the only difference between group training protocols being whether the cues were on the treadmill (TG) or on the ground (OG). In order to remove any other potential confounds, all other variables such as intensity, required step length, frequency of training, and duration of training were kept identical between groups.

Parkinsonian gait has previously been theorized to be the result of a deficient connection between the basal ganglia and supplementary motor area (SMA). The interactions between these two structures are commonly associated with controlling well-learned movements. However, in PD, this disconnect is believed to cause impaired internal cueing within the basal ganglia, often manifesting itself into problematic walking. Visual cues are proposed to bypass this deficient loop and use visual motor pathways in the lateral premotor cortex (PMC) and posterior parietal cortex (PPC), as these areas are activated through externally cued movements and paradoxical movements, respectively [21]. Similar gait results in both training groups is evidence that usual optic flow is not essential, but rather, the transverse lines may be activating these areas regardless of surrounding environmental information.

It is important to acknowledge however, that we did not completely remove optic flow in the treadmill training group. Rather we were able to reduce the amount of optic flow available in the treadmill group relative to the overground group. Thus, some researchers might argue that as long as some optic flow is available, gait improvements can still be achieved.

The findings of our study confirm that transverse lines have a positive impact on gait parameters [15, 17, 19, 22, 23] and contributes to the existing PD literature on the long-term effects of visual cue training protocols. Step length was shown to improve after six weeks and was maintained after an additional six-week retention period in both the TG and OG. Findings indicate that this spatial gait improvement is not the result of short-term training effects but rather a lasting change in the subjects walking. The fact that step length improvement was maintained even after the non-exercising period suggests that cueing provides potential for greater long-term retention gains [24]. The present study also rules out any potential strength gains that may have contributed to step length improvements. The 30-second chair stand was used as a tool to assess lower limb strength and gait performance [25] and showed no change across all groups.

A significant interaction revealed that both intervention groups achieved faster walking speeds upon completing the current study. Moreover, these same groups also experienced no change in cadence. In many cueing and treadmill studies, increase in step length is often accompanied by an increase in cadence [17, 26, 27]. However, it is unknown as to what extent each variable (step length or cadence) influences gait velocity. Our study reveals that PD individuals are achieving faster walking speeds due to taking larger steps rather than increasing the frequency of stepping. Thus, their velocity improvements were a result of step length gains rather than a compensatory reaction to cadence.

Although walking measures were similar across the two intervention groups, the TUG test did reveal an important difference. The TUG test has been shown to significantly correlate with the Berg balance scale, implying that improvement in TUG times may suggest an improvement in dynamic balance as well [28]. Our study revealed that only the OG significantly improved TUG times. This may be due to the nature of the overground walking protocol, which required the participant to turn at the end of the visual cue carpet, mimicking the constant movement found in people walking on a treadmill. By having individuals turn at the end of the 16-meter carpet, the OG may have developed strategies for turning. The participants could have used the cues on the carpet to compete their turn, similar to the way they use transverse lines during straight line walking. The lines may have acted as a critical feedback tool for completing a successful turn, which is essential in optimizing motor performance [29]. This would suggest that this group may
be simply using an attentional strategy in which the cues are used to focus ones attention on completing the required gait sequence [17]. Alternatively, it is possible that the OG had more opportunity to practise turns relative to the TG (since no turns are made on a treadmill). These results provide some important implications for rehabilitation professionals, as turning movements have been problematic in PD and closely linked to falling incidences and freezing episodes [30, 31]. These effects, however, did not persist past the posttest, which could be due to the complex nature of turning in general compared to straight walking.

In assessing symptom severity, the UPDRS motor score displayed a trend towards a significant interaction ($P = 0.06$). More importantly, there is a hint of symptom improvement in the TG, while the OG and CG displayed worsening of symptoms that often accompanies the progression of the disease [32]. It is important to consider that the improvements in the TG may be caused by the treadmill belt driving proprioceptive inputs [33], when the lower limbs are actively and passively taken through the walking cycle. Impaired proprioception has been previously reported in PD individuals [34], and perhaps, the treadmill belt is externally stimulating the afferent inputs that may help overcome the secondary effects of the disease. Hence, future research might also consider how external drive may be related to treadmill training, while overground training might be more internally driven. Animal model studies looking at treadmill training have been shown to acutely increase dopamine release [35] and chronically upregulate D2 receptors in the striatum of rats [36]. The motor symptom improvement found in the TG may similarly be the result of this overall availability and utilization of dopamine.

5. Conclusions

The overall improvements found in the treadmill and overground groups as compared to the control group are indicative of the positive impact transverse lines have on gait. However, similar step length and velocity improvements in both training groups suggests that typical optic flow is not necessarily required to achieve short- and/or long-term benefits associated with PD gait training. Rather than using optic flow information, PD participants may be using vision as a strategy to overcome lower limb proprioceptive deficit and/or focus attention on consciously achieving the stepping process. Interestingly, hints of motor severity improvement in the TG seem to be driven by additional proprioceptive input fed by the belt, while functional tests such as the TUG improved for those that repetitively practised turning. The results of our study reveal that a reduced amount of optic flow can produce similar benefits during gait training, and clinically, the implementation of transverse lines as a long-term cueing therapy for Parkinson’s disease seems appropriate. Furthermore, future work should focus on implementing visual cueing therapy during functional aspects of walking such as gait initiation, termination, and turning.

Author’s Contributions

Each of the coauthors contributed equally to the development and completion of this project.

Conflict of Interests

The authors declare no potential conflict of interests with respect to the authorship and/or publication of this paper.

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References

Parkinson’s Disease


Research Article

Walking Ability Is a Major Contributor to Fear of Falling in People with Parkinson’s Disease: Implications for Rehabilitation

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Although fear of falling (FOF) is common in people with Parkinson’s disease (PD), there is a lack of research investigating potential predictors of FOF. This study explored the impact of motor, nonmotor, and demographic factors as well as complications of drug therapy on FOF among people with PD. Postal survey data (including the Falls Efficacy Scale, FES) from 154 nondemented people with PD were analyzed using multiple regression analyses. Five significant independent variables were identified explaining 74% of the variance in FES scores. The strongest contributing factor to FOF was walking difficulties (explaining 68%), followed by fatigue, turning hesitations, need for help in daily activities, and motor fluctuations. Exploring specific aspects of walking identified three significant variables explaining 59% of FOF: balance problems, limited ability to climb stairs, and turning hesitations. These results have implications for rehabilitation clinicians and suggest that walking ability is the primary target in order to reduce FOF. Specifically, balance, climbing stairs, and turning seem to be of particular importance.

1. Introduction

People with Parkinson’s disease (PD) have an increased risk of falling [1], and fear of falling (FOF) is also more common and pronounced compared to controls [2–6]. FOF has been described as an ongoing concern about falling, a loss of balance confidence, low fall-related self-efficacy, or as activity avoidance [7–11].

The prevalence of FOF in people with PD has been reported to range from 35% to 59% [2, 12–16], although a study that included only men reported a lower prevalence (18%) [17]. It is even more common and pronounced among fallers [2, 6, 12–14, 17–19]. FOF can cause social isolation [20], and up to 70% of people with PD report activity limitations due to FOF [2, 21]. It is thus important for rehabilitation clinicians to understand the factors contributing to FOF.

Successful interventions need to be based on an understanding of factors associated with (and potentially influencing) the target of the intervention. That is, if rehabilitation aims to reduce FOF, it should target factors that may influence FOF. With respect to FOF in PD, weak to moderate associations (Spearman correlations \( r_s \)) have been found between FOF and age \( (r_s, \leq 0.08) \), PD duration \( (r_s, <0.29) \), and disease severity \( (r_s, 0.47) \) [14, 22]. Previous studies have also shown that FOF relates to freezing of gait (FOG) [15, 23], physical functioning [14], gait tests [5, 14, 22, 24], balance [3, 14, 22], mobility, activities of daily living (ADL) [14, 21], and sex [14]. However, those studies have relied on bivariate analyses, and none has simultaneously taken a broader range of independent variables (e.g., motor symptoms, drug therapy complications such as motor fluctuations and dyskinesias, nonmotor symptoms, and demographic factors) into account. The objective of this study was to
2. Participants and Methods

Data were collected by a postal survey to a sample of people with idiopathic PD [25]. All individuals with PD that received care at a Swedish university hospital were considered for inclusion in the study. Exclusion criteria constituted dementia or severe cognitive impairment as determined by their respective PD-specialized nurse clinicians. The survey was sent to 282 individuals (39% women) followed by a reminder about ten days later. Of 231 returned questionnaires, 38 were returned blank and two were returned to sender due to a change of address. There were thus 191 survey respondents (43% women; conservative total response rate, 68%). Six of these had left the included FOG-questionnaire completely blank, and total scores could not be computed for another 31 participants due to missing data. These 37 persons were excluded from the analysis. Excluded participants did not differ ($P \geq 0.153$) from those included with respect to sex, age, and PD duration. Characteristics of the final study sample ($n = 154$) are presented in Table 1. The investigators did not have access to patient details (beyond those provided by survey responders) or addresses. The study was conducted in accordance with the Declaration of Helsinki, and all participants gave their informed consent.

2.1. Survey Questions and Instruments. In addition to demographic questions, the survey included a set of questions on the presence or absence (no/yes) of motor fluctuations (i.e., a fluctuating effect of anti-PD medications with periods of more severe motor symptoms), dyskinesias (i.e., involuntary, irregular, twisting, and/or jerky movements), comorbidity, FOF, falls during the past six months (described and defined as by Lamb et al. [26]), near falls (described and defined as by Gray and Hildebrand [27]), and need of help from others in daily activities. Overall perceived PD severity was self-rated as “mild,” “moderate,” or “severe.” In addition, participants were asked whether they had responded to the survey themselves (with or without assistance in reading and/or writing).

A battery of self-administered questionnaires was included. The Falls Efficacy Scale (FES) conceptualizes FOF as low fall-related self-efficacy [8]. The Swedish version, FES(S), includes 13 items (activities) rated from 0 (not confident at all) to 10 (completely confident) [14, 28]. The maximum total score is 130 points, and a higher score denotes “better” balance confidence. The Functional Assessment of Chronic Illness Therapy-Fatigue scale (FACIT-F) consists of 13 items with a total score ranging between 0–52 (higher scores = less fatigue) [29, 30]. The physical functioning (PF) scale from the Short Form-36 (SF-36) includes ten items, and the total score can range between 0–100 (higher scores = better) [31, 32]. The self-administered version of the FOG Questionnaire (FOGQsa) consists of six items graded 0–4 (higher = worse) [15]. In this study we only used items 3 (freezing: “Do you feel that your feet get glued to the floor while walking, making a turn or when trying to initiate walking (freezing?)”) and 6 (turning hesitations: “During the past week, how long have your typical “freezing” episodes been when making a turn?”) of the FOGQsa. Those scoring ≥ 1 on item 3 were categorized as “freezers,” and those scoring ≥ 1 on item 6 were considered to have turning hesitations. The generic version of the Walking-12 (Walk-12G) assesses walking difficulties in everyday life from the individual’s perspective [33–35]. The total Walk-12G score ranges between 0–42 points (higher scores = worse). In this study, item 6 (“Have you had problems balancing when standing or walking?”) of the Walk-12G (graded 0–4) was specifically used to identify and describe balance problems. Those scoring ≥ 1 were considered having balance problems. The pain section of the Nottingham Health Profile (NHP-Pain) has eight items and yields a total score between 0–100 (higher scores = more pain) [36, 37].

All included patient-reported rating scales have previously been found to have acceptable validity and reliability in people with PD [14, 15, 30, 32, 35, 37]. Reliabilities (coefficient alpha) in this study were as follows: FES(S), 0.98; FACIT-F, 0.85; PF, 0.93; Walk-12G, 0.96; NHP-Pain, 0.85. Corrected item-total correlations in this study were all ≥ 0.30. These data support the adequacies of scores used in this study [38].

2.2. Statistical Analysis. Data were checked regarding underlying assumptions and described and analyzed accordingly using PASW version 18 (SPSS Inc., Chicago, IL). The alpha level of significance was set at 0.05 (2-tailed, exact P-values were used).

Spearman correlations ($r_s$) and Mann-Whitney U-tests were used for bivariate analyses of associations with FOF, that is, FES(S). Variables significantly associated with FES(S) scores in bivariate analyses were then entered as independent variables in regression models with FES(S) scores as the dependent variable. To ease interpretation, all scores were adjusted to be in the same direction (higher scores = more problems) before being entered into the regression analyses.

A first regression model (method: forward) included motor, nonmotor, and demographic factors as well as drug therapy complications (i.e., fluctuations and dyskinesias) as independent variables. Further details about the included independent variables are provided as footnotes in Table 2. Based on results from the first model, a second model was explored (method: enter with manual backward deletion) consisting of items from scales found significant in the first model. These items (independent variables) were selected based on whether they appeared to represent specific aspects potentially suitable for rehabilitation interventions, in combination with clinical considerations. Details about the included independent variables are provided as footnotes in Table 3.

3. Results

Eighty-five % (131/154) of the participants responded completely independently to the postal survey, whereas the
rest attained assistance in reading or writing. The included 154 participants had a median FES(S) score of 114 (q1–q3, 69–130; min-max, 0–130) and 29% scored at maximum, that is, 130. According to the dichotomous FOQ-question, 45% (67 out of 149) perceived themselves as having FOQ. In addition, 76% (112/148) of the participants experienced balance problems when standing or walking. Perceived PD severity was rated as “moderate” by 96 participants and ranged from “mild” (n = 43) to “severe” (n = 14).

Bivariate analyses are presented in Table 1. FES(S) scores demonstrated the weakest correlation with age (rS = −0.24) and the strongest (rS = −0.82) with walking difficulties. Those reporting the presence of motor fluctuations and dyskinesias had significantly (P ≤ 0.010) lower FES scores (i.e., more FOQ) than those who did not (Table 1). Needing help from others in daily activities and experiencing FOQ, turning hesitations, prior falls or near falls were also associated with more (P < 0.001) FOQ (Table 1).

Table 1: Sample characteristics and bivariate associations with FES(S) scores (n = 154).

<table>
<thead>
<tr>
<th></th>
<th>Total sample</th>
<th>Spearman correlations with FES(S) scores</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mean (SD) age, years</strong></td>
<td>70 (9.1)</td>
<td>−0.24</td>
<td>0.003</td>
</tr>
<tr>
<td><strong>Mean (SD) PD duration, years</strong></td>
<td>6 (5.4)</td>
<td>−0.42</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Fatigue (FACIT-F), median (q1–q3)</strong></td>
<td>36 (27–42)</td>
<td>0.67</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Physical function (PF), median (q1–q3)</strong></td>
<td>65 (40–84)</td>
<td>0.79</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Pain (NHP), median (q1–q3)</strong></td>
<td>0 (0–25)</td>
<td>−0.50</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Walk-12G, median (q1–q3)</strong></td>
<td>13 (6–23)</td>
<td>−0.82</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

**n*/total* % Median (q1–q3) FES(S) scores P-value**

<table>
<thead>
<tr>
<th>Dichotomous variables</th>
<th>n</th>
<th>total</th>
<th>No</th>
<th>Yes</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Education: university degree</td>
<td>37/153</td>
<td>24</td>
<td>115 (69–130)</td>
<td>112 (70–130)</td>
<td>0.941</td>
</tr>
<tr>
<td>Living alone</td>
<td>38/150</td>
<td>25</td>
<td>119 (80–130)</td>
<td>96 (55–130)</td>
<td>0.125</td>
</tr>
<tr>
<td>Comorbidity</td>
<td>77/142</td>
<td>50</td>
<td>107 (60–130)</td>
<td>120 (74–130)</td>
<td>0.271</td>
</tr>
<tr>
<td>Motor fluctuations</td>
<td>90/152</td>
<td>58</td>
<td>124 (86–130)</td>
<td>104 (64–128)</td>
<td>0.010</td>
</tr>
<tr>
<td>Dyskinesia</td>
<td>57/153</td>
<td>37</td>
<td>124 (85–130)</td>
<td>93 (53–117)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Freezing of gait</td>
<td>57/152</td>
<td>37</td>
<td>128 (112–130)</td>
<td>69 (47–101)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Turning hesitations</td>
<td>58/150</td>
<td>38</td>
<td>128 (113–130)</td>
<td>69 (48–102)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Experienced falls</td>
<td>50/149</td>
<td>33</td>
<td>123 (90–130)</td>
<td>81 (44–113)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Experienced near falls</td>
<td>69/147</td>
<td>45</td>
<td>129 (111–130)</td>
<td>84 (52–115)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Needing help from others in daily activities</td>
<td>42/153</td>
<td>27</td>
<td>124 (104–130)</td>
<td>59 (35–91)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Sex, women</td>
<td>62/152</td>
<td>41</td>
<td>Women</td>
<td>116 (52–130)</td>
<td>112 (77–130)</td>
</tr>
</tbody>
</table>

Possible score ranges: FACIT-F, 0–52 (higher = better); PF, 0–100 (higher = better); NHP-Pain, 0–100 (higher = worse); Walk-12G, 0–42 (higher = worse); FES(S), 0–130 (higher = better).

* Mann Whitney U-test.

**A** As assessed by item 3 (“freezing”) of the FOQsa (Freezing of Gait Questionnaire, self-administered version). Those scoring ≥ 1 were categorized as freezers.

**B** As assessed by item 6 (“turning hesitations”) of the FOQsa. Those scoring ≥ 1 were categorized as having turning hesitations.

**C** As assessed by item 6 (“turning hesitations”) of the FOQsa. Those scoring ≥ 1 were categorized as having turning hesitations.

**D** As assessed by item 3 (“freezing”) of the FOQsa (Freezing of Gait Questionnaire, self-administered version). Those scoring ≥ 1 were categorized as freezers.

**E** As assessed by item 3 (“freezing”) of the FOQsa (Freezing of Gait Questionnaire, self-administered version). Those scoring ≥ 1 were categorized as freezers.

**F** As assessed by item 6 (“turning hesitations”) of the FOQsa. Those scoring ≥ 1 were categorized as having turning hesitations.

**G** As assessed by item 6 (“turning hesitations”) of the FOQsa. Those scoring ≥ 1 were categorized as having turning hesitations.

**H** As assessed by item 6 (“turning hesitations”) of the FOQsa. Those scoring ≥ 1 were categorized as having turning hesitations.

**I** As assessed by item 6 (“turning hesitations”) of the FOQsa. Those scoring ≥ 1 were categorized as having turning hesitations.

**J** As assessed by item 6 (“turning hesitations”) of the FOQsa. Those scoring ≥ 1 were categorized as having turning hesitations.

**K** As assessed by item 6 (“turning hesitations”) of the FOQsa. Those scoring ≥ 1 were categorized as having turning hesitations.

**L** As assessed by item 6 (“turning hesitations”) of the FOQsa. Those scoring ≥ 1 were categorized as having turning hesitations.

**M** As assessed by item 6 (“turning hesitations”) of the FOQsa. Those scoring ≥ 1 were categorized as having turning hesitations.

**N** As assessed by item 6 (“turning hesitations”) of the FOQsa. Those scoring ≥ 1 were categorized as having turning hesitations.

**O** As assessed by item 6 (“turning hesitations”) of the FOQsa. Those scoring ≥ 1 were categorized as having turning hesitations.

**P** As assessed by item 6 (“turning hesitations”) of the FOQsa. Those scoring ≥ 1 were categorized as having turning hesitations.

**Q** As assessed by item 6 (“turning hesitations”) of the FOQsa. Those scoring ≥ 1 were categorized as having turning hesitations.

**R** As assessed by item 6 (“turning hesitations”) of the FOQsa. Those scoring ≥ 1 were categorized as having turning hesitations.

**S** As assessed by item 6 (“turning hesitations”) of the FOQsa. Those scoring ≥ 1 were categorized as having turning hesitations.

**T** As assessed by item 6 (“turning hesitations”) of the FOQsa. Those scoring ≥ 1 were categorized as turning hesitations.

**U** As assessed by item 6 (“turning hesitations”) of the FOQsa. Those scoring ≥ 1 were categorized as turning hesitations.

**V** As assessed by item 6 (“turning hesitations”) of the FOQsa. Those scoring ≥ 1 were categorized as turning hesitations.

**W** As assessed by item 6 (“turning hesitations”) of the FOQsa. Those scoring ≥ 1 were categorized as turning hesitations.

**X** As assessed by item 6 (“turning hesitations”) of the FOQsa. Those scoring ≥ 1 were categorized as turning hesitations.

**Y** As assessed by item 6 (“turning hesitations”) of the FOQsa. Those scoring ≥ 1 were categorized as turning hesitations.

**Z** As assessed by item 6 (“turning hesitations”) of the FOQsa. Those scoring ≥ 1 were categorized as turning hesitations.

Table 2: Multiple linear regression with fear of falling (FES(S) scores) as the dependent variable among people with Parkinson’s disease.

<table>
<thead>
<tr>
<th>Significant independent variables</th>
<th>B (95% CI)</th>
<th>β</th>
<th>P-value</th>
<th>Adjusted R²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Walking difficulties (Walk 12-G)</td>
<td>1.7 (1.2, 2.2)</td>
<td>0.55</td>
<td>&lt;0.001</td>
<td>0.680</td>
</tr>
<tr>
<td>Fatigue (FACIT-F)</td>
<td>0.74 (0.26, 1.2)</td>
<td>0.22</td>
<td>0.003</td>
<td>0.023</td>
</tr>
<tr>
<td>Turning hesitations (item 6, FOQsa)</td>
<td>11 (2.5, 19.6)</td>
<td>0.15</td>
<td>0.012</td>
<td>0.014</td>
</tr>
<tr>
<td>Need help from others in daily activities</td>
<td>10 (0.96, 19)</td>
<td>0.13</td>
<td>0.030</td>
<td>0.010</td>
</tr>
<tr>
<td>Fluctuations</td>
<td>−7.6 (−15, −0.48)</td>
<td>−0.11</td>
<td>0.037</td>
<td>0.008</td>
</tr>
</tbody>
</table>

* For the regression analysis, scores were adjusted to be in the same direction: higher scores = more problems.

**B** Independent variables in the analysis were fatigue (FACIT-F), age (years), PD-duration (years), pain (NHP), turning hesitations (item 6, FOQsa: dichotomized, 1 = turning hesitations), fluctuations (1 = yes), dyskinesia (1 = yes), freezing (item 3, FOQsa: dichotomized, 1 = freezing), falls (1 = yes), near falls (1 = yes), need help from others in daily activities (1 = yes), and walking difficulties (Walk12-G).

**C** Listed by order of entry into the model (forward method).

**D** B: regression coefficient; CI: confidence interval; β: standardized regression coefficient.
In the first regression model, there were signs of multicollinearity between PF and Walk-12G scores (data not shown). PF was therefore omitted from the model in favor of the Walk-12G. This was done because the Walk-12G represents a more specific variable and exhibited a somewhat better reliability than the PF (0.96 versus 0.93). This resulted in a model with five significant independent variables, explaining 74% of the variance in FES(S) scores (Table 2). The strongest independent variable (as assessed by the standardized regression coefficients, β) was walking difficulties, which alone explained 68% of the variance in FES(S) scores. This was followed by fatigue, turning hesitations, needing help from others in daily activities, and motor fluctuations (Table 2).

In the second explorative regression model, specific gait and balance items were entered as independent variables (Table 3). In this model, the original five response categories of Walk-12G were recoded and entered as dummy variables: “not at all” (reference category), “a little,” and “moderately/quite a bit/extremely,” that is, the three worst categories were merged into one (due to skewed response distributions). Two Walk-12G items were omitted from the model: item 11 (“Have you been limited in how far you are able to walk?”) due to signs of multicollinearity and item 12 (“Has your walking been slow?”) which was not significant. The final model included three significant independent variables explaining 59% of the variance in FES(S) scores (Table 3). The two strongest independent variables were (moderate to extreme) limitations in climbing stairs and balance impairment rather than on fall prevention per se in order to reduce FOF. Arguably, such interventions may benefit from specifically targeting balance problems, stair climbing, and turning hesitations. These issues are of particular relevance for the physical therapist within the interdisciplinary team.

The present finding of balance problems contributing independently to FOF is in accordance with previous results based on bivariate analyses [3, 14, 22]. It is noteworthy that prior falls or near falls were not independently associated to FOF when controlling for the other independent variables, despite the highly significant bivariate relationship demonstrated. This finding illustrates a major pitfall in relying on bivariate analyses. However, we did not register falls prospectively (as has been recommended [26]), and our sample had a relatively low proportion of fallers. Still, although further confirmatory studies are needed, our findings suggest that focus primarily should be put on perceived balance impairment rather than on fall prevention per se in order to reduce FOF.

Impaired balance is common among people with PD, which is confirmed by the fact that 76% of the participants in our study reported balance problems. This corresponds to the finding of Schrag et al., who reported that 65% of people with a PD duration of five years or more experience a postural instability [40]. Although gait and balance training are common in rehabilitation for people with PD, very few studies have investigated the effects on FOF. Some studies reported improvements after training [41–44], but it is unclear whether these were of clinical significance. In people with PD. That is, variations in self-rated walking ability could account for a high proportion (68%) of the variance in FES(S) scores. This is in line with previous studies showing a relationship between FOF and clinical gait tests [5, 14, 22, 24]. Furthermore, a mixed method pilot study found that FOF was universally reported in connection to everyday walking [39]. Our results have important implications for rehabilitation and suggest that walking difficulties should be the main target in order to reduce FOF. Arguably, such interventions may benefit from specifically targeting balance problems, stair climbing, and turning hesitations. These issues are of particular relevance for the physical therapist within the interdisciplinary team.

4. Discussion

This study identified that walking disabilities contributed the strongest to FOF (i.e., low fall-related self-efficacy) in people with PD. That is, variations in self-rated walking ability could account for a high proportion (68%) of the variance in FES(S) scores. This is in line with previous studies showing a relationship between FOF and clinical gait tests [5, 14, 22, 24]. Furthermore, a mixed method pilot study found that FOF was universally reported in connection to everyday walking [39]. Our results have important implications for rehabilitation and suggest that walking difficulties should be the main target in order to reduce FOF. Arguably, such interventions may benefit from specifically targeting balance problems, stair climbing, and turning hesitations. These issues are of particular relevance for the physical therapist within the interdisciplinary team.

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addition, none of these studies included a long-term follow-up and all used different outcome measures, which limit their comparability. Further studies are therefore warranted, which are of importance since pharmacological treatments have insufficient effects on gait and balance problems [45–47]. In addition, although deep brain stimulation in the subthalamic nuclei has been shown to positively influence FOF [48, 49], it is a surgical option only eligible for a minority of people with PD.

We identified turning hesitations to be independently associated with FOF. While turning hesitations are related to FOG, it is noteworthy that freezing was not associated with FOF when controlling for the other independent variables in the identified model, despite the highly significant bivariate relationship demonstrated between FOF and FOG. This further illustrates the pitfall in relying on bivariate analyses. The present results suggest that turning hesitations should be more specifically addressed than FOG per se in order to reduce FOF. Turning is in fact impaired in mild PD [50], and rehabilitation clinicians (such as physical therapists) should therefore consider this already early on. Furthermore, moderate to extreme limitations in climbing stairs were also independently associated with FOF, and a previous study showed that stairs can cause considerable anxiety among people with PD [39]. This suggests that stair climbing should be considered more specifically both when assessing and treating people with PD.

In addition to walking difficulties, our primary regression model identified fatigue, need for help in daily activities, and fluctuations as additional but relatively minor factors associated with FOF. Although the contributions were small (≤2.3% for each of the variables), this is, as far as we know, the first study showing that fatigue and motor fluctuations may be associated with FOF in PD. These results support the value of an interdisciplinary approach in the management of FOF including, for example, an optimization of anti-PD medications and efforts targeting independence in activities of daily living.

There are some methodological concerns associated with this study. All data were self-reported, and future studies should consider including also clinical tests and assessments in order to provide a more complete and detailed picture. For example, “having balance problems when standing or walking” (item 6, Walk-12G) is a coarse indicator of a very complex issue. This item does not take into account the complex interaction between the person, environment and the activity at hand, and it cannot separate balance problems in standing from those connected with walking. Although this study considered a relatively broad variety of aspects, we acknowledge that there may be additional aspects influencing FOF in PD (e.g., cognitive problems, executive dysfunctions, and environmental factors). In addition, our sample was relatively limited and drawn from a university clinic. It is unknown to what extent such a sample is representative for the PD population at large, which may influence the external validity of our findings. Finally, the response rate of 68% may potentially have introduced a bias, particularly since the study design did not allow for a thorough analysis of responders versus nonresponders.

However, excluded responders did not differ from those included with respect to sex, age, and PD duration, and the prevalence of FOF found here (close to 50%) is in agreement with that reported in other studies [2, 12–16]. Nevertheless, in order to gain a deeper understanding and reach firmer conclusions, additional quantitative and qualitative work is needed within this area.

5. Conclusions

This is to our knowledge the first study using multivariate analysis to explore factors associated with FOF in people with PD. The present results suggest that walking ability is the primary target in order to reduce FOF. Specifically, balance, climbing stairs, and turning seem to be of particular importance. Additional studies are warranted in order to further improve our understanding of FOF and how to best approach it in rehabilitation.

Acknowledgments

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Research Article

Impaired Economy of Gait and Decreased Six-Minute Walk Distance in Parkinson’s Disease

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Changes in the biomechanics of gait may alter the energy requirements of walking in Parkinson’s Disease (PD). This study investigated economy of gait during submaximal treadmill walking in 79 subjects with mild to moderate PD and the relationship between gait economy and 6-minute walk distance (6 MW). Oxygen consumption (VO2) at the self-selected treadmill walking speed averaged 64% of peak oxygen consumption (VO2 peak). Submaximal VO2 levels exceeded 70% of VO2 peak in 30% of the subjects. Overall the mean submaximal VO2 was 51% higher than VO2 levels expected for the speed and grade consistent with severe impairment in economy of gait. There was an inverse relationship between economy of gait and 6MW (r = −0.31, P < 0.01) and with the self-selected walking speed (r = −0.35, P < 0.01). Thus, the impairment in economy of gait and decreased physiologic reserve result in routine walking being performed at a high percentage of VO2 peak.

1. Introduction

Walking capacity is central to the performance of many activities of daily living. Difficulty with walking is one of the cardinal symptoms of Parkinson’s Disease (PD). Alterations in the biomechanics of gait, such as decreased stride length, increased stride length variability, and reduced gait speed, are common even in early stages of PD [1–3]. Most often, PD patients attempt to compensate for short steps by increasing gait cadence, thereby potentially altering energy requirements. This higher energy cost of movement is often referred to as a lower economy of gait and is a function of abnormal gait patterns that accompany aging and neurological disability. Reduced economy of gait has been associated with impaired function and fatigue in non-PD populations [4–9], but there is currently scant information on how parkinsonian gait affects energy expenditure or economy of gait using direct measures of oxygen consumption [10]. Further, little is known about the relationship between economy of gait and mobility. Hence, the purpose of this study was to investigate economy of gait during submaximal treadmill walking in mild to moderate PD, and the relationship between economy of gait and the distance covered during the 6-minute walk (6 MW).

2. Methods

2.1. Subjects. Participants for this study were recruited from the University of Maryland Parkinson’s Disease Center and the Baltimore VA Medical Center neurology clinics as part of an exercise intervention trial in PD [11]. Inclusion criteria were (1) diagnosis of levodopa-responsive PD characterized by 2 of 3 cardinal signs (resting tremor, bradykinesia, rigidity), (2) Hoehn and Yahr (HY) [12] stage 1 to 3 (while “on” for motor fluctuations), and (3) presence of mild to moderate gait impairment, (score of 1 or 2 on Unified Parkinson’s Disease Rating Scale (UPDRS) [13] questions no.
29 Gait or no. 30 Postural Stability, (4) Age ≥ 40, (5) Folstein mini-mental state examination [14] score ≥ 23, and (6) unlikely to require PD medication adjustment for 4 months. Exclusion criteria were (1) unstable cardiac, pulmonary, liver, or renal disease, (2) unstable hypertension or diabetes, (3) anemia, orthopedic, or chronic pain-restricting exercise, (4) unstable psychiatric illness, or (5) >20 minutes of aerobic exercise more than 3 times per week (to avoid prior training effect). This study was approved by the Institutional Review Board at the University of Maryland, Baltimore, and written informed consent was obtained from each participant.

All physical performance measures, rating scales, and functional tests were performed while the subjects were “on” or within 3 hours of medication intake. Subjects used an additional dose of medication to maintain the “on” state when necessary.

2.2. Assessments. The UPDRS was administered by a neurologist with expertise in movement disorders (LS). The Total UPDRS includes three subscales: Mentation, Behavior, and Mood (Part I), Activities of Daily Living (Part II), and the Motor Examination (Part III). Short distance ambulatory function was assessed with three-timed 10 meter walks. The self-selected walking speed was defined as the average velocity of the three tests. This short-distance test is widely recognized as a valid index of mobility recovery and simulates the distance required for many home-based daily functions. The 6 MW is a distance that is more representative of community-based daily activities. Participants were instructed to cover as much distance as possible in 6 minutes, turning every 100 feet, as prompted by orange traffic cones set apart across a flat, clear space.

2.3. Exercise Treadmill Testing

Screening Treadmill Test. A screening graded-treadmill test to voluntary exhaustion without measurement of the rate of oxygen consumption (VO2) was performed using a manual protocol as previously described [15, 16]. All treadmill testing was performed in the early afternoon while the subjects were “on”. This screening exercise treadmill test served to (1) acclimate the subjects to walking on a treadmill (2) evaluate for symptoms of overt coronary disease or to detect silent myocardial ischemia (3) evaluate hemodynamic heart rate and blood pressure response to exercise (4) observe gait patterns and (5) determine whether there were any issues that would preclude their ability to safely exercise. All subjects wore a gait belt for safety, and a spotter stood behind subjects during the treadmill evaluations. Subjects were instructed to use the minimum level of handrail support for balance during the test.

The initial target speed for treadmill testing was the subject’s self-selected over ground walking velocity, with the incline set at 0%. The first stage was conducted for 2 minutes at 0% grade, the next stage was conducted for 2 minutes at 4% grade, and then the grade was subsequently advanced by 2% every minute until voluntary exhaustion. In frailer subjects, the second stage was conducted at 2% instead of 4% for a more gradual increase in workload. Once the grade reached 10%, subjects were asked if the speed of the treadmill could be simultaneously advanced with grade (generally by 0.2 mph). The electrocardiogram (ECG) was monitored continuously, and blood pressure was measured during the first 3 stages of the tests and every 2 minutes during recovery.

Exercise Treadmill Test with Measurement of Peak Oxygen Consumption. At the next study visit one week later, subjects underwent a progressive-graded exercise treadmill test to voluntary exhaustion as described above with measurement of peak oxygen consumption (VO2 peak using a Quark Cardio Pulmonary Exercise Testing metabolic analyzer (Cosmed, Rome, Italy)). In some subjects, the initial treadmill speed was adjusted slightly based on the results of the screening treadmill test and feedback from the research subjects. As a result, the average self-selected walking speed on the treadmill was 94% of their self-selected over ground speed (2.31 ± 0.59 miles per hour (mph) versus 2.46 ± 0.53 mph). The first stage was conducted for 2 minutes at 0% grade (first submaximal treadmill stage), and then advanced as described above. VO2 consumption, CO2 production, and minute ventilation were measured breath-by-breath, and values averaged for 20 second intervals. Subjects were instructed not to talk during the test as this is known to affect the depth of breathing and gas exchange. Based on our pilot study [15], we anticipated that we would not be able to measure true maximal aerobic capacity (defined as a plateau in oxygen consumption during the final stage, maximal heart rate >85% of age-adjusted predicted maximal heart rate, and respiratory quotient (RQ) or respiratory exchange ratio (RER) > 1.10) in many of these deconditioned subjects. The VO2 peak was based on the mean of the final two 20-second averages obtained during the final stage of the test.

2.4. Economy of Gait. We used the average O2 consumption values obtained over the final 40 seconds of the first submaximal treadmill stage to measure economy of gait. The 2-minute duration of this stage is similar to the time spent on many activities of daily living. Economy of gait was calculated as the measured VO2 during the first treadmill stage divided by the predicted VO2 for non-PD age-matched subjects based on commonly accepted American College of Sports Medicines equations for subjects walking accounting for treadmill speed and grade [17].

\[
VO2 = \text{horizontal component} + \text{vertical component} + \text{resting component},
\]

\[
\text{VO2 (mL/kg/min)} = 0.1 \text{ (speed)} + 1.8 \text{ (speed) (fractional grade)} + 3.5,
\]

\[
\text{Speed} = \text{speed in meter/minute}, \text{to convert to mph,} 1 \text{ mph} = 26.8 \text{ meter/minute}.
\]

Higher oxygen consumption levels for any given speed and treadmill grade imply increased energy expenditure and impaired economy of gait.

2.5. Statistics. SAS version 9.2 (SAS Institute, Inc, Cary, NC, USA) was used for the statistical analyses. Descriptive
statistics are expressed as mean ± standard deviation (SD). Pearson’s correlation coefficients were used to calculate strength of relationship between variables. All statistical tests were two sided and performed at a significance level of 0.05.

3. Results

Seventy-nine subjects (57 men and 22 women) completed this cross-sectional study. Physical characteristics and PD severity scores are summarized in Table 1. Based on the UPDRS and HY ratings, the subjects had a broad range of disease severity from mild to moderately severe PD. Eleven subjects (7%) had received deep brain stimulation surgery for PD. The level of medical comorbidity in the sample was low, with only five individuals (6%) with prior history of stable coronary artery disease, seven (10%) on medication for diabetes, and only one was a current smoker (1%). Twenty-nine subjects (37%) were on medications for hypertension, including five on betablockers.

The VO2 at the self-selected treadmill walking speed averaged 64% of their VO2 peak. There were, however, a wide range of values (31% to 89% of VO2 peak). Interestingly, 24 of 79 subjects had submaximal VO2 levels that exceeded 70% of their VO2 peak, indicating severe reduction in economy of gait, with 3 subjects approaching 90% of their VO2 peak. Overall the subjects had mean submaximal, self-selected walking speed VO2 values that were 51% higher than the VO2 levels expected for the same speed and grade for non-PD subjects (13.0 ± 3.3 mL/kg/min versus 9.7 ± 1.6 mL/kg/min). This observation provides clear evidence of the large decreases in economy caused by parkinsonian gait patterns (Figure 1).

We examined whether PD severity was associated with economy of gait (the ratio of measured VO2 and predicted VO2). There was a significant correlation of HY stage with economy of gait (Figure 2) with more advanced PD severity associated with lower economy of gait. There was no relationship between economy of gait with total or motor UPDRS. There was an inverse relationship between economy of gait and the distance covered during the 6MW (r = −0.31, P < 0.01). Specifically, individuals whose measured VO2 was a higher percentage of their VO2 peak during their self-selected walking speed covered less distance walking for six minutes (Figure 3). There was also an inverse relationship between walking speed on the treadmill test and economy of gait (r = −0.35, P < 0.01).

4. Discussion

Our results demonstrate that economy of gait is markedly impaired in people with mild to moderate PD that increases the energy demands of physical activity. Our subjects walking at their self-selected pace on the treadmill required on average 64% of their VO2 peak. Indeed, 30% of our subjects used over 70% of their VO2 peak during their self-selected treadmill speed, and several subjects approached 90% of their VO2 peak. By contrast in healthy younger and older individuals, most activities require a small percentage of

<table>
<thead>
<tr>
<th>Parameter (N = 79*)</th>
<th>Mean ± SD</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>65.1 ± 10.7</td>
<td>42 to 86</td>
</tr>
<tr>
<td>UPDRS total</td>
<td>47.2 ± 14</td>
<td>15 to 96</td>
</tr>
<tr>
<td>UPDRS motor</td>
<td>32.4 ± 10.2</td>
<td>11 to 66</td>
</tr>
<tr>
<td>Hoehn and Yahr stage</td>
<td>2.2 ± 0.4</td>
<td>1.5 to 3.0</td>
</tr>
<tr>
<td>Hoehn and Yahr Stage 1.5</td>
<td>N = 1 (1%)</td>
<td>—</td>
</tr>
<tr>
<td>Hoehn and Yahr Stage 2.0</td>
<td>N = 61 (77%)</td>
<td>—</td>
</tr>
<tr>
<td>Hoehn and Yahr Stage 2.5</td>
<td>N = 5 (6%)</td>
<td>—</td>
</tr>
<tr>
<td>Hoehn and Yahr Stage 3.0</td>
<td>N = 12 (15%)</td>
<td>—</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>28.1 ± 4.9</td>
<td>18.0 to 41.6</td>
</tr>
<tr>
<td>VO2 peak (mL/kg/min)</td>
<td>22.4 ± 4.8</td>
<td>12.6 to 37.4</td>
</tr>
<tr>
<td>Submaximal VO2 (mL/kg/min)</td>
<td>13.0 ± 3.3</td>
<td>5.1 to 21.6</td>
</tr>
<tr>
<td>Walking speed (mph)</td>
<td>2.31 ± 0.59</td>
<td>1.0 to 3.8</td>
</tr>
<tr>
<td>6 min walk distance (meters)</td>
<td>424 ± 106</td>
<td>122 to 695</td>
</tr>
</tbody>
</table>

* 6-min walk performed in 75 subjects.

The VO2 at the self-selected treadmill walking speed exceeded the VO2 levels expected for the same speed and grade for non-PD subjects (13.0 ± 3.3 mL/kg/min versus 9.7 ± 1.6 mL/kg/min). This observation provides clear evidence of the large decreases in economy caused by parkinsonian gait patterns (Figure 1).

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There was a relationship between HY stage and economy of gait, such that individuals with more severe PD had poorer economy of gait. Impairments in gait and mobility impact on the ability of subjects with PD to perform a number of gait-dependent daily activities including housework, dressing, and transferring in and out of bed [21]. Impaired gait
economy may result from many factors including abnormal gait biomechanics and altered spatiotemporal aspects of gait associated with PD, that is, slow, short-stepped shuffling gait with decreased stride length, asymmetric arm [22] swing, tremor and rigidity, postural instability, loss of range of motion of axial structures, impaired sensorimotor integration, and so forth. The modest association between economy of gait and disease severity and economy of gait and distance covered during the 6MW test also indicates that other factors such as balance problems, difficulty with turning, and physical deconditioning contribute to impaired mobility in these subjects [1–3].

Few studies have directly measured walking economy in PD. Christiansen et al. examined walking economy at a number of walking speeds in subjects with PD compared to healthy subjects without PD [10]. VO2 was found to be 6 to 10% higher in people with PD at walking speeds above 1 mph. We report much greater impairments in walking economy than Christiansen et al. The VO2 for our subjects at 2 mph is 12.5 mL/kg/min, whereas Christiansen et al. reported a VO2 of 11 mL/kg/min at this speed. This difference may be explained by greater PD severity in our population (mean total UPDRS score, 47 versus 32). We used published equations for VO2 rather than direct measurement in a control population. The predicted VO2 for a given walking speed derived from younger individuals may underestimate the energy cost of walking in healthy older adults [19]. Protas et al. [23] also studied submaximal oxygen consumption during steady-state exercise in PD. Exercise performance was assessed using cycle ergometry in PD and non-PD. The PD group was unable to perform the same level of exercise as rated by maximum power when compared with the control group, even though the peak VO2 and heart rate were similar. The authors concluded that there was poorer exercise efficiency in the PD group than in controls. Over a range of submaximal cycling intensities, rates of energy expenditure were about 20% higher in PD than in controls. Thus, our results support previous findings of reduced economy of gait and exercise efficiency in PD.

There is growing interest in the effects of aging and medical comorbidities on bioenergetics and their impact on mobility and other measures of physical performance [18, 24]. We have previously reported that subjects with mild to moderate PD have VO2 peak values 20 to 25% lower than healthy age-matched controls [16]. This impairment in VO2 peak, in combination with the higher energy demands of walking (lower economy of gait), reduces the physiologic reserve in PD. The decreased physiologic reserve and lower VO2 peak make it more difficult to perform everyday tasks. The higher energy cost of walking necessitates the use of anaerobic pathways to meet ordinary energy demands, which may be associated with fatigue [18, 20]. Clearly, the decreased physiological reserve shown in this study has functional consequences as evidenced by impaired 6MW distance and slow self-selected walking speed, particularly in those with more severe PD. The predicted 6MW distance for healthy subjects without PD using the equation of Enrichi and Sherrill [25] that takes into consideration age, gender, height, and weight was 509 meters compared to the measured 424 meters, a difference of 85 meters, or 17% lower in PD. The 6MW distance in our subjects is comparable to the values reported by Falvo and Earhart [26] who reported a 6MW distance of 394.1 ± 98.4 m in PD patients of similar age to our subjects.

This study has limitations that may result in an underestimation of the severity of the impairment of economy of gait. (1) The submaximal O2 utilization was measured by using O2 utilization during the last 40 seconds of the first stage of the treadmill test, when subjects walked at their self-selected speed and 0% grade. We chose this time as representative of the time period in which our subjects typically walked. A number of investigators have advocated measuring submaximal O2 for longer periods of time [7, 18, 27]. For example, Alexander et al. measured O2 kinetics in frail and non-frail older adults during a 6-minute submaximal exercise bout on the treadmill [7]. The Baltimore Longitudinal Study of Aging employs a 5-minute stage, but the data from the first 1.5 minutes is discarded [18]. This allows for a longer period of time for the subjects to come to equilibrium and plateau during the bout of submaximal exercise. We recognize that it is possible that some of subjects
did not plateau during the second minute of the exercise due to a lag in O2 uptake at the start of exercise reflecting impaired O2 kinetics. However, any error introduced would have biased our measuring less O2 utilization as subjects with delayed O2 kinetics would take longer to come to equilibrium [7, 27]. Hence, we potentially understated the degree of inefficiency of our patient sample with respect to economy of gait. (2) Another limitation is that the O2 consumption during exercise includes a resting component for the resting metabolic rate. Indeed this resting component is included in the American College of Sports Medicine equation [17]. This resting component is often measured with the subjects in the supine position [28], but others have advocated measuring it by having the subject stand for 5 minutes prior to the walking test [9] as this allows an examination of the incremental O2 utilization attributable to the exercise itself. The resting metabolic rate in subjects with PD might be affected by age-related changes in body composition, sarcopenia, as well as other changes attributable to PD (i.e., resting tremor and medication effects). Changes in resting metabolic rate in PD may be clinically significant as a higher resting metabolic rate is associated with increased mortality in older adults [28]. Even if the increased metabolic needs during exercise are partially explained by an increased resting metabolic rate, the net effect on ambulatory function is the same; more energy is needed for a given level of ambulation. (3) Another potential confound is the use of handrail support during this study. Subjects were instructed to walk on the treadmill with minimal hand support. Subjects varied in the extent to which they used the side rails for balance support. The use of hand support reduces O2 consumption, again leading to a possible underestimate of their O2 utilization (VO2) and subsequent underestimate of the degree of impairment of their economy of gait. (4) These measures were performed with subjects walking on treadmills. Frenkel-Toledo et al. have proposed that treadmill walking may act as an external pacemaker to improve gait variability [29]. If gait biomechanics improve on the treadmill, this would reduce oxygen utilization and lead to an overestimate of their economy of gait. The gait biomechanics and energetics might be different in overground walking. (5) Lastly the 6-minute walk test required subjects to make tight turns around a cone. This might have adversely impacted the distance covered, particularly in subjects that had limited ability to turn, that is, turning “en bloc”. Future studies employing portable metabolic systems could be employed to examine economy of gait during overground walking.

There is substantial interest in whether the abnormalities in gait and functional performance in PD can be improved by treadmill exercise training [30–32]. In a pilot study by Pelosin et al. [32], 10 patients with idiopathic PD underwent 4 weeks of treadmill training (30 min, three times a week for 4 weeks). Walking performance (Timed Up and Go, 6-min and 10-m walking tests) and metabolic function (oxygen uptake and heart and respiratory rate) were evaluated before training, at the end of treatment and after 30 days with two different graded exercises (treadmill and cycle ergometer). Training significantly improved walking performance. Oxygen uptake, and heart and respiratory rates were significantly decreased only during graded exercise on the treadmill but not on the cycle ergometer consistent with improved economy of gait, but the data are difficult to interpret due to the way they are displayed in the paper.

In summary, this study reinforces prior evidence showing impaired economy of gait in PD that is associated with impairment of ambulation at both short and long distance. Reduced economy of gait combined with the reduced VO2 peak results in lower physiologic reserve where even comfortable gait is performed at a high percentage of VO2 peak. Future research should examine the biomechanical and neuromuscular factors that contribute to impaired walking economy in PD. A better understanding of these factors may lead to new approaches to improve functional performance and quality of life in PD.

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