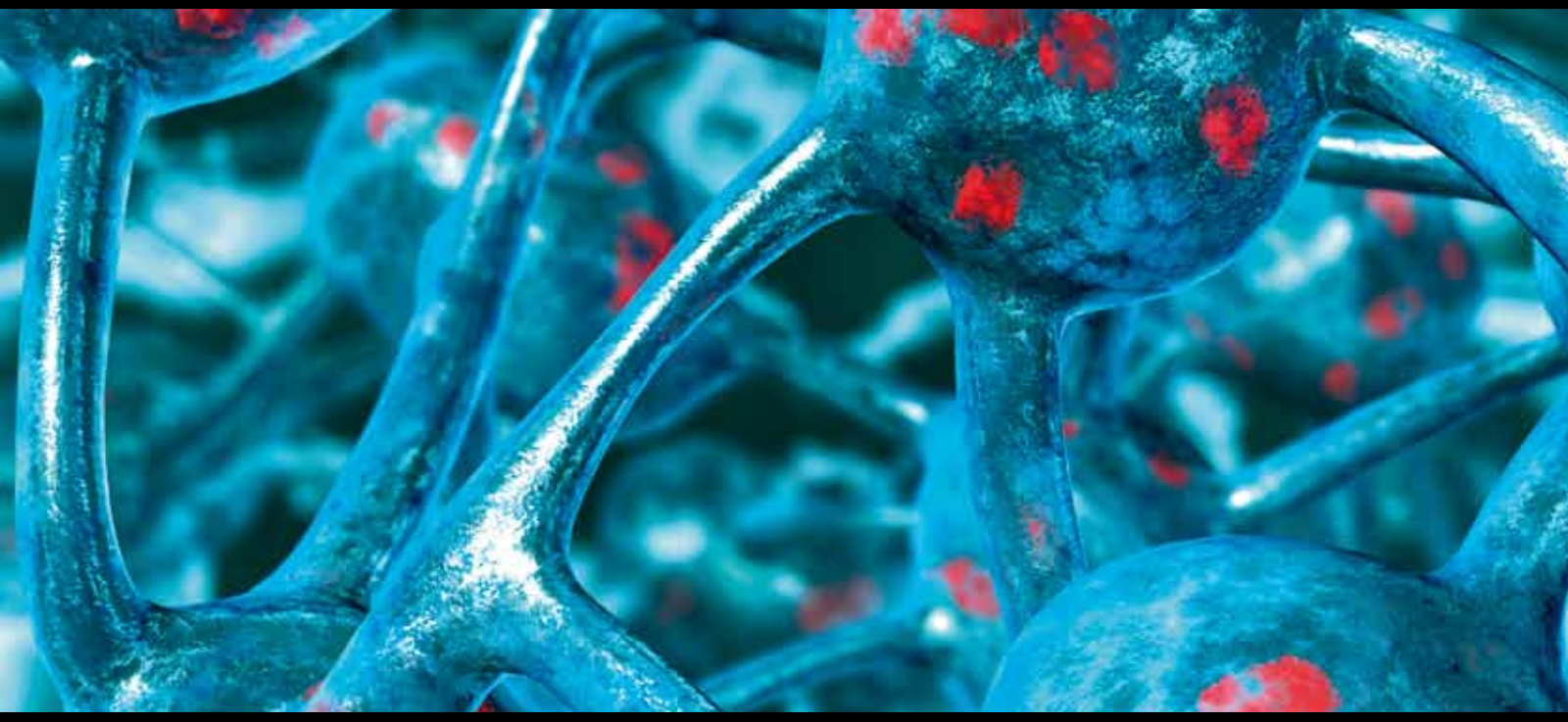
Parkinson's Disease

Rehabilitation and Parkinson's Disease 2013

Guest Editors: Gammon M. Earhart, Leland E. Dibble, Terry Ellis, and Alice Nieuwboer



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Editorial

Rehabilitation and Parkinson's Disease 2013

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Parkinson's disease (PD) is the second most common neurodegenerative disorder, and increasing age is a major risk factor for development of PD. As such, PD is expected to become increasingly prevalent in coming years as the aged population grows in number. PD is typically treated with pharmacological and sometimes surgical approaches, but these treatments do not adequately address many aspects of the disease. As such, rehabilitation may play a key role in the management of PD. The nine articles in this special issue illustrate the broad spectrum of important rehabilitation issues for people with PD. M. H. Nilsson et al. report relationships between health and housing in very old individuals with PD, examining the impact of environmental barriers and accessibility problems on daily life. A. Letanneux et al. focus on the psychosocial impact of speech impairment in PD, presenting a French version of the Dysarthria Impact Profile. K. B. Foreman et al. also address speech issues, examining the effects of concurrent performance of a speech task and a postural control task in individuals with PD. Postural control is also addressed by G. Vervoort et al., who present evidence of differences in specific aspects of postural control in people with PD who experience freezing of gait compared to those with PD who have no history of freezing of gait. S. T. Nemanich et al. also focus on gait in PD, examining utility of walking speeds for identifying fallers and determining predictors of preferred and fast pace walking speeds. A. Williams et al. examine the relationships between gait and upper extremity movements in PD, studying the effects of amplitude and cadence manipulations. B. K. Randhawa et al. also examine upper extremity performance as assessed by handwriting, demonstrating the acute changes in handwriting following a single intervention session using transcranial magnetic stimulation. L. A. King et al. examine two different exercise interventions, focusing on which outcome measures were most effective for measuring change following agility boot camp or treadmill training. Finally, G. Frazzitta et al. report the effects of a four-week multidisciplinary inpatient rehabilitation program on gait and balance function after completion of the intervention and one year later. The broad scope of work in this special issue is reflective of the far-reaching impact that rehabilitation may have on many aspects of PD, from the individual to the environmental level. Last but not least, the presented work will provide a multilevel understanding of PD motor problems which will feed into the clinical care and optimal rehabilitation for patients with this complex disease.

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Clinical Study

Upper Extremity Freezing and Dyscoordination in Parkinson's Disease: Effects of Amplitude and Cadence Manipulations

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Purpose. Motor freezing, the inability to produce effective movement, is associated with decreasing amplitude, hastening of movement, and poor coordination. We investigated how manipulations of movement amplitude and cadence affect upper extremity (UE) coordination as measured by the phase coordination index (PCI)—only previously measured in gait—and freezing of the upper extremity (FO-UE) in people with Parkinson's disease (PD) who experience freezing of gait (PD + FOG), do not experience FOG (PD-FOG), and healthy controls. *Methods*. Twenty-seven participants with PD and 18 healthy older adults made alternating bimanual movements between targets under four conditions: Baseline; Fast; Small; SmallFast. Kinematic data were recorded and analyzed for PCI and FO-UE events. PCI and FO-UE were compared across groups and conditions. Correlations between UE PCI, gait PCI, FO-UE, and Freezing of Gait Questionnaire (FOG-Q) were determined. *Results*. PD + FOG had poorer coordination than healthy old during SmallFast. UE coordination correlated with number of FO-UE episodes in two conditions and FOG-Q score in one. No differences existed between PD−/+FOG in coordination or number of FO-UE episodes. *Conclusions*. Dyscoordination and FO-UE can be elicited by manipulating cadence and amplitude of an alternating bimanual task. It remains unclear whether FO-UE and FOG share common mechanisms.

1. Introduction

A motor block, or "freezing" event, is the sudden inability to produce effective movement, which has been documented during speech, upper extremity (UE) movements, and gait, and is often experienced by individuals with Parkinson's disease (PD) [1–4]. Freezing of gait (FOG) is arguably the most debilitating motor block, as it contributes to increased risk of falls and is associated with reduced quality of life and depression [5]. FOG is difficult to study because it is not easily elicited within the laboratory setting. Individuals with PD who experience FOG (PD+FOG) often demonstrate decreasing steplength in combination with increased cadence prior to a freezing event [4, 6]. Additionally, studies have demonstrated that people with PD+FOG exhibit greater steplength variability, increased cadence, increased step-time asymmetry, and poorer coordination compared to individuals with PD who do not experience FOG (PD-FOG) [7–9]. Plotnik et al. suggest that each of these gait parameters may have a certain level of dependency on each other, and that decline in one or more of these parameters can push an individual past the threshold for functional gait resulting in an episode of FOG [9].

Recent research investigated a possible shared mechanism between FOG and impaired upper extremity (UE) movements [10–12]. Nieuwboer et al. observed trends towards decreased coordination and increased variability of movement in freezers, nonfreezers, and controls during an alternating, high speed, and small amplitude bimanual task compared to an alternating, normal speed, and large amplitude task [11]. Additionally, they showed a strong correlation between UE freezing and Freezing of Gait Questionnaire (FOG-Q) scores. Similarly, Vercruysse et al. [10] observed UE freezing most often during alternating flexion/extension

Table 1: Final sample characteristics.

Characteristic	Healthy old $N = 18$	PD-FOG $N = 16$	PD + FOG $N = 11$
Sex (M/F)*†	6/12	5/11	10/1
Age (yrs)‡	68.4 ± 7.5	67.6 ± 9.5	70.8 ± 6.9
Average baseline amplitude (cm)*	13.5 ± 2.4	11.4 ± 2.8	9.2 ± 2.9
Average baseline cadence (taps per minute)	114.4 ± 10.5	156.1 ± 23.9	151.71 ± 31.5
Hoehn and Yahr OFF¥		2.2 ± 0.44	2.2 ± 0.26
MDS-UPDRS-3 OFF*§		26.1 ± 9.4	44.8 ± 11.8
FOG-Q score*¥		2.8 ± 1.8	11.3 ± 2.2

*All group(s) significantly different; $P < 0.05$.
†Chi-square analysis; ‡one-way ANOVA; ¥Mann-Whitney U Test; §Independent samples t-test.
Abbreviations:
M: male.
F: female.
Yrs: years.
MDS-UPDRS-3: Movement Disorder Society Unified Parkinson Disease Rating Scale Motor Subscale 3.
FOG-Q: Freezing of Gait Questionnaire.

movements of the index finger during small, fast movements. Most recently, the same group [12] observed the effects of manipulating amplitude, frequency, and movement complexity (in-phase versus antiphase) during alternating flexion/extension movements of the index finger with and without auditory cueing in PD-FOG and PD+FOG. They noted that the PD+FOG group demonstrated the most movement variability during small amplitude tasks.

These results suggest that variability of UE movement and freezing of the UE (FO-UE) during bimanual tasks may be related to FOG. Additionally, FO-UE may be influenced by manipulations of amplitude and cadence that reflect characteristics of FOG, that is, small amplitude and fast cadence. However, the extent to which small amplitude or increased cadence in isolation or in combination contributes to dyscoordination of UE movement or FO-UE has yet to be determined. Further, no studies to date have compared similar manipulations of amplitude and cadence of the UE and of gait in order to gain insight into potential shared mechanisms of motor blocks in the UE and during gait.

The purpose of this study was (1) to investigate how specific manipulations of amplitude and cadence during an alternating bimanual task affect UE coordination, as measured by the phase coordination index (PCI), and number of FO-UE events and (2) to gain further insight into potential shared mechanisms between UE and gait coordination in people with PD and healthy controls. We hypothesized that decreasing amplitude or increasing cadence would decrease coordination in people with PD compared to healthy controls, with the combination of small amplitude and fast cadence eliciting the poorest coordination. Furthermore, we hypothesized that the PD+FOG group would be more affected by amplitude and cadence manipulations thereby exhibiting worse coordination and increased FO-UE episodes compared to PD-FOG and healthy controls. Finally, we hypothesized that coordination during each UE task would be correlated with coordination of a parallel gait task.

2. Methods

2.1. Participants. Twenty-eight participants with idiopathic PD (16 PD-FOG, 12 PD+FOG) and 19 healthy older adults participated. Sex, age, and disease severity characteristics are included in Table 1. Participants were recruited from the Movement Disorders Center database at Washington University in St. Louis School of Medicine (WUSM). All participants with PD had a diagnosis of idiopathic PD according to established criteria [13, 14]. Inclusion criteria included the ability to independently ambulate a minimum of twenty feet and normal or corrected to normal vision. Exclusion criteria included the presence of a diagnosed neurological or medical condition (aside from PD) and an inability to withhold anti-Parkinson medication for a limited duration. Data were collected following a minimum 12-hour overnight withdrawal of anti-Parkinson medication. Healthy older adults (>30 years old) were often the spouses of participants with PD. All healthy individuals met the above inclusion and exclusion criteria except those specific to PD. Healthy older adults were age-matched to participants with PD. Data from these individuals has been previously reported elsewhere [15]. Data were collected in the Locomotor Control Laboratory at WUSM Program in Physical Therapy. All participants gave informed consent as approved by the WUSM Human Research Protection Office.

Participants with PD were further divided into two groups, those who experience freezing of gait (PD+FOG) and those who do not (PD-FOG), based upon a score of ≥2 on item three of the Freezing of Gait Questionnaire (FOG-Q), which indicated at least weekly freezing episodes [16]. All participants with PD participated "OFF" medication (≥12 hour withdrawal of anti-Parkinson medication). One healthy older adult was excluded from all analyses due to the inability to follow directions adequately. One participant with PD+FOG was excluded from all analyses due to inability to perform the tasks. Two additional participants with PD+FOG were excluded only from UE PCI analyses due to the inability to perform continuous alternating bilateral UE movements during one or more of the conditions.

2.2. Procedure: Upper Extremity and Gait Tasks. Participants with PD were assessed by a trained research physical therapist using the Movement Disorder Society Unified Parkinson's

Disease Rating Scale Motor Subscale III (MDS-UPDRS-3) to quantify disease severity [13] and completed the FOG-Q [16] to quantify frequency and severity of FOG events. All participants completed four UE tasks and four gait tasks: Baseline, Fast, Small, and SmallFast.

A full description of the methods used during the parallel gait tasks are reported in Williams et al [15]. In short, all participants were assessed while walking at a preferred speed across a 4.9 m GAITRite instrumented walkway (CIR Systems, Inc., Sparta, NJ, USA) placed on a level surface in a large open room. For this experiment, these data were used to determine the cadence of each individual's UE task. Ten trials were performed to obtain an average baseline cadence for each individual and each trial was visually monitored for FOG events or atypical gait events such as stumbles, falls, or lateral deviation off of the GAITRite mat. Any trials consisting of these events were removed and repeated.

During the UE tasks, participants were seated comfortably at a table in an open room. Each individual performed alternating, bilateral UE movements under four conditions: Baseline (baseline cadence, 10 cm target), Fast (+50% baseline cadence, 10 cm target), Small (baseline cadence, 5 cm target), and SmallFast (+50% baseline cadence, 5 cm target). Baseline UE cadence was determined by an individual's cadence during preferred gait as reported in Williams et al. [15]. That is, if a person walked at a rate of one step per second, we had him/her perform UE movements to one reach per second. All conditions were randomized.

Five, 15-second trials of kinematic data for each condition were captured using 8 Hawk cameras and Cortex data acquisition software (Motion Analysis Corporation, Santa Rosa, CA, USA). Prior to each recorded trial, the participant was given a 20.32 cm × 27.94 cm (8 × 11 in) sheet marked with the appropriate targets (Figure 1). Instructions were given to use his/her index fingers to tap the targets, alternately tapping the left front/right rear targets and then the left rear/right front targets simultaneously. A metronome was turned on to the appropriate cadence while the individual tapped the targets. Once the individual practiced with the targets and metronome, the metronome was turned off and the targets were removed without the individual stopping his/her UE movement. The 15-second trial was captured after the visual and auditory cues were removed. This allowed for observation of the participant's internally generated movement state during each condition. Further, auditory and visual cues were removed as these cues are known to enhance performance in individuals with PD [14, 17, 18], and the purpose of this study was to observe each participant's internally generated movement without external cues.

2.3. Outcome Variables. A quantitative assessment of freezing episodes based upon established definitions [10] and phase coordination index (PCI) were the primary outcomes. PCI was developed to quantify interlimb coordination during gait by taking into account the accuracy and consistency of the timing of stepping phases [19]. Higher PCI values indicate poorer coordination. Previous investigations have used PCI to quantify temporal coordination of steps during gait by measuring the timing of consecutive footfalls [8, 19].

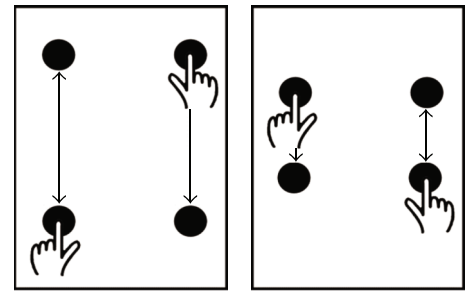

Figure 1: Schematic of targets and movements for the bilateral, alternating upper extremity task. Baseline (left, 10 cm); Small (right, 5 cm).

In the current study, we use the same metric to assess the temporal coordination of alternating UE movements. In this case, each "footfall" in the standard PCI calculation was represented by the index finger making contact with the target furthest from the body. Therefore, only the time of taps aimed at the target furthest from the body were analyzed. A "stride" was defined as two consecutive taps of the same finger. A "step" was defined as consecutive taps of alternating fingers and from hereon will be referred to as a "cycle." For three consecutive taps, the phase (φ) was determined as cycle time divided by "stride" time and scaled to 360° (φ_i):

$$\varphi_i = 360 \times \frac{t_{Si} - t_{Li}}{t_{L(i+1)} - t_{Li}}, \quad (1)$$

where $t_{S(i)}$ and $t_{L(i)}$ represent the timing of the ith finger contact of the UE with shorter and longer average "step" times, respectively. Once φ_i had been determined, 180 was subtracted from each φ_i value. The absolute value of each data point was calculated, and the mean of the array was taken to produce a measure of temporal accuracy (φ_{ABS}):

$$\varphi_{ABS} = \overline{\left|(\varphi_i) - 180^\circ\right|} \quad (2)$$

The degree of consistency of φ was calculated as the coefficient of variation of φ values (φ_{CV}) and given as a percentage. PCI was then calculated as

$$\text{PCI} = \varphi_{CV} + P\varphi_{ABS}, \quad (3)$$

where $P\varphi_{ABS} = 100(\varphi_{ABS}/180)$. Periods of freezing, as defined in the following paragraph, were not included in the PCI analysis.

For the quantitative assessment of FO-UE episodes, trials were analyzed for the presence of FO-UE episodes by a blinded rater. In order to assess FO-UE episodes, we determined the duration and amplitude of the average antiphase cycle (AAPC) [10]. The AAPC was calculated using the first six consecutive cycles of alternating UE movement in each trial. FO-UE episodes were then defined using the calculated AAPC for a given trial. FO-UE episodes were defined as a sudden halt or decrease in amplitude of movement, which deviated from the calculated AAPC in one of two ways: (1) UE movement halted for ≥75% of the AAPC duration or

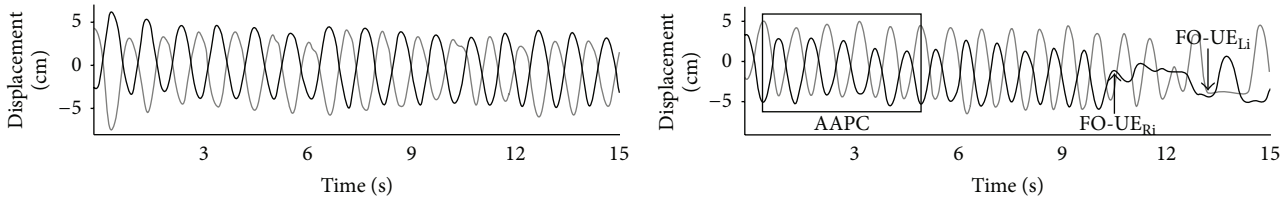

Figure 2: Kinematic trajectories (a) healthy older adult and (b) individual with PD-FOG with an FO-UE event. AAPC: average antiphase cycle; FO-UE$_{Ri}$: initiation of right upper extremity freeze; FO-UE$_{Li}$: initiation of left upper extremity freeze.

(2) UE movement amplitude that was ≤50% of the AAPC amplitude, was accompanied by an irregular cycle frequency, and continued as such for at least twice the AAPC duration [10]. Additionally, voluntary stops and in-phase movements were excluded from assessment. A normal and an FO-UE event trajectory are illustrated in Figure 2.

As a secondary analysis, we determined correlations between FO-UE, UE PCI, PCI during parallel gait tasks (as reported in Williams et al. [15]), and FOG-Q score.

2.4. Data Processing. Kinematic data were processed using Motion Monitor software (Innovative Sports Training, Inc., Chicago, IL, USA) and analyzed with custom written Matlab software (MathWorks, Natick, MA, USA). Position and velocity data were low pass filtered at 10 Hz before kinematic analyses. Each group's average amplitude, cadence, and PCI values for each task were determined.

2.5. Statistical Approach. The same statistical approach as reported in Williams et al. [15] was used to analyze UE PCI. Mixed model repeated measures ANOVA with an unstructured covariance structure was implemented using SAS v 9.3 (SAS Institute, Inc., Cary, NC, USA). Group was used as the between subject factor and condition as the within-subject factor. We corrected for multiple comparisons by dividing $\alpha = 0.05$ by the number of comparisons made (Bonferroni correction); a post hoc P value of 0.004 was considered significant for evaluating interactions. Additionally, we compared number of FO-UE episodes between PD−/+FOG groups, which was analyzed as percent of trials with FO-UE episodes. Data were rank-transformed prior to performing a repeated measures ANOVA.

Spearman's correlation was used to determine relationships of FO-UE events with UE PCI, PCI during gait, and FOG-Q score and of UE PCI with PCI during gait as reported in Williams et al. [15]. Aside from evaluating interactions, a P value of ≤0.05 was considered significant for all statistical analyses.

3. Results

Mean performance ± standard deviation of each group is shown in Figures 3(a) and 3(b). Values are expressed as percent difference from instructed baseline. As such, ideal performance in the Baseline condition would have cadence and amplitude values of 0%. Ideal performance in the Fast condition would have cadence values of +50% and amplitude values of 0%. Ideal performance in the Small condition would have cadence values of 0% and amplitude values of −50%. Ideal performance in the SmallFast condition would have values of +50% for cadence and −50% for amplitude. Overall, there was no between-group difference in performance of cadence ($P = 0.21$), while there was a difference between healthy older adults and individuals with PD in performance of amplitude ($P \leq 0.02$).

3.1. Quantitative Assessment of FO-UE. Total numbers of FO-UE episodes for each group are reported in Table 2. There was no difference between conditions ($P = 0.61$) in percent of trials with FO-UE. A trend toward significance was present between PD-FOG and PD+FOG in percent of trials with FO-UE ($P = 0.07$).

3.2. Phase Coordination Index (PCI) during Upper Extremity Tasks. Overall, UE PCI values were different between groups ($P = 0.005$) and conditions ($P < 0.001$), and a group by condition interaction effect was observed ($P = 0.05$) (Figure 4). Post hoc analyses showed that PD+FOG had poorer coordination compared to healthy older adults during the SmallFast condition ($P < 0.001$).

3.3. Correlational Analyses. All groups were included in the analysis between UE PCI and gait PCI. Healthy older adults were excluded from analysis of FO-UE and FOG-Q, as freezing is specific to PD. UE PCI was correlated with the number of FO-UE events in the Baseline and Small conditions (Table 3). Gait PCI was correlated with UE PCI for the SmallFast (rho = 0.34; $P = 0.03$) condition. Furthermore, FOG-Q scores were correlated with FO-UE events during Fast (rho = 0.45; $P = 0.02$). FOG-Q scores were not correlated with UE PCI. Additionally, UPDRS scores were correlated with UE PCI (rho = 0.41, $P = 0.04$) but were not correlated with the number of FO-UE episodes (rho = 0.21, $P = 0.29$).

4. Discussion

The results from this study demonstrate that dyscoordination and FO-UE can be elicited by manipulating cadence and amplitude of an alternating UE bimanual task. Contrary

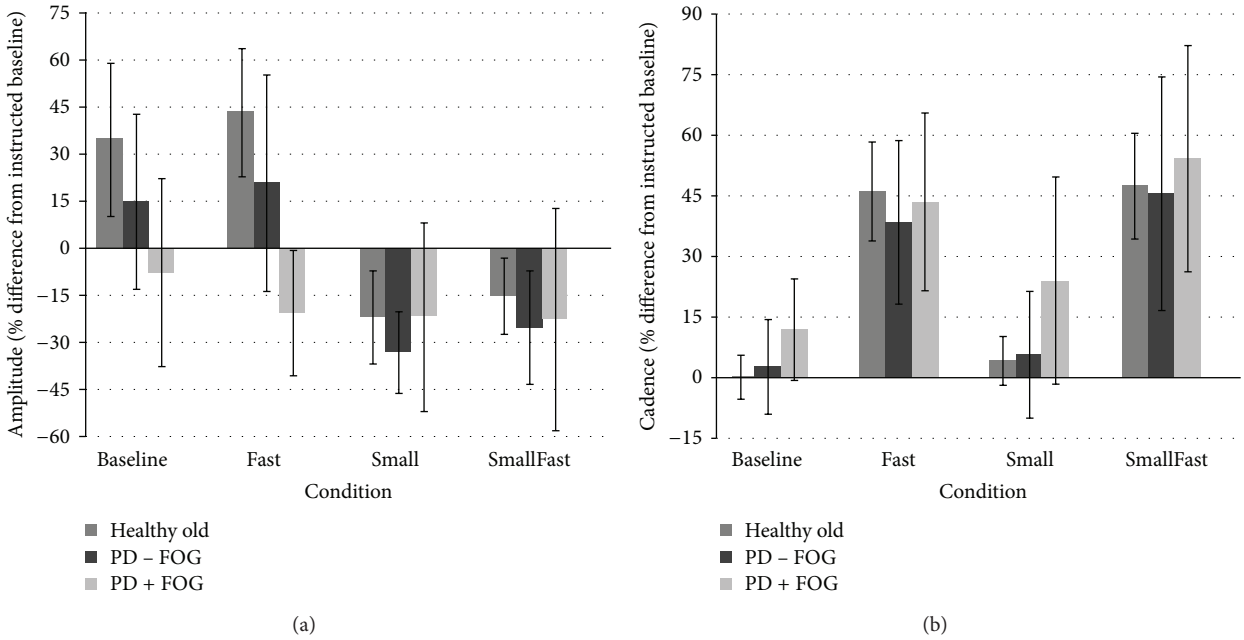

Figure 3: Task performance amplitude (a) expressed as percent difference from baseline (10 cm) and cadence (b) expressed as percent difference from each participant's baseline gait cadence (i.e., baseline). Bars represent standard deviations. Healthy old were different from PD−/+FOG in amplitude; there were no differences between groups in cadence.

Table 2: Number of FO-UE episodes.

Condition	Group		
	Healthy old (n = 18)	PD-FOG (n = 16)	PD + FOG (n = 11)
Baseline			
FO-UE	0 (0%)	4 (3.7%)	10 (11.0%)
N	0	2	4
Fast			
FO-UE	0 (0%)	5 (6.2%)	12 (21.8%)
N	0	4	6
Small			
FO-UE	0 (0%)	4 (3.7%)	8 (14.5%)
N	2	5	
SmallFast			
FO-UE	1 (0.01%)	12 (11.2%)	6 (9.5%)
N	1	6	3

Values are number of episodes of freezing per condition (percent of total trials with at least one episode in parentheses). *N*: total number of individuals experiencing ≥1 episode of FO-UE.
Abbreviations:
FO-UE: freezing of the upper extremity.
PD-FOG: Parkinson disease without freezing of gait.
PD + FOG: Parkinson disease with freezing of gait.

Table 3: Spearman's correlations between UE PCI, Gait PCI, FOG-Q, and number of FO-UE events.

	FO-UE	UE PCI
Baseline		
UE PCI	0.41*	—
Gait PCI	−0.22	0.18
FOG-Q	0.27	0.09
Fast		
UE PCI	0.10	—
Gait PCI	0.04	0.15
FOG-Q	0.45*	−0.05
Small		
UE PCI	0.66**	—
Gait PCI	0.28	0.19
FOG-Q	0.30	0.27
SmallFast		
UE PCI	−0.32	—
Gait PCI	0.06	0.34*
FOG-Q	−0.12	0.21

*$P < 0.05$.
**$P < 0.01$.
Abbreviations:
UE: upper extremity.
PCI: phase coordination index.
FOG-Q: freezing of gait questionnaire.
FO-UE: freezing of upper extremity.

to our hypothesis, there was no difference between participants with PD and healthy controls in PCI during Small or Fast conditions. Additionally, there was no difference between PD−/+ FOG in PCI during any condition. However, PD+FOG were more affected by the combination of SmallFast, which resulted in poorer coordination in PD+FOG compared to healthy older adults. A trend toward significance between PD−/+FOG was also observed in the percent of trials exhibiting FO-UE episodes. Although periods of freezing were excluded from the PCI calculation, UE PCI and the quantitative assessment of FO-UE events were correlated during the Baseline and Fast conditions. An additional relationship was demonstrated between PCI during the SmallFast

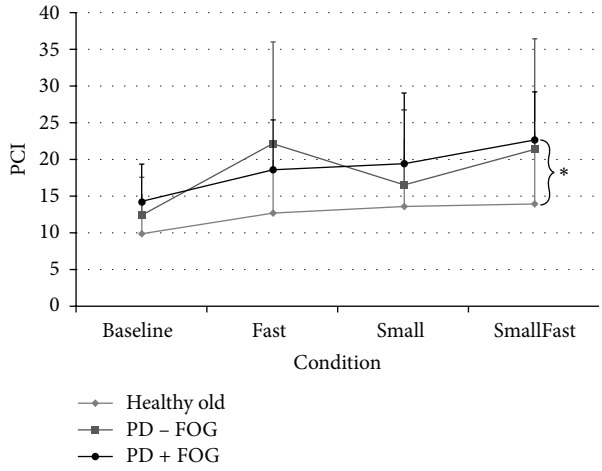

Figure 4: Phase coordination indices (PCI) for PD−/+ FOG and healthy older adults. *Group significantly different, $P < 0.004$.

gait task and the parallel SmallFast UE task. Further, FOG-Q scores were correlated with FO-UE during the Fast condition.

Previous work demonstrated that bimanual, antiphase movement coordination is impaired in people with PD compared to healthy controls [3, 10, 12]. In keeping with this, a number of FO-UE events were elicited in this study and people with PD+FOG had poorer coordination during the SmallFast task compared to healthy controls. Further, FOG was not elicited during the parallel gait tasks reported in Williams et al. [15]. This suggests that FO-UE may be elicited more easily than FOG in individuals with PD [3, 10–12].

Previous work demonstrated that FO-UE was more common in more complex tasks, that is, anti-phase movement with a small amplitude and fast frequency [10], and participants with PD+FOG exhibited increased difficulty with coordination compared to participants with PD-FOG [12]. This work also suggested that FO-UE increased with small amplitude movements [10]. However, in the present study, there were no significant differences between conditions in number of FO-UE events. Only 27% of participants with PD+FOG exhibited FO-UE during the SmallFast condition, while 54% exhibited FO-UE during the Fast condition. For individuals with PD, the Small condition only accounted for 20% of the total number of FO-UE events. Additionally, there was no significant difference between the PD−/+FOG groups in the assessment of PCI and only a trend toward significance in the quantitative assessment of FO-UE episodes. In fact, two participants with PD-FOG exhibited FO-UE in each of the four conditions, and 37% of PD-FOG exhibited FO-UE during the SmallFast condition. This difference may be due to the way the participants with PD−/+FOG were qualified.

Prior studies have qualified individuals with PD+FOG as experiencing monthly or more frequent FOG episodes [10, 12]. In the present study, we defined PD+FOG as those individuals with PD experiencing weekly or more frequent FOG episodes (score of ≥2 on item 3 of the FOG-Q). Four participants in this study reported experiencing FOG once per month (score of ≥1 on item 3 of the FOG-Q). To determine if these individuals were indeed driving the difference between our work and prior studies, we did a secondary analysis wherein the four participants with FOG once per month were placed in the PD+FOG group. Using this alternate classification scheme, we again analyzed differences in the percent of trials with FO-UE between the PD−/+FOG. This analysis yielded the same results as the original analysis; that is, there was no difference between PD−/+FOG in percent of trials with FO-UE episodes. There was also no difference between conditions of percent of trials with FO-UE events. As such, the differences in results of the present study compared to results of previous work are unlikely due to PD−/+FOG method of classification.

It has been hypothesized that freezing may be a somatotopic phenomenon, which initially affects the UE or LE and may eventually come to impact both UE and LE tasks [10, 11]. Interestingly, two of the four participants in the PD-FOG group who reported FOG once per month accounted for 67% of FO-UE events in the Baseline and Small condition and 40% of FO-UE events in the Fast condition. Though none of the four experienced FO-UE during the SmallFast condition, those in the PD-FOG group who did may experience motor blocks of the UE and not yet experience FOG. This may also explain why not all of those with PD+FOG experienced FO-UE.

Based upon the results of the present study, it remains unclear whether FO-UE and FOG are related. However, FO-UE can be elicited by manipulating amplitude and frequency characteristics in a way that mimics changes in these variables just before an episode of FOG. The group of Nieuwboer et al. demonstrated a strong correlation between FO-UE episodes and the FOG-Q [10–12]. There may be common mechanisms underlying FO-UE and FOG, but further research is needed to investigate this, as the FOG-Q score was correlated with number of FO-UE events only during the Fast condition. Additionally, the number of FO-UE events was correlated with poor gait coordination (i.e., gait PCI) during the parallel SmallFast task, but no FOG episodes were elicited during this gait task.

To our knowledge, this is the first time that gait coordination, that is, PCI, has been used to correlate interlimb coordination during UE tasks with gait coordination of parallel tasks. Prior work demonstrated that individuals with PD+FOG exhibit ongoing movement impairments during gait, that is, greater steplength variability and increased cadence compared to individuals with PD-FOG [7–9]. Our work supports this as participants with PD+FOG made, on average, smaller movements during the Fast condition and faster movements during the Small condition than the two other groups.

It remains unclear whether decreased amplitude, increased cadence, or a combination of the two is associated with the freezing mechanism of the UE. Vercruysee et al. [10] conclude that smaller amplitudes elicit more FO-UE, but there were no significant differences between conditions in the present study. The differences between the present study and the previous literature suggest that small amplitude, fast cadence, or a combination of small, fast movements may not be the sole contributors to FO-UE episodes. As Plotnik et al.

suggest with FOG [9], we suggest that FO-UE episodes may represent a culmination of breakdown in several aspects of control. This breakdown can be elicited by alternating bimanual Small tasks, Fast tasks, or SmallFast tasks in people with PD as measured by our quantitative assessment of FO-UE events. Though cadence and amplitude immediately prior to a FO-UE event were not measured in this study, as with FOG, we hypothesize that FO-UE is preceded by involuntary simultaneous decreasing amplitude with an accompanying hastened cadence that either a Fast, Small, or SmallFast task has the potential to elicit this response in the UE.

Functional, complex, rhythmical tasks that require manual coordination include typing, handwriting, playing an instrument, and certain forms of exercise such as UE strength training. These tasks can replicate Small, Fast, or SmallFast conditions depending on an individual's ability. As demonstrated in the present study, decreased amplitude and increased cadence alone or together can elicit FO-UE. FO-UE during daily tasks can severely impact an individual's form of communication, hobbies, and quality of life. It is therefore important to educate patients with PD regarding these functional tasks that may elicit FO-UE.

Limitations of this study are acknowledged. First, only one independent rater determined the presence of FO-UE based upon established definitions [10], and reliability of this method was not established. Further, preselected amplitudes and cadence were utilized and we cannot say whether a large amplitude or slow cadence would have elicited the same or lesser amount of dyscoordination or FO-UE. Additionally, cadence was determined from a gait task rather than from an UE movement task. This methodology was employed as the gait task provided a parallel motor task, without introducing the UE task and allowing for motor learning effects to bias the study. We acknowledge the difference between UE and lower extremity tasks and that perhaps movement frequency may be a higher in UE tasks. Additionally, participants were not sex-matched, participants with PD were not matched for disease severity, and UPDRS scores were correlated with PCI. We cannot conclude definitively whether our measures of dyscoordination or FO-UE are due to disease severity, FOG status, or both. Finally, the sample size of this study was relatively small with large amounts of variation within each condition per group, which makes it difficult to detect significant differences between groups and conditions.

5. Conclusions and Future Direction

Imposed manipulations of cadence and amplitude that mimic changes in gait associated with FOG can affect UE coordination and elicit FO-UE episodes in people with PD. People with PD+FOG have poorer coordination compared to healthy controls during a SmallFast task, but no other differences in UE coordination were noted between healthy controls and individuals with PD. FO-UE and FOG may be related, but future research is needed to explore potential links between the two. Future clinical studies could also examine the utility of instructions to increase movement amplitude and decrease movement cadence as a means of enhancing coordination and reducing FO-UE and FOG.

Funding

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Research Article

Which Aspects of Postural Control Differentiate between Patients with Parkinson's Disease with and without Freezing of Gait?

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This exploratory study aimed to identify which aspects of postural control are able to distinguish between subgroups of patients with Parkinson's disease (PD) and controls. Balance was tested using static and dynamic posturography. Freezers ($n = 9$), nonfreezers ($n = 10$), and controls ($n = 10$) stood on a movable force platform and performed 3 randomly assigned tests: (1) sensory organization test (SOT) to evaluate the effective use of sensory information, (2) motor control test (MCT) to assess automatic postural reactions in response to platform perturbations, and (3) rhythmic weight shift test (RWS) to evaluate the ability to voluntarily move the center of gravity (COG) mediolaterally and anterior-posteriorly (AP). The respective outcome measures were equilibrium and postural strategy scores, response strength and amplitude of weight shift. Patients were in the "on" phase of the medication cycle. In general, freezers performed similarly on SOT and MCT compared to nonfreezers. Freezers showed an intact postural strategy during sensory manipulations and an appropriate response to external perturbations. However, during voluntary weight shifting, freezers showed poorer directional control compared to nonfreezers and controls. This suggests that freezers have adequate automatic postural control and sensory integration abilities in quiet stance, but show specific directional control deficits when weight shifting is voluntary.

1. Introduction

Patients with Parkinson's disease (PD) are prone to falling during daily activities. Recurrent falls are a frequent cause of injuries and hospital admissions for patients with PD and an important factor that negatively influences quality of life [1, 2]. The extent of this problem was shown in a meta-analysis of prospective studies that reported that 46% of the patient population with PD had one or more falls in a 3-month time frame [3].

In order to prevent recurrent falls it is important to gain more insight in the underlying deficits. Recently, a number of prediction studies have shown that postural control deficits and freezing of gait (FOG) are powerful determinants of recurrent falls [4, 5]. Although both signs were previously linked to falls, there are, to our knowledge, no conclusive reports on the relationship between postural control deficits and FOG.

FOG is defined as an episodic inability to generate effective stepping while having the intention to walk [6]. It is most commonly experienced during turning and step initiation, but also when faced with spatial constraints, stress, and distraction [6]. A FOG episode can present itself by a significant step size reduction (shuffling gait), knee trembling, or complete akinesia, all leading to a sudden arrest of walking [7]. During freezing, it sometimes happens that the center of gravity (COG) continues to move forward while the feet stop moving. This can lead to imbalance, which cannot be corrected by compensatory steps and therefore increases the risk of falling [1, 7]. This was supported by Jacobs et al. [8], who showed that patients with PD, compared to controls, fail to initiate compensatory stepping and present with FOG-like trembling knee movements when balance was challenged using a sudden forward platform translation. These findings were interpreted as being indicative of a postural control

deficit and, more specifically, a failure to couple balance and voluntary locomotor synergies [8].

Postural control deficits in freezers were also reported by Nantel and coworkers [9]. During voluntary weight shifts as part of a repetitive stepping task, freezers showed rapid, small, and inefficient weight transfers between both legs, which were associated with freezing episodes [9]. In addition, both peripheral proprioceptive feedback and central sensory processing abnormalities have been attributed to postural control deficits in PD [10]. Since both FOG and postural control deficits are associated with increased fall risk, elucidating their relationship is an important step in understanding the problem of recurrent falls in PD.

Therefore, the purpose of this exploratory study was to study both sensory and motor aspects of voluntary and automatic postural control using a moveable balance platform in a group of freezers, nonfreezers, and age-matched controls. This enabled objective quantification of sensory organization processes and postural responses to external perturbations (automatic) and voluntary weight shifting to determine if differences exist between freezers and nonfreezers.

We expected freezers to experience more problems in both voluntary and automatic postural control tasks compared to nonfreezers given the reported greater impairment during automatic task performance and underscaled voluntary body weight transfer during repetitive stepping in place [9]. Additionally, we expected both freezers and nonfreezers to perform worse on these tasks compared to controls [11].

2. Materials and Methods

2.1. Participants. Nineteen patients with PD and 10 age-matched healthy controls participated in this study. All patients were recruited through the University Hospitals Leuven. Patients were included if they had a Hoehn and Yahr (H&Y) stage between II and IV during the "on" state of the medication cycle and were able to stand independently without interfering dyskinesias. Patients with low back pain, orthostatic hypotension, dementia (Mini Mental State Examination < 24), neurosurgical intervention (subthalamic stimulator), and other diseases affecting postural control and/or proprioception were excluded. The patient group consisted of 9 patients with PD experiencing FOG and 10 patients with PD without FOG as confirmed by a score of 1 or higher on the third question of the freezing of gait questionnaire (FOGQ). The freezer and nonfreezer groups were matched for age and disease severity by means of the Hoehn and Yahr (H&Y) stage and Unified Parkinson's Disease Rating Scale (UPDRS) part III. Those patients on levodopa were tested in the "on" state, about 1-2 hours after medication intake. Each participant signed a written informed consent. The research procedures were approved by the local review board according to the declaration of Helsinki.

2.2. Experimental Design. The baseline clinical examination consisted of administering the UPDRS (part III, motor subscale) and the FOGQ [12]. Fall frequency in the past three months was determined retrospectively and patients were assigned one of three fall status categories: (1) no falls or near falls, (2) no falls but at least one near fall, and (3) one fall or more in the last 3 months. A fall was defined as an event resulting in a person coming to rest unintentionally on the ground or other level and not as the result of a major intrinsic event or overwhelming hazard [13, 14]. A near fall was defined as any loss of balance without hitting the floor or other lower surface (fall arrested by seeking support) [15].

To account for possible proprioceptive differences between freezers and nonfreezers, position sense was measured with a lower limb matching task. During this task, participants were blindfolded and instructed to match the position of one lower limb with the position of the other limb, which was held in a fixed position by the investigator. Differences in alignment between both limbs (expressed in degrees) were measured for a range of knee angles during 5 trials and expressed as an average [16]. To avoid muscle fatigue, a short period of rest was given between all trials.

Postural control was measured using the SMART Equi-Test System (Neurocom International Inc., Clackamas, OR, USA). Three tests were assigned in random order: (1) the Sensory Organization Test (SOT), (2) the Motor Control Test (MCT), and (3) the Rhythmic Weight Shift test (RWS). These tests were selected to address global postural control, that is, static and dynamic postural (automatic and voluntary control), as well as the influence of the various sensory modalities. Participants were allowed to rest between tests to avoid muscle fatigue. They were placed bare-footed on the moveable force plate and were instructed to stand still during SOT and MCT conditions leaving their hands hanging besides their body, looking straight ahead. Foot placement was adapted as a function of body height, so taller participants had a wider base of support. To avoid falls, a harness was fitted onto the participant and a second examiner was standing nearby.

The Sensory Organization Test (SOT) was used to assess postural control and the ability to integrate sensory (visual, vestibular, and proprioceptive) information under 6 systematically manipulated conditions [11]. Each condition consisted of 3 trials of 20 seconds during which the postural sway and the postural strategy (relative amount of ankle to hip movement where 100% indicated ankle movement only and 0% hip movement only) were measured. The outcome measure generated from this test was the equilibrium score, which was averaged for 3 trials of the 6 conditions in which sensory information was manipulated. The equilibrium score is a valid measure for postural stability comparing the participants' sway with their theoretical limits of stability (LOS) (12.5°) calculated by the formula $(12.5(\theta_{\max} - \theta_{\min}) \times 100)/12.5$ where θ reflects the sway angle in response to the perturbation [17]. A higher equilibrium score represented a better ability to maintain balance.

The Motor Control Test (MCT) assessed the automatic postural reactions in response to platform translations of various sizes (small, medium, and large) in forward and backward directions. Translation of the surface resulted in displacement of the COG, in response to which participants were instructed to restore their balance [18]. Each size of platform translation in forward and backward direction was offered 3 times, randomly ordered with a random time

Table 1: Clinical variables of nonfreezers, freezers, and controls.

	Nonfreezers ($n = 10$)	Freezers ($n = 9$)	Controls ($n = 10$)	P value
Gender (m/f)	10/0	7/2	3/7	0.003*
Age (y)	68 (58–75)	65 (62–73)	66 (63–74)	0.90
Height (cm)	174 (169–178)	173 (166–176)	174 (168–179)	0.90
H&Y				0.49
H&Y 2	4	1	NA	
H&Y 2.5	2	5	NA	
H&Y 3	4	2	NA	
H&Y 4	0	1	NA	
DD (y)	6 (5–8)	12 (10–14)	NA	0.09
FOGQ tot (0–28)	2.5 (2–4)	13 (6–14)	NA	0.006**
MMSE (24–30)	29 (28–30)	29 (28–30)	NA	0.83
Fall frequency	1/10	4/9	NA	0.008**
UPDRS (III) (0–108)	25.5 (19–27)	26 (23–28)	NA	0.71
Knee proprioception#	2.4 (1.8–3.6)	2.2 (2-3)	1.6 (1-2)	0.02*

Median and 25th percentile and 75th percentile (Q25 and Q75) are presented between brackets.
#Larger difference in degrees indicates greater difference between right and left leg and thus greater proprioceptive deficit.
Abbreviations: H&Y: Hoehn and Yahr stadium; DD: disease duration; FOGQ tot: total score of the freezing of gait questionnaire; MMSE: mini mental state examination; UPDRS: unified Parkinson's disease rating scale; NA: not applicable; *significant difference (K-W: $P < 0.05$) between 3 groups (group effect); **significant difference (M-WU: $P < 0.05$) between freezers and nonfreezers (post hoc effects).

interval. Latency times (ms) and response strength (°/s) were measured for each of the 3 trials and averaged for the 6 combinations of the size and direction of platform translation. The response strength reported the participants' active response at each size and direction of the translation, defined as the amount of angular momentum needed to counteract sway (approximately twice the angular momentum of the platform in opposite direction) induced by the platform translation. Low response strength represented adequate amplitude scaling in response to platform translations [18].

The Rhythmic Weight Shift (RWS) test evaluated the voluntary ability to move the COG from right to left and forward to backward between two targets (preset at 50% at the measured LOS of the participant) at slow (3 seconds peak to peak), medium (2 seconds peak to peak), and fast (1 second peak to peak) pacing [11]. Movement velocities of the target were 2.67°/s (slow mediolateral), 4°/s (medium mediolateral), 8°/s (fast mediolateral), 1.78°/s (slow anterior-posterior), 2.68°/s (medium anterior-posterior), and 5.35°/s (fast anterior-posterior). Participants were instructed to move the cursor towards a star on the screen by moving their pelvis (COG) left/right or forward/backward without moving their feet or other body parts. The outcome variable was directional control. This is a ratio of the amount of movement in the intended direction to the amount of deviation from the ideal movement trajectory. It is expressed as a percentage, calculated for every combination of movement direction and speed. The percentage reflects the average score of 6 movement repetitions in one plane (as shown in Figure 4). Higher scores indicate better directional control.

2.3. Statistical Analysis. Overall group differences in the freezer, nonfreezer, and control group for descriptive variables (gender, age, and length), SOT (equilibrium score and postural strategy), MCT (latency time and response strength), and RWS (directional control) outcome measures were analyzed using the nonparametric Kruskal-Wallis (K-W) ANOVA by ranks test due to small sample size and abnormal distribution of data. Post hoc Mann Whitney U-tests (M-WU) were used to compare individual between-group differences for clinical variables (between patient groups), SOT, MCT, and RWS. Additional within-group analyses for the MCT were carried out using the Wilcoxon matched pairs test. All tests were performed using Statistica (Statistical analysis Software, version 8) at an α-level of 0.05.

3. Results

Demographic characteristics of both groups are shown in Table 1. A significant difference was found between freezers and nonfreezers on FOGQ scores ($P = 0.006$). Freezers showed a higher frequency of falls (4/9) and near falls (5/9) in the preceding 3 months compared to nonfreezers (1/10 and 3/10, resp.) ($P = 0.008$). No significant differences were found for UPDRS score (part III, motor subscale), MMSE score, and disease duration between subgroups. Nevertheless, freezers had a twofold longer median disease duration compared to nonfreezers. Knee proprioception mean scores were significantly worse in freezers (2.4°) compared to controls (1.6°) ($P = 0.02$), but not to nonfreezers ($P > 0.05$).

Patients were taking their normal daily doses of anti-Parkinson medication. Eight of 9 freezers took levodopa with a mean active dose of 359.72 mg/day. Nine out of 10 freezers took levodopa with a mean active dose of 315 mg/day. Other medication intake was not significantly different between groups.

3.1. Automatic Postural Control: SOT-Test. Equilibrium scores showed a significant difference between the 3

Table 2: SOT equilibrium score descriptive variables.

Test	Freezers	Nonfreezers	Controls	*P* value
SOT1	94.3 (92.7–94.7)	93.2 (92.0–94.3)	94.3 (93.0–96.0)	0.20
SOT2	92.0 (90.7–92.3)	89.3 (88.0–93.0)	92.2 (90.0–93.7)	0.52
SOT3	90.0 (87.7–92.3)	88.0 (88.0–92.0)	89.7 (88.3–91.7)	0.82
SOT4	75.7 (70.7–84.3)	74.8 (68.3–82.0)	75.5 (65.7–81.3)	0.82
SOT5	55.0 (43.0–69.3)	55.0 (48.3–61.3)	56.2 (50.7–69.0)	0.61
SOT6	54.0 (52.0–65.0)	53.0 (42.3–58.0)	58.9 (58.0–61.0)	<0.01*

Estimated median interquartile range of the SOT equilibrium scores is presented in percentage (%). *Significant differences ($P < 0.05$) for Kruskal-Wallis ANOVA overall group analysis.

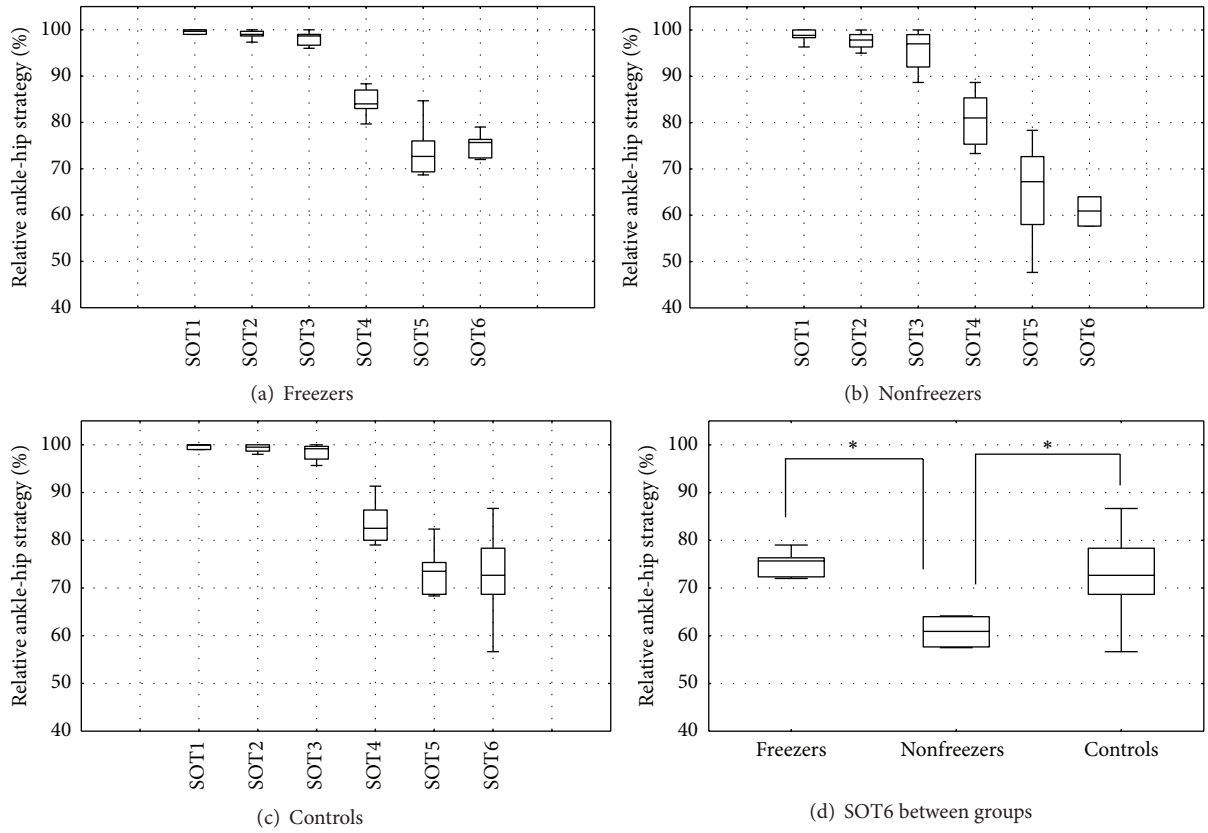

Figure 1: Group comparison of ankle-hip strategy in SOT conditions. Boxes represent median values and interquartile ranges (Q25–Q75), with error bars indicating the nonoutlier ranges. Panels (a), (b), and (c) show the relative ankle-hip strategy (with 100% ankle strategy only and 0% hip strategy only) for each SOT test. Panel (d) shows the relative ankle-hip strategy for SOT6 between freezers, nonfreezers, and controls. *Significant difference ($P < 0.05$) between two groups (post hoc).

groups for SOT6 (K-W: $P = 0.008$). Post hoc analysis indicated that both freezers and nonfreezers had lower equilibrium scores for SOT6 compared to controls (M-WU: $P = 0.02$; $P = 0.005$), but no PD subgroup difference was found. No significant overall group differences were found for SOT1–SOT5 (Table 2). All groups showed very similar and minimal sway in all conditions, even during conditions where the balance platform was moving and sensory information was compromised (SOT4–SOT6). In SOT5 and SOT6, data were omitted if a near fall occurred which was prevented by the tester. Two freezers and 1 nonfreezer tended to fall during each trial of SOT5 and 1 control did so during 1 trial of SOT5. In addition, 3 freezers almost fell during 1 or more trials of SOT6, similar to 3 nonfreezers and 5 controls.

The postural control strategy used by participants to maintain balance during the SOT is shown in Figure 1. An overall group comparison showed a significant difference between groups for SOT6 (K-W: $P = 0.02$). Freezers (75.67% ± 4) and controls (72.67% ± 9.67) relied significantly more on the ankle strategy compared to nonfreezers (60.92% ± 6.33) in SOT6 (M-WU: freezers: $P = 0.02$; controls: $P = 0.02$). There were no significant differences between groups for SOT1, SOT2, SOT3, SOT4, and SOT5. In general, all groups increased the amount of hip strategy from SOT1 to SOT6.

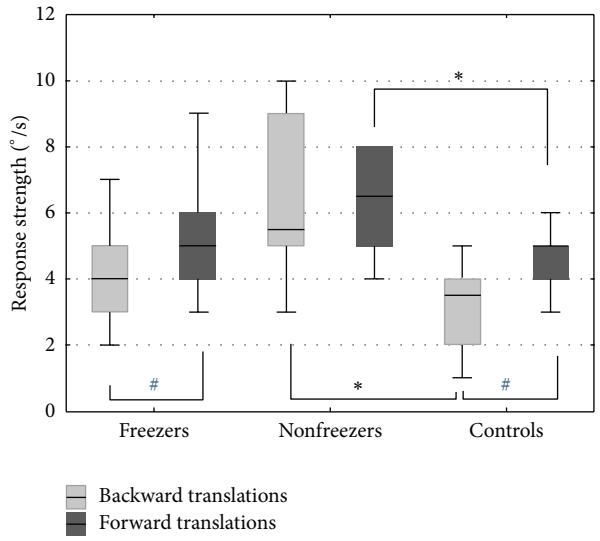

Figure 2: Group differences in MCT performance. Response strength of the left leg in forward and backward translations during MCT (pooled for small, medium, and large conditions). Boxes represent median values and interquartile ranges (Q25–Q75) with error bars indicating the nonoutlier range. *Significant difference ($P < 0.05$) between two groups (post hoc), #significant difference ($P < 0.05$) within groups.

3.2. Automatic Postural Control: MCT-Test. Figure 2 displays the response strength to translations during the MCT. As the results for both legs were very similar, the data are presented for one leg only.

Statistical testing indicated overall group differences in response strength for backward translations in the 3 conditions (K-W: small: $P = 0.02$; medium: $P = 0.01$; large: $P = 0.03$). Between-group analysis showed that, in all backward conditions, the response strength of the nonfreezer group was larger than that of the freezer and control groups, indicative of poorer automatic postural control in nonfreezers (Figure 2). Backward translations brought on significantly stronger responses in nonfreezers than in controls during small (M-WU: $P = 0.007$), medium (M-WU: $P = 0.005$), and large (M-WU: $P = 0.01$) translations (Figure 3). Comparing freezers and nonfreezers, a significant difference was found in the medium backward translation (M-WU: $P = 0.047$) in which nonfreezers showed larger responses. No significant differences were found between freezers and controls.

3.3. Voluntary Postural Control: RWS-Test. The RWS test was utilized to gain insight in the voluntary intentional shifting of the COG. Figure 4 shows an example of the movement pathway in the mediolateral direction of a representative participant of each group. It shows that freezers performed worse and had a more irregular pathway compared to nonfreezers and controls.

Statistical analysis revealed overall group differences for directional control in the moderate mediolateral direction (K-W: $P = 0.01$) and the slow, moderate, and average anterior-posterior direction (K-W: $P = 0.002$, $P = 0.05$, $P = 0.006$). Table 3 shows the results of the between-group

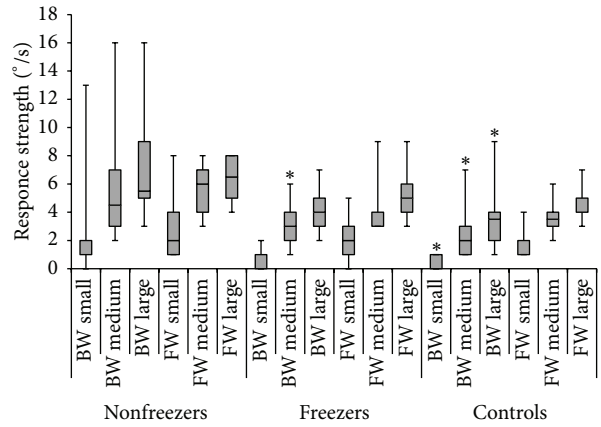

Figure 3: Group differences in MCT performance per condition. Response strength of the left leg in forward (FW) and backward (BW) translations for small, medium, and large conditions separately. Boxes represent median values and interquartile ranges (Q25–Q75) with error bars indicating range. *Significant difference ($P < 0.05$) with nonfreezers (post hoc).

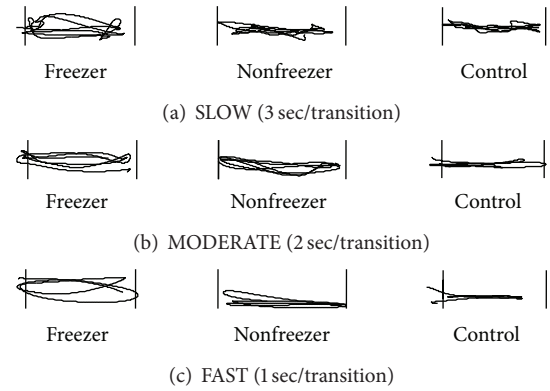

Figure 4: COG pattern during mediolateral RWS. Each graph shows a representative COG movement pattern for a freezer, nonfreezer, and control participants. The vertical bars indicate the distance of the shift the participants were instructed to make and are set at 50% of the participants' limit of stability. Panels (a), (b), and (c) show the COG pattern when a cue was given with respectively a 3 second, 2 second, and 1 second interval.

analysis indicating significantly less directional control for the slow anterior-posterior shift in freezers compared to nonfreezers (M-WU: $P = 0.02$) and controls (M-WU: $P = 0.0009$). Additionally, freezers showed significantly less directional control for average anterior-posterior (M-WU: $P = 0.002$) and average mediolateral (M-WU: $P = 0.02$) shifts compared to controls. There were no significant differences between nonfreezers and freezers except for the slow anterior-posterior condition in which nonfreezers had better directional control. No significant differences were found in movement velocity between groups.

4. Discussion

The purpose of this study was to investigate for the first time differences in voluntary and automatic postural control

Table 3: Directional control during rhythmic weight shift.

	Freezers	Nonfreezers	Controls	P value (Freezers versus nonfreezers)	P value (Freezers versus controls)	P value (Nonfreezers versus controls)
Slow mediolateral	77 (62–77)	74.5 (69–81)	79.5 (76–83)	0.24	0.07	0.28
Moderate mediolateral	74 (71–79)	83 (76–86)	86.5 (82–88)	0.07	<0.01**	0.35
Fast mediolateral	84 (77–87)	88.5 (87–90)	87 (83–91)	0.13	0.24	0.80
Average mediolateral	79 (71–82)	80.5 (78–96)	83.5 (81–85)	0.13	0.01*	0.48
Slow anterioposterior	49 (22–67)	70 (62–79)	77 (72–83)	0.02*	<0.01**	0.089
Moderate anterioposterior	61 (38–77)	75 (70–80)	82.5 (66–87)	0.16	0.01*	0.25
Fast anterioposterior	76 (64–82)	81 (68–82)	82.5 (79–87)	0.50	0.07	0.39
Average anterioposterior	62 (43–74)	73 (70–79)	81 (76–84)	0.09	<0.01**	0.052

Estimated median interquartile range of the directional control is presented in percentage (%). *Significant difference ($P < 0.05$); **significant difference ($P < 0.01$). Measurement unit is % of optimal performance.

between freezers, nonfreezers, and controls to gain insight in the connection between postural control deficits and freezing of gait (FOG).

In contrast to our hypothesis, we found that freezers did not have a greater problem with automatic postural control compared to nonfreezers, even in situations with both unreliable visual and proprioceptive input. This points to a similar ability to integrate sensory information during quiet stance in patients with freezing compared to patient without freezing. Contrary to the lack of differences in response strengths between freezers and nonfreezers, we did find a significant difference between PD subgroups for the strategy used to maintain balance. A shift from an ankle to hip strategy is normal when changing from quiet stance in stable conditions to situations where balance becomes compromised [19]. Freezers showed similar strategies to maintain balance compared to controls throughout the SOT. Nonfreezers showed less ankle strategy during SOT6 compared to freezers and controls, which indicates more balance problems in both normal balance condition and condition where vision and proprioception (SOT6) are compromised. These results are surprising and suggest that, in this sample, nonfreezers had poorer postural control or more difficulty with sensory integration to maintain postural control compared to freezers and controls. However, because of the lack of differences in other SOT conditions, this conclusion cannot be generalized. Contrary to our results, Tan et al. [20] reported that freezers show a greater proprioceptive deficit compared to nonfreezers and controls in a force target task with a tendon vibration protocol. When we assessed proprioception separately by the lower limb position sense test, we found larger errors for freezers compared to controls, but not compared to nonfreezers. Combined with the SOT results, this favours the conclusion of poorer postural control in nonfreezers compared to freezers and controls. However, we did not separately assess other sensory modalities.

Nevertheless, similar results were found during the MCT. There were no significant differences in response strengths between freezers and nonfreezers except for the backward translation of medium size, confirming that nonfreezers tended to have less adequate postural control. In addition, there were significant differences in response strengths between nonfreezers and controls in almost all forward and backward translations. The more normal pattern of response strengths in freezers may be explained by an increased alertness of freezers to the possibility of losing balance. Snijders et al. [21] showed that freezers anticipated an upcoming obstacle more quickly during treadmill gait. Nonfreezers on the other hand may have expected the perturbations less, leading to exaggerated response strengths. We found no response time differences between freezers and nonfreezers during the MCT, indicating no movement initiation differences between groups.

Overall, the pattern that nonfreezers had more impaired postural control is particularly notable, given that UPDRS and H&Y scores were similar between groups and that freezers tended to have longer disease duration. Freezers were taking a higher levodopa dose (not significant), which is consistent with the contention that FOG may be relatively less levodopa responsive than other PD symptoms [22]. The fact that the present exploratory study was conducted in "on" phase may explain these findings since a higher levodopa dose may have contributed to the better balance in freezers compared to nonfreezers. However, other studies [23, 24] showed no significant improvement in postural control with levodopa treatment and even increased postural sway in levodopa-treated patients.

The RWS task was used to test the participants' voluntary ability to move the COG in an intended direction at different velocities [11]. In this task, freezers had strikingly worse directional control compared to the other groups and more so in the anterior-posterior than in the mediolateral direction. Nevertheless, they were able to perform the weight shifts at an adequate speed, and therefore this deficit cannot be interpreted as an expression of bradykinesia. When performing the intended movement trajectories, freezers may have opted to prioritize optimal velocity resulting in neglect of adequate directional control [25]. Another study suggested that patients with PD display a speed/accuracy tradeoff during repetitive movement tasks, but this has never been shown to be more present in freezers [26]. In addition, the task involved a visual target, which may have served as an external cue. Freezers and nonfreezers are known to increase gait speed in response to an external trigger. The impaired

voluntary COG control, particularly in the sagittal plane, may be a contributing factor to loss of balance during freezing and festination when patients cannot counteract the forward propulsion inherent to hastening of gait. In this respect, Bloem et al. [1] suggested that this pattern, followed by a sudden arrest of walking, may be one of the reasons why falling and freezing are related [1].

Interestingly, in controlled situations (SOT and MCT), no differences were found in "fall frequency" (representing the number of uncompleted trials) between freezers, nonfreezers, and controls. This may point to the fundamental deficit of automatic motor control in PD, which is difficult to capture during laboratory testing. The fall frequency questionnaire showed that 4/9 of the patients in the freezer group fell during the past three months in daily life compared to 1/10 of the nonfreezers, which is in line with earlier work [1, 3, 8].

Several limitations of the study should be taken into account when interpreting the present findings. The relatively modest differences in balance performance between freezers and nonfreezers found in our exploratory study may be related to the small sample size and could have underestimated actual differences between freezers and nonfreezers. In addition, no multiple testing corrections were applied because of the hypothesis-generating nature of this study. Furthermore, all tests were done in the "on" state, providing insufficient contrast between both patient groups. However, several studies have reported that patients still experience a deterioration of balance when they are in the "on" state [24, 27]. We only studied limited aspects of postural control, not taking into account other components like balance during gait tasks, lower extremity strength, and ankle range of motion. Therefore, to fully elucidate the differences in postural control between freezers and nonfreezers we recommend that future studies be conducted in larger sample sizes in both "on" and "off" state. Additionally, we suggest using appropriate multiple testing corrections and including different aspects of postural control to fully understand postural control problems in patients with PD with and without freezing. Finally, the significant difference in gender distribution between groups could have influenced our results as previous research has shown differences in postural sway between men and women [28].

5. Conclusion

Freezers performed better than nonfreezers on a balance platform requiring sensory integration and response to unexpected translations. They did show a particular impairment in voluntary weight shifting, mainly in the anterior-posterior direction. Future research is needed to pinpoint differences in automatic postural control between freezers and nonfreezers and to unravel whether proprioceptive deficits underlie these problems. Additionally, it needs to be elucidated why patients with freezing have a higher fall frequency.

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Clinical Study

The Effects of Practice on the Concurrent Performance of a Speech and Postural Task in Persons with Parkinson Disease and Healthy Controls

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Purpose. Persons with Parkinson disease (PD) demonstrate deficits in motor learning as well as bidirectional interference (the performance of one task concurrently interferes with the performance of another task) during dual-task performance. Few studies have examined the practice dosages necessary for behavioral change in rehabilitation relevant tasks. Therefore, to compare the effects of age and PD on motor learning during dual-task performance, this pilot study examined persons with PD as well as neurologically healthy participants during concurrent performance of postural and speaking tasks. *Methods*. Seven persons with PD and 7 healthy age-matched and 10 healthy young control subjects were tested in a motion capture facility. Task performances were performed concurrently and recorded during 3 time periods (acquisition (beginning and ending), 48-hour retention, and 1-week retention). Postural control and speech articulatory acoustic variables were measured. *Results*. Healthy young participants consistently performed better than other groups on all measured postural and speech variables. Healthy young participants showed decreased variability at retention, while persons with PD and healthy age-matched controls were unable to consistently improve their performance as a result of practice. No changes were noted in the speech variables. *Conclusion*. The lack of consistent changes in motor performance in any of the tasks, except in the healthy young group, suggests a decreased efficiency of motor learning in the age-matched and PD groups and argues for increased practice dosages during balance training.

1. Introduction

Parkinson disease (PD) is thought to begin in the peripheral nervous system and progress to the central nervous system through the enteric, autonomic, and olfactory pathways [1]. Only with neuronal cell loss in the midbrain does PD begin to manifest its cardinal motor signs (akinesia, bradykinesia, tremor, rigidity, and postural instability). Although these motor signs are the most recognizable features of PD, the neurology community is developing a greater appreciation of deficits that extend beyond motor function [2].

Two signs of PD that may have profound implications for rehabilitation potential are the impairments of motor learning and difficulty with performance of concurrent motor tasks (dual-task deficits) [3, 4]. Previous research suggests that persons with PD can demonstrate retention of practiced tasks (defined as learning) [5]. However, the retention is generally not as good as the retention for persons without the disease, and the overall rate of skill acquisition is slowed [6].

One cause for disappointing intervention effects in neurologic rehabilitation may be the lack of appropriate dosage [7]. In support of this idea, studies that examined increased practice of single task activities such as balance reactions and volitional weight shifts in persons with PD have demonstrated improved center of mass control and protective stepping responses [8, 9]. Although persons with PD appear to benefit from single-task practice, less is known about their ability to benefit from practice in dual-task conditions.

Dual task conditions acutely degrade postural performance [10–12] as well as gait steadiness and symmetry [13, 14] in individuals with PD.

While a recent study demonstrated that persons with PD could benefit from dual-task practice during gait [5], to our knowledge, no studies have examined changes in measures of anticipatory postural control and stability as a result of practice in dual-task conditions. In addition, it is unclear if persons with PD can improve performance and retain these changes over time when exposed to dosages of practice commonly utilized in the clinic [15, 16].

To address this issue, this study examined the effects of age and PD on practice-based changes in concurrent postural task and speech motor task performance (dual-task condition). The postural control and speech tasks were chosen because of their limited response to pharmacological treatment [17, 18]. Given the limitations of pharmacological treatments, behavioural interventions such as practice may be the most promising means of improving postural control and speech in individuals with PD. Specifically, based on previous research [11, 13], we hypothesized that persons with PD would demonstrate performance deficits in concurrently performed postural and speaking tasks when compared to healthy age-matched and healthy young controls. In addition, based on a research examining motor learning in PD [6], we hypothesized that the effects of practice on concurrently performed postural and speaking tasks would be different for individuals with PD compared to neurologically healthy individuals.

2. Methods

2.1. Design and Selection of Participants. This study included 3 groups: (1) persons with PD (PD group), (2) healthy age-matched control participants (AM group), and (3) healthy young adult control participants (HY group). Utilizing movement velocity outcomes for between group effect sizes from Dromey et al. [11] (Cohen's $d = 1.6$) and Jessop et al. [8] (Cohen's $d = 1.4$) a priori power calculations indicated that between 7 and 10 individuals in each group were needed to provide 80% power with an alpha level of 0.05. The accessible population for the PD group was individuals from our facility's Movement Disorders clinic. Inclusion criteria for the PD group included a confirmed diagnosis of idiopathic PD and mild to moderate disease severity (Hoehn and Yahr Stage I–III). For the HY group, participants had to be between 18 and 40 years of age. All three groups had to have the physical and cognitive abilities to actively participate in the study procedures. Exclusion criteria included individuals who were cognitively unable to understand or follow study instructions, previous surgical management of PD, or individuals with significant orthopaedic (i.e., fracture, moderate-to-severe osteoarthritis) or neurological (i.e., stroke, traumatic brain injury, and neuropathy) injury. The accessible population for the AM and HY groups was from the university community or relatives of the individuals with PD. A general exclusion criterion for all groups was a history of concomitant medical conditions that limited their ability to perform the proposed testing.

2.2. Tasks, Instrumentation, and Procedures. All subjects signed an IRB-approved consent form prior to participating. The postural control task was a stationary base of support rise to toes (RTT) movement during which participants were instructed to the following "rise to your toes as fast as you can and stay as high and stable as you can for 5 seconds." This task was selected because it required participants to voluntarily move from a stable (full foot-to-ground contact) to an unstable posture (only forefoot-to-ground contact) and maintain a stable position. The RTT movement has been used as a measure of postural control in previous studies [11, 17]. The speech task involved the repetitive reading of standardized sentences that were selected because they allowed inferences about lingual excursions [11, 19, 20]. All testing was performed in the Motion Capture Core Facility using an 8-camera Vicon Motion Analysis System (Vicon Motion Systems, Centennial, CO, USA) and an Advanced Medical Technologies Inc. force platform (OR6-7 series, AMTI, Watertown, MA, USA). Speaking tasks were recorded using a stereo headset with a microphone (Logitech, Inc., Newark, CA, USA) and a computer-based audio recording program (Audacity, version 1.3.5). For testing, participants wore black tight fitting clothing and no shoes. Passive reflective markers were placed on bony prominences utilizing a 15-segment full body standardized gait analysis marker set (Plug-In Gait marker set; Vicon Motion Systems, Centennial, CO) [21, 22]. Following marker placement, participants were asked to stand in a comfortable position on the force plate, which was covered with solid color butcher paper. To insure standardized foot position between test periods, each individual's feet were traced with a marking pen, and these tracings were used as the starting position for all trials. In addition, all subjects were instructed to begin trials with their arms positioned comfortably at their side. Motion capture data (marker trajectories and kinetic data) were synchronized using Vicon Nexus Software (Vicon Motion Systems, Centennial, CO, USA).

Individual performance of the postural control and speech tasks was tested prior to the initial trials of dual-task practice. A substantial dual-task deficit in both posture and speech measures has been reported on previously [11]. For this study, the postural control and speech tasks were performed simultaneously and were synchronized using an auditory cue triggered from loading a second force plate that emitted a loud sound when loaded over 10 Newtons. This trigger placed a timestamp in both the auditory and motion capture data for synchronization purposes and signaled the subject to simultaneously perform the postural control and speech tasks.

Testing was performed over three time periods utilizing a classic motor learning paradigm that used an acquisition phase with a larger number of practice trials separated in time from two retention phases with fewer trials [23, 24]. The first time period was the acquisition phase (day 1) in which participants completed 21 dual-task trials segregated into 7 blocks of 3 trials with 30 seconds rest between trials and 2 minutes rest between blocks. The second and third time periods were the 48-hour retention phase and the 1-week retention phase, respectively. For both retention phases,

participants completed 9 dual-task trials segregated into 3 blocks of 3 trials with 30 seconds rest between trials and 2 minutes rest between blocks. Testing (including participant and laboratory setup) took approximately 45–60 minutes for the acquisition phase and 20–30 minutes for the retention phases. For each trial, data were collected from the time an auditory cue was given until after the movement task was completed. Participants were supervised closely during all trials in order to prevent falls. Data gathered during trials were stored on the laboratory computer for later analysis. In order to control for dopamine replacement medication effects, persons with PD were tested at the same time each day with testing of the PD subjects beginning approximately 1 hour after taking their medications.

2.3. Data Processing and Analysis. The independent variables used for analysis were group assignment (PD group, AM group, and HY group) and practice phase (beginning of acquisition, end of acquisition, 48-hour retention, and 1-week retention). The dependent variables used for data analyses for the postural task were related to motor planning, postural coordination, and postural stability.

Reaction time (RT) reflected the time from the go signal until the onset of COP movement. Previous motor control research supports that the processing time taken from a go signal until movement onset reflects motor planning [23, 25]. Longer reaction times taken prior to the beginning of movement are considered to reflect increased motor planning demands.

In order to visualize the biomechanical coordination of the center of pressure during movement from the foot flat to the on toes position, we chose two postural coordination variables (center of pressure velocity (COP Vel) as well as center of mass (COM) and center of pressure (COP) difference) [26]. Center of pressure velocity was calculated as the rate of change of the net center of pressure during the initial 0.25 seconds of anterior COP movement. Greater COP velocity was interpreted as improved postural coordination while reduced COP velocity was interpreted as bradykinetic postural coordination. Center of pressure-COM difference (COP-COM difference) was calculated as the maximal difference between the sagittal plane locations of the COP and the vertical projection of the COM onto the floor. Previous research has shown that persons with greater postural coordination allow a larger separation of the COP and COM positions during postural control tasks than less stable individuals [17, 27].

Once participants had reached the peak of their RTT position, they were asked to remain stable for 5 seconds. The variable selected to reflect postural stability in peak heel raise position was the vertical heel position coefficient of variation (HH CV). The HH CV was calculated by dividing the standard deviation of the heel position by the average heel position during the middle 3 seconds of the RTT task [26]. In the context of the task constraints to remain as "stable as possible," increases in linear measures of variability such as the coefficient of variation reflect reduced stability [28].

The speaking task involved the production of two target sentences that were read from a sheet of paper at a comfortable rate and loudness. The sentences on the paper were printed using a large font and positioned on a stand at a comfortable reading position for each subject. These sentences were: "the boot on top is packed to keep" and "the boy gave a shout at the sight of the cake". These sentences were selected because they included the corner vowels and several diphthongs that allowed inferences about lingual excursions via measurement of the first and second formants. The speech-specific dependent variables were articulatory acoustic measures that reflected movements of the tongue [29]. A diphthong is sometimes called a *gliding vowel* because it is a combination of two adjacent vowels (as in *boy*). Diphthong duration was chosen to reflect diphthong transition time in msec, which is a measure of how long it takes to transition from the first to the second vowel. Formants are prominent acoustic features in the speech signal that change in frequency as the tongue moves during diphthong articulation. The first and second formant (F1 or F2) frequency change during the diphthong (transition extent in Hz) was chosen to reflect tongue displacement; therefore, lower frequency change reflected smaller articulatory excursions. The slopes of each formant transition (Hz/ms) were chosen to reflect tongue velocity; therefore, smaller slopes reflect lower velocities. The first formant reflected superior/inferior and the second formant reflected anterior/posterior movement of the tongue [29, 30]. The diphthong analyzed in the standardized sentences included /ɔɪ/ (boy).

The recordings were analyzed with Praat software (version 5.0.47; Amsterdam, Netherlands). The methods for data reduction and analysis have been detailed previously [11]. The speech acoustic measures were selected because they have been associated in previous studies with changes in articulatory function in speakers with PD and have appeared to be sensitive to dual-task interference and practice-mediated improvements [11, 19, 20].

For each variable, the average of 3 consecutive trials (or one "block") was used as the representative dependent variable. During the acquisition phase, the first block was used to represent the baseline, and the seventh block was used to represent the end of acquisition. In order to examine the participants' initial performance on the retention day, rather than have their performance be confounded by additional practice, we utilized the first block for analysis during both the 48-hour and one-week retention phases.

Changes in performance were defined as changes that occurred during the acquisition phase, that is, between block 1 and block 7 of acquisition. Motor learning was defined as changes that occurred between the acquisition phase and the retention phases. Short-term learning was defined as the difference between block 1 of acquisition and block 1 of the 48-hour retention testing, while long-term learning was defined as the difference between block 1 of acquisition and block 1 of the one-week retention testing [23].

Because of the small sample size and the potential for violations of the assumptions of parametric statistical tests, we utilized nonparametric analyses. To examine between group differences at baseline, for each dependent variable we compared each group's acquisition block 1 performance using separate Kruskal-Wallis ANOVAs. Post hoc testing

was performed as needed using Mann-Whitney U tests. To examine changes in performance during the acquisition phase and between acquisition and retention phases within groups, we compared acquisition block 1, acquisition block 7, 48-hour retention block 1, and 1-week retention block 1 using separate Friedman ANOVAs. Post hoc testing was performed as needed using Wilcoxon matched pairs tests.

For all dependent variables, the magnitude of change was estimated by calculating the percent change from acquisition block 1. The level of significance for all comparisons was set at 0.05. All statistical analyses were performed with SPSS 19 (IBM Inc; Armonk, NY,USA) for Macintosh.

3. Results

Overall, 24 participants completed the study (7 persons with PD, 7 neurologically healthy age-matched controls, and 10 neurologically healthy young participants) (Table 1). All participants that were recruited completed all testing periods.

3.1. Motor Planning. Analysis of reaction time results showed no statistical differences between groups or over time ($P > 0.05$). The observed reaction times were consistent with those observed in other studies of dual-task paradigms [31] (Table 2).

3.2. Postural Coordination. COP velocity results for block 1 of the acquisition phase (baseline) demonstrated a significant difference between the groups ($P = 0.006$). Post hoc testing revealed that the HY group demonstrated significantly faster COP velocity at baseline relative to the AM and PD groups ($P < 0.04$). The PD group demonstrated the slowest velocity at baseline (Table 2).

Within-group analysis demonstrated that only the HY group showed a significant difference as a result of practice (comparison between acquisition and retention phases) ($P = 0.02$). Post hoc testing revealed that the HY group significantly increased their COP velocity from baseline to the end of the acquisition phase by 18.7% ($P = 0.03$). Center of pressure velocity for the AM and PD groups was not significantly altered at any phase of the study (Table 2).

A significant difference was found between the groups in COP-COM difference for block 1 of the acquisition phase (baseline) ($P = 0.003$). Post hoc testing revealed the HY and AM groups demonstrated a significantly larger COP-COM difference relative to the PD group ($P < 0.01$). The PD group demonstrated the smallest COP-COM difference at baseline.

Within group-analysis demonstrated that none of the groups showed significant differences in COP-COM difference as a result of practice (comparison between acquisition and retention phases) (Table 2).

3.3. Postural Stability. A significant difference was found between the groups in HH CV for block 1 of the acquisition phase (baseline) ($P = 0.02$). Post hoc testing revealed that the HY and AM groups demonstrated significantly less variability at baseline relative to the PD group ($P < 0.02$). The HY group demonstrated the lowest HH CV value, and the PD group had the highest HH CV at baseline (Table 2).

Within-group analysis demonstrated a significant difference as a result of practice (comparison between acquisition and retention phases). Post hoc testing revealed that the greatest improvements in HH CV were seen in the HY group with significant decreases of 38% and 50% at 48-hour and one-week followups, respectively, relative to acquisition ($P < 0.05$). In contrast, there was no significant effect on HH CV in the AM or the PD groups.

3.4. Articulatory Acoustic Measures. A significant difference was found between the groups for /ɔɪ/ F2 slope for block 1 of the acquisition phase (baseline) ($P = 0.04$). Post hoc testing revealed that the PD group produced significantly different values relative to the AM and HY groups (Table 3).

Within-group analysis demonstrated no significant differences as a result of practice (comparison between acquisition and retention phases) in any of the three groups ($P > 0.05$) (Table 3).

4. Discussion

Based on our interest in the effects of motor learning deficits on the ability to improve components of postural task performance in persons with PD, in this preliminary study we subjected persons with and without PD to commonly utilized practice dosage amounts [15] of dual-task practice. As we hypothesized, persons with PD demonstrated performance deficits in concurrently performed postural and speaking tasks when compared to healthy age-matched and healthy young controls. In addition, we hypothesized that persons with PD would respond differently to practice than neurologically healthy participants. Despite having the least variability in measures of postural stability, the healthy young participants were the only group that improved in HH CV during acquisition and retention. Such results suggest that the amount of practice necessary for postural task motor learning in healthy young individuals does not appear sufficient to drive changes in persons with PD or healthy elders. No consistent effect of practice was noted in any of the groups for the articulatory acoustic measures.

4.1. The Effects of Age and PD on the Efficiency of Acquisition and Retention. Neurologically healthy young participants consistently performed better on all measured postural and speech variables. As evidence of the adverse effect of age on the measured variables, most commonly the neurologically healthy age-matched control participants demonstrated impaired postural control and speech performance relative to the young participants. The effects of Parkinson's disease beyond age was specifically evident for our measures of COP velocity and heel height variability where participants in the PD group demonstrated substantially greater bradykinesia and variability than the neurologically health groups (COP velocity: PD = 155.49 mm/sec, AM = 247.84 mm/sec, HY = 369.31 mm/sec at block one of acquisition; heel height

Table 1: Participant demographics.

Variable	Groups		
	HY group	AM group	PD group
n (gender)	10 (M = 4; F = 6)	7 (M = 5; F = 2)	7 (M = 7; F = 0)
Age	25.50 (2.40)	70.50 (11.90)	68.70 (9.20)
Time since diagnosis			4.11 (2.31)
Disease severity* (modified HY)			2 (1.5–3)
Taking carbidopa/levodopa			Yes: 6 No: 1
Dysarthria severity (1–10)*			4.1 (1–7)
6-month fall history			>2 falls: 3 0–2 falls: 4

HY group: healthy young adult controls; AM group: healthy age-matched controls; PD group: persons with PD.
*Median (range).

Table 2: Values (SD) for each postural control measure at acquisition and retention phases for each group.

	Acquisition (baseline) Block 1 mean (SD)	Acquisition (ending) Block 7 mean (SD)	Retention 48 hrs Block 1 mean (SD)	Retention 1 week Block 1 mean (SD)
Reaction time (sec)				
HY group	0.66 (0.16)	0.59 (0.14)	0.61 (0.10)	0.67 (0.11)
AM group	0.76 (0.21)	0.74 (0.36)	0.70 (0.25)	0.75 (0.29)
PD group	0.79 (0.20)	0.67 (0.36)	0.78 (0.22)	0.73 (0.10)
COP Vel (mm/sec)				
HY group	381.39 (166.64)*,#	473.26 (146.95)	446.85 (179.12)	503.16 (217.22)
AM group	263.30 (184.21)	227.08 (227.76)	331.05 (301.86)	238.58 (229.46)
PD group	97.13 (261.83)	113.45 (235.31)	108.02 (219.66)	139.39 (219.58)
COP_COM diff (mm)				
HY group	52.84 (21.69)*	62.74 (26.56)	59.97 (24.40)	62.65 (22.95)
AM group	41.18 (26.45)	40.58 (9.75)	44.88 (19.60)	43.73 (14.40)
PD group	18.43 (25.80)	23.40 (23.15)	27.72 (21.49)	31.23 (26.52)
Heel Height CV (%)				
HY group	3.86 (2.50)*,**	2.79 (4.10)	2.58 (1.70)	2.07 (3.30)
AM group	2.43 (4.70)	3.72 (8.80)	3.01 (22.50)	2.18 (13.80)
PD group	14.35 (5.08)	24.74 (43.30)	13.59 (43.90)	9.03 (27.50)

HY group: healthy young adult controls; AM group: healthy age-matched controls; PD group: persons with PD.
All values: median (interquartile range).
*Significant difference between groups.
**Significant difference between acquisition block 1 (baseline) and block 1 at 48 hr retention and block 1 at 1 wk retention.
#Significant difference between acquisition block 1 and 7.

variability: PD = 26.40, AM = 6.80, HY = 4.20 at block one of acquisition).

In this study we examined a concurrently performed postural control task and a speech task using a classic motor learning paradigm [23, 24]. The postural control and speech tasks were chosen because of their limited response to pharmacological treatment [17, 18]. Given the limitations of pharmacological treatments, behavioural interventions such as practice may be the most promising means of improving postural control and speech in individuals with PD. However, since deficits in motor learning in individuals with PD or with basal ganglia lesions may be due to limited amount of practice [32], by limiting the number of practice trials, we introduced a commonly utilized practice dosage to the research design. We theorized that the bidirectional interference [11] that occurs between concurrently performed tasks would confound any differences in motor learning between the groups. The lack of consistent changes in motor performance in any of the postural tasks, except in the HY group, suggests a decreased efficiency of motor learning in the AM and PD groups and would suggest that additional amount of practice may be necessary. While previous research has utilized differing motor tasks and practice paradigms and typically examines the single-task performance [33–35], our results add evidence to the theory that a deficit in the retention of motor skill may necessitate additional amounts of practice [4, 36].

Table 3: Articulatory acoustic measures for /ɔɪ/ diphthong at acquisition and retention phases for each group.

	Acquisition (Baseline) Block 1 mean (SD)	Acquisition (Ending) Block 7 mean (SD)	Retention 48 hrs Block 1 mean (SD)	Retention 1 week Block 1 mean (SD)
/ɔɪ/ duration (sec)				
HY group	0.11 (0.03)	0.09 (0.04)	0.10 (0.03)	0.10 (0.03)
AM group	0.11 (0.05)	0.11 (0.04)	0.11 (0.04)	0.11 (0.04)
PD group	0.12 (0.03)	0.11 (0.02)	0.12 (0.02)	0.12 (0.03)
/ɔɪ/ F1 ext (Hz)				
HY group	87.17 (60.83)	66.83 (84.08)	63.17 (44.42)	56.83 (77.75)
AM group	108.66 (66.39)	75.67 (45.25)	61.67 (77.00)	59.00 (68.50)
PD group	78.67 (80.83)	74.16 (48.33)	44.50 (56.12)	47.67 (24.67)
/ɔɪ/ F2 ext (Hz)				
HY group	1066.00 (404.83)	938.17 (331.63)	997.33 (332.00)	915.00 (404.08)
AM group	1062.67 (302.67)	966.33 (248.08)	967.33 (273.92)	914.67 (231.17)
PD group	859.67 (219.00)	807.67 (290.00)	864.67 (268.33)	810.00 (308.17)
/ɔɪ/ F1 slope (Hz/ms)				
HY group	−0.78 (0.46)	−0.80 (1.01)	−0.67 (0.52)	−0.65 (1.12)
AM group	−0.89 (1.34)	−0.70 (0.68)	−0.49 (1.20)	−0.76 (1.14)
PD group	−0.68 (0.96)	−0.70 (0.47)	−0.30 (0.70)	−0.39 (0.63)
/ɔɪ/ F2 slope (Hz/ms)				
HY group	9.72 (3.20)	9.96 (4.22)	10.77 (4.58)	9.65 (4.93)
AM group	11.19 (6.16)	9.64 (4.68)	10.13 (4.79)	10.96 (3.76)
PD group	7.11 (2.62)*	7.41 (2.67)	6.96 (1.04)	6.44 (3.46)

HY group: healthy young adult controls; AM group: healthy age-matched controls; PD group: persons with PD.
All values: median (interquartile range).
*Significant difference between groups.

4.2. Task Difficulty. Although the HY group demonstrated improvements in postural coordination and postural stability as a result of practice, consistent changes in speech task performance in any group as a result of practice were lacking. One potential reason for this was that the stereotyped speaking tasks that were used in this study utilized well-practiced words for primary English speakers. Because our measures of speech performance came from sentence production, the extensive familiarity the subjects had with these words likely limited our ability to observe any practice-related improvement [37]. Another potential reason for the lack of practice-related change in speech performance is that due to the acute consequences of falls, participants chose to prioritize postural stability over speaking. This lack of attention to a nonprimary task could have diminished any practice-related improvements. However, our previous research using these tasks suggests that in the absence of explicit instructions for prioritization, there appears to be bidirectional interference on both tasks [11]. That is, performance of both tasks at the same time resulted in concurrent performance deficits compared to individual performances of each task [38, 39].

4.3. Limitations and Directions for Future Research. While these results suggest that practice dosages for motor learning may need to be different for persons with PD or advanced age, they should be interpreted with caution. Based on our research design, type I and type II statistical errors are possible. Because of the exploratory nature of this project, we did not perform corrections for multiple comparisons. Although our sample size was calculated using a priori power calculations, the effect sizes calculated from this data were smaller than those that we used and therefore we cannot ruleout type II statistical errors. These smaller effect sizes suggest that dual tasking may reduce the practice effect on skill acquisition and imply that future studies will need to employ design features to address this effect (increased practice, larger samples). In addition, for the sake of internal validity, the tasks used were constrained measurements of postural and inferred vocal tract movement that were used for both practice and testing. Our selected speaking task may not have been challenging enough to reveal practice-mediated improvements in articulatory acoustic measures. Lastly, formal cognitive testing was not performed to assess learning abilities. Future research should include a larger number of subjects, utilize retention and transfer tasks, perform formal cognitive testing, and examine varied dosages of practice to elucidate the adequate dosage of practice to induce lasting changes in postural and speech task performance in both persons with PD and neurologically healthy elders.

5. Conclusion

When asked to perform dual-task practice of postural motor and speaking tasks, persons with PD and neurologically

healthy age-matched controls were unable to improve their performance during the acquisition phase or the retention phases. In contrast, when exposed to the same practice dosage, neurologically healthy young participants improved and retained improved postural stability over a one-week period.

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Clinical Study

Predictors of Gait Speeds and the Relationship of Gait Speeds to Falls in Men and Women with Parkinson Disease

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Gait difficulties and falls are commonly reported in people with Parkinson disease (PD). Reduction in gait speed is a major characteristic of Parkinsonian gait, yet little is known about its underlying determinants, its ability to reflect an internal reservation about walking, or its relationship to falls. To study these issues, we selected age, disease severity, and nonmotor factors (i.e., depression, quality of life, balance confidence, and exercise beliefs and attitudes) to predict self-selected (SELF), fast-as-possible (FAST), and the difference (DIFF) between these walking speeds in 78 individuals with PD. We also examined gender differences in gait speeds and evaluated how gait speeds were related to a retrospective fall report. Age, disease severity, and balance confidence were strong predictors of SELF, FAST, and, to a lesser extent, DIFF. All three parameters were strongly associated with falling. DIFF was significantly greater in men compared to women and was significantly associated with male but not female fallers. The results supported the clinical utility of using a suite of gait speed parameters to provide insight into the gait difficulties and differentiating between fallers in people with PD.

1. Introduction

Gait difficulties are one of the first problems reported in people with PD, indicating the onset of disability [1]. Parkinsonian gait is often slow and characterized by short shuffling steps, which may contribute to postural instability. As such, problems with walking are often accompanied by falling, which occurs in 40–70% of people with PD [2]. Fallers have higher incidences of skeletal fracture, social isolation, and reduction in exercise [3]. These consequences of a fall can in turn contribute to declines in gait and balance and lead to an additional increased risk of falling. Understanding these difficulties and developing criteria to identify people with PD who are at risk for falling are crucial to interrupt this devastating cycle of falls and injuries.

Complex gait analyses use 3-dimensional kinematics to quantify the biomechanical and rhythmic impairments of gait in people with PD [4, 5]. These evaluations require sophisticated equipment and require higher level analysis. Within clinical settings, therapists currently use objective balance rating scales to measure gait and balance because they assess a wide range of postural and balance characteristics, are highly reproducible and predictive of falls [6]. However, clinical balance scales require trained raters and can be time consuming. As an alternative to the above methods, gait speed is a simple measurement to assess gait function and

perhaps fall risk, in people with PD. Furthermore, gait speed can be easily obtained with only a measuring tape and stopwatch.

Self-selected gait speed (SELF) of people with PD has been associated with disability level (UPDRS) [7] as well as nonmotor characteristics, such as age and executive attention [8]. However, limited data is available to show which (and to what extent) nonmotor factors are associated with gait speeds. SELF was found to be both weakly [9] and moderately [10] correlated with Part II of the UPDRS, which assesses activities of daily living (ADL). Elbers et al. also showed that anxiety, depression, and reduced motivation were associated with community walking in 153 individuals with PD cohort [11]. These results suggest that gait may be in part determined by nonmotor behavior, such as lack of confidence about walking, depression, quality of life, or general aversive attitudes about activity.

Fast-as-possible gait speed (FAST) is important to consider because, when compared to SELF, it measures one's ability to adapt gait speed to environmental demands [12]. However, it has not been studied frequently, mainly because it correlates with age and disease severity to a similar extent as comfortable gait speed [10, 13]. We believe that a third gait speed, DIFF (i.e., the difference between FAST and SELF), may uniquely provide insight into an individual's willingness and ability to change gait speed. Presumably, DIFF could be influenced by nonmotor factors, such as depression, quality of life, balance confidence, and/or exercise beliefs and attitudes. Thus, our first aim was to identify the predictors of three gait speeds SELF, FAST, and DIFF. We postulated that SELF and FAST would be best predicted by age and MDS-UPDRS, while DIFF would be better predicted by nonmotor factors.

SELF has further been studied as an important indicator of community ambulation [11] and fall risk [14] in people with PD. In the latter study, Paul et al. developed a powerful three-variable model which included self-selected gait speed to predict fallers with PD [14]. However, to our knowledge, no one has similarly shown how FAST and DIFF gait speed parameters are related to falling. The second aim of this work, therefore, was to assess the relationship between SELF, FAST, and DIFF gait speeds and fall history in individuals with PD. We hypothesized that, in comparison to SELF and FAST, DIFF would be a better discriminator between fallers and nonfallers because of its potential to reflect the ability to adapt walking speed to changes in environmental demands that could precipitate a fall.

2. Materials and Methods

2.1. Participants. Of 81 participants, full data sets from 78 individuals with "idiopathic" PD [15], recruited from the Washington University Movement Disorders Clinic, were analyzed. All participants were greater than 40 years of age, had a confirmed diagnosis of idiopathic PD from a neurologist, and were at a Hoehn and Yahr (H&Y) stage [16] between 1 and 4. Participants were included/excluded based on criteria defined previously [17]. All evaluations were performed during a single two-hour period during the "on" state, which was 1-2 hours after the administration of levodopa medication. Participants provided written consent after being screened for eligibility. This study was approved by the Human Research Protection Office at Washington University.

2.2. Clinical Evaluations and Questionnaires. All data were collected by a single assessor as part of a larger longitudinal study to monitor the outcomes of a cohort of people with PD [17]. Demographic information and medical history were obtained from each participant at the beginning of evaluation, including age, disease duration, medications, fall history, and exercise history. The full, revised Unified Parkinson's Disease Rating Scale (MDS-UPDRS) was administered to assess overall disease severity. Participants completed a battery of surveys and questionnaires during their visit. The Geriatric Depression Scale (GDS) was used to evaluate participants' emotional state and the Parkinson Disease Questionnaire-39 (PDQ-39) was used to indicate overall quality of life; high scores for the GDS are associated with greater levels of depression while high scores for the PDQ-39 reflect poorer quality of life. These two surveys have previously been validated in PD [18] and elderly adults [19]. To quantify balance confidence, participants completed the Activities and Balance Confidence (ABC) scale, a 16-point questionnaire in which participants are asked about their balance confidence during certain activities [20]; high scores indicate greater balance confidence. Finally, participants answered several questionnaires regarding their attitudes and beliefs about exercise, including confidence about ability to maintain an exercise program (CONF), exercise control beliefs (BEL) [21], and the self-efficacy for exercise scale (EFFIC) [22]. High scores are associated with greater confidence about exercise programs (CONF), more negative beliefs about exercise (BEL), and positive exercise self-efficacy (EFFIC).

Outcome variables, which included SELF, FAST, and DIFF (i.e., FAST-SELF), were calculated based upon timed 10-meter walks on a straight path. For each walk, participants were given a 2-meter initiation and termination phase for a total walking distance of 14 meters; walking speed was measured for the 10-meter distance between the initiation and termination phases. For SELF, participants were instructed to walk at a comfortable pace after "Ready" and "Go" cues. For FAST, participants were told to walk as quickly and safely as possible after "Ready" and "Go" cues. Participants always started with SELF and performed one trial at each speed. Gait speeds were normalized for subject height [23]. We performed analyses on both normalized and raw gait speeds and were met with similar results. As such, normalized gait speeds were used for all subsequent analyses.

2.3. Regression Model Selection. To determine the significant predictors of SELF, FAST, and DIFF gait speeds, we used block-entry linear regression. Potential variables for inclusion in the regression were first determined using bivariate analyses. A variable was removed from consideration in the regression analysis if its Pearson correlation coefficient with any of SELF, FAST, or DIFF gait speed was less than 0.25. This cut-off criterion ensured that each variable would explain

a minimum of 6% of the variability in gait speed, not accounting for collinearity. After filtering out unrelated variables, we ensured that all measures were not different between men and women. For variables in which there were differences between men and women (DIFF, see Results), a separate gender-stratified regression model was developed. All predictor variables were rescreened for this model using a bivariate coefficient cutoff of 0.35 (to account for reduction in the sample size).

After filtering variables with low correlation to gait speeds, we constructed the models using a hybrid approach. *A priori* predictors age, and MDS-UPDRS were selected first based on previous reports describing the relationships between gait performance, age and disease severity [10, 24, 25]. The entire MDS-UPDRS score (sum of all four subscales) was used because it includes motor and nonmotor aspects of the disease as well as activities of daily living and motor complications. Our hypothesis-driven predictors included ABC, GDS, PDQ, and three exercise-attitude scales (BEL, CONF, and EFFIC).

Table 1 defines the blocks and included variables for each regression model predicting SELF, FAST, and DIFF. We grouped predictors into the following blocks: (1) age, (2) disease severity (MDS-UPDRS); (3) balance confidence (ABC); (4) quality of life/mood (PDQ-39 and GDS); (5) attitudes about exercise (CONF, BEL, and EFFIC). The blocks for the stratified analysis of DIFF were as follows: (1) disease severity (MDS-UPDRS); (2) balance confidence (ABC), (3) quality of life (GDS and PDQ), and (4) attitudes about exercise (BEL). Age, CONF, and EFFIC were not included in the gender-stratified DIFF model because they did not meet the inclusion criterion ($r > 0.35$) for both men and women. We evaluated each model based on the adjusted R^2 change and the change in overall model F statistic after the addition of each block and by the statistically significant predictors in the final model.

Table 1: Regression model specification.

Block	Predictor variable(s)	Outcome variable(s)
(1) Age	Age	SELF, FAST, DIFF
(2) Disease severity	MDS-UPDRS	SELF, FAST, DIFF
(3) Balance confidence	ABC	SELF, FAST, DIFF
(4) Mood/quality of life	GDS PDQ	SELF, FAST, DIFF
(5) Attitudes about exercise	BEL CONF EFFIC	SELF, FAST, DIFF
(1) Disease severity	MDS-UPDRS	DIFF M/F
(2) Balance confidence	ABC	DIFF M/F
(3) Mood/quality of life	GDS PDQ	DIFF M/F
(4) Attitudes about exercise	BEL	DIFF M/F

2.4. ROC Analyses. To determine if gait speed could discriminate among fallers in our sample, we generated receiver operator characteristic (ROC) curves and calculated area under the curve (AUC), cut-off scores, sensitivity, specificity, and likelihood ratios (see [26]) for SELF, FAST, and DIFF speeds, and also for DIFF separately in men and women. Cut-off scores were calculated by:

$$\frac{\ln\left(p/\left(1-p\right)\right)-a}{B} * h, \tag{1}$$

where p is the probability of falling associated with the maximum sensitivity and specificity; a is the intercept coefficient from the logistic regression of normalized gait speed to predict falling; B is coefficient of regression; and h is the mean height (m). Fall data were taken from a questionnaire inquiring how often the participant had fallen in the past 6 months. A fall was described as an unexpected event in which any part of the body contacted the ground [27, 28]. Fallers were defined as those who fell two or more times over the past 6 months as assessed via self-report. As such, in our study, fallers were categorized as recurrent fallers. This criterion ensured that we could distinguish actual fallers who have significant gait and balance impairment from those who fell randomly [29].

All statistical analyses were performed using SPSS version 20 (IBM, Chicago, IL, USA). Differences in variables between genders were determined using independent sample t-tests or Mann-Whitney U tests for categorical or nonnormally distributed data. The level of significance was set at $\alpha = 0.05$ unless otherwise noted.

3. Results

Participant demographics and experimental variables are shown in Table 2 for men, women, and the total sample. The average SELF gait speed was 1.10 m/s, while the average fast-as-possible gait speed was 1.53 m/s. DIFF was significantly greater in men compared to women (0.51 ± 0.28 m/s versus 0.32 ± 0.18 m/s; independent sample t-test; $P < 0.001$) after controlling for height differences. All other measures were not different between men and women.

Table 3 summarizes the regression model predicting SELF, FAST, and DIFF gait speeds in the total sample. The model was able to predict 51.9% and 54.1% of the variation in SELF and FAST, respectively, while the same model only accounted for 20.2% of the variability in DIFF. Blocks 1–3 (age, disease severity, and balance confidence) were significant contributors to the model predicting SELF and DIFF, while all except block 5 (attitudes about exercise) made significant contributions in explaining FAST. Despite the overall model potency, only age and ABC were significant predictors of SELF and FAST after accounting for all other variables. There were no significant regressors in the final model of DIFF.

After noting gender differences in DIFF, we created a separate model to describe DIFF in men and in women. Table 4 shows the model results for DIFF in men and women using four blocks. Overall, the model accounted for 20.7%

Table 2: Participant demographics and experimental variables.

Characteristic (scale)	Total	Males	Females	P (M versus F)
Sex, N	78	45	33	—
Age, yr	68.18 ± 9.35 (45, 88)	67.84 ± 8.84 (48, 88)	68.63 ± 10.12 (45, 85)	0.714
Disease duration, yr	8.50 ± 4.88 (0, 25)	8.82 ± 5.33 (0, 25)	8.06 ± 4.22 (1, 20)	0.499
Fallers, N (% total)	25 (32%)	16 (36%)	9 (27%)	0.439[d]
MDS-UPDRS (0–260)	72.96 ± 24.99 (25, 135)	74.78 ± 26.71 (26, 131)	70.48 ± 22.60 (25, 135)	0.457
MDS-UPDRS-III (0–132)	41.52 ± 14.77 (9, 83)	43.02 ± 14.30 (17, 70)	39.48 ± 15.37 (9, 83)	0.299
H&Y[a] (0–5)	2.50 (0.63)	2.50 (0.5)	2.50 (1.0)	0.473[c]
FOGQ (0–24)	6.97 ± 5.85 (0, 20)	6.78 ± 5.82 (0, 20)	7.24 ± 5.97 (0, 19)	0.731
GDS (0–30)	8.47 ± 6.28 (0, 24)	8.87 ± 6.42 (0, 24)	7.93 ± 6.15 (0, 24)	0.523
PDQ-39 (0–100)	22.83 ± 13.72 (0.52, 63.13)	22.05 ± 15.00 (0.52, 66.13)	23.91 ± 11.90 (2.86, 51.77)	0.558
FGA (0–30)	18.41 ± 7.10 (0, 29)	19.29 ± 6.99 (4, 29)	17.21 ± 7.20 (0, 29)	0.204
ABC (0–100)	68.27 ± 25.01 (16, 100)	72.51 ± 23.87 (17, 100)	62.48 ± 25.73 (16, 100)	0.08
BEL (0–25)	8.19 ± 2.96 (5, 16)	8.22 ± 3.14 (5, 16)	8.15 ± 2.74 (5, 15)	0.838[c]
CONF (0–40)	28.21 ± 8.66 (8, 40)	29.71 ± 7.90 (8, 40)	26.18 ± 9.35 (9, 40)	0.08[c]
EFFIC (0–10)	5.48 ± 2.26 (0.33, 9.44)	5.62 ± 2.38 (0.78, 9.44)	5.30 ± 2.12 (0.33, 8.89)	0.536
SELF, m/s	1.10 ± 0.29 (0.37, 1.66)	1.15 ± 0.29 (0.49, 1.67)	1.04 ± 0.29 (0.37, 1.44)	0.822[b]
FAST, m/s	1.53 ± 0.47 (0.54, 2.80)	1.66 ± 0.49 (0.67, 2.80)	1.36 ± 0.40 (0.54, 2.18)	0.104[b]
DIFF, m/s	0.43 ± 0.26 (−0.05, 1.27)	0.51 ± 0.28 (0.04, 1.27)	0.32 ± 0.18 (−0.05, 0.74)	**0.008**[b]

[a]Data presented as median (IQR).

[b]P values represent differences in normalized gait speed.

[c]Mann-Whitney U test; [d]Chi-square test.

All other data presented as mean ± SD (Min, Max).

Gender differences were determined by independent samples t-test unless otherwise noted.

MDS-UPDRS: Movement Disorder Society Unified Parkinson Disease Rating Scale; H&Y: Hoehn and Yahr stage; FOGQ: Freezing of Gait Questionnaire; GDS: Geriatric Depression Scale; PDQ-30: Parkinson Disease Questionnaire-39; FGA: Functional Gait Assessment; ABC: Activities and Balance Confidence Scale; BEL: Beliefs about control over one's exercise behavior; CONF: confidence about maintaining an exercise program; EFFIC: self-efficacy exercise scale; SELF: self-selected gait speed; FAST: fast-as-possible gait speed; DIFF: difference between FAST and SELF.

of the variability in men's DIFF walking speed. Block 1 (disease severity) was a significant contributor while block 3 (mood/quality of life) was marginally significant ($P = 0.066$). For women, only block 1 (disease severity) was a significant block ($P = 0.012$). Overall, 15.8% of the variability in DIFF walking speed was explained by the model for females, which was not significantly different ($P = 0.084$) from the null model, that is, a model without any predictor variables. Moreover, the addition of block 3 (mood/quality of life) reduced the potency of the model, as shown in the relatively large and negative change in R^2.

To determine the value of gait speed alone to discriminate among fallers and nonfallers, we generated ROC curves (Figure 1) for SELF, FAST, and DIFF in the total sample. Table 5 shows the AUC, cut-off score, sensitivity, specificity, and likelihood ratios associated with each test. SELF ($P < 0.001$), FAST ($P < 0.001$), and DIFF ($P = 0.004$) were all significantly associated with fallers in the total sample, according to the AUC. Due to the aforementioned gender differences, we further investigated if DIFF was a better predictor of fallers in men or women (Figure 1). DIFF was a strong predictor of male fallers (AUC = 0.806, $P = 0.001$; sensitivity = 0.828; specificity = 0.813) but a relatively weaker predictor of female fallers (AUC = 0.569, $P = 0.544$; sensitivity = 0.667; specificity = 0.583).

4. Discussion

In this work, we identified significant non-gait-related predictors of comfortable, fast-as-possible, and the difference between these walking speeds in individuals with PD. We showed that age, disease severity, and balance confidence were significantly related to all three gait speeds. Furthermore, we showed how gait speeds were significantly associated with a history of falls in the past 6 months. Gender-stratified analyses indicated that DIFF was well explained by disease severity and in part by mood/quality of life in men, but not in women.

We determined that age, disease severity (i.e., MDS-UPDRS), and balance confidence (i.e., ABC) were important predictors of SELF, FAST, and DIFF gait speeds. When considering both genders together, our data expanded upon previous research [7, 8] identifying age and disease severity not only as predictors of SELF, but also as predictors of FAST and DIFF. In addition, although we had hypothesized that non-motor factors (e.g., low balance confidence) would influence DIFF, our data suggested that balance confidence is significantly related to overall gait performance in people with PD. This finding was in agreement with other studies examining the relationship between ABC and gait [30, 31] but was not surprising, given that several items on the ABC pertain to everyday gait activities such as walking around the house.

Table 3: Regression model results for SELF, FAST, and DIFF walking speeds.

Block	Variable	B_{unstd}	B_{std}	P	R^2 change	P (block)
			SELF			
1	Age	−0.005	−0.277	**0.004**	0.189	<**0.001**
2	UPDRS	0.001	0.016	0.906	0.18	<**0.001**
3	ABC	0.003	0.448	**0.001**	0.155	<**0.001**
4	GDS	−0.002	−0.092	0.411	0.002	0.328
	PDQ-39	−0.002	−0.146	0.349		
5	CONF	0.003	0.144	0.228	−0.007	0.565
	BEL	0.001	0.021	0.851		
	EFFIC	−0.009	−0.117	0.258		
					Total $R^2 = 0.519^{**}$	
			FAST			
1	Age	−0.008	−0.288	**0.002**	0.179	<**0.001**
2	UPDRS	0.001	0.083	0.529	0.184	<**0.001**
3	ABC	0.004	0.342	**0.009**	0.146	<**0.001**
4	GDS	−0.004	−0.085	0.438	0.035	**0.026**
	PDQ-39	−0.005	−0.283	0.065		
5	CONF	0.004	0.124	0.286	−0.003	0.478
	BEL	−0.006	−0.063	0.554		
	EFFIC	−0.009	−0.079	0.430		
					Total $R^2 = 0.541^{**}$	
			DIFF			
1	Age	−0.003	−0.196	0.109	0.057	**0.02**
2	UPDRS	0.001	0.129	0.458	0.07	**0.01**
3	ABC	0.001	0.098	0.564	0.045	**0.028**
4	GDS	−0.001	−0.046	0.750	0.042	0.058
	PDQ-39	−0.004	−0.336	0.095		
5	CONF	0.001	0.057	0.710	−0.012	0.584
	BEL	−0.007	−0.136	0.337		
	EFFIC	−0.001	−0.008	0.951		
					Total $R^2 = 0.202^{*}$	

$^{**}P < 0.001$, $^{*}P < 0.05$ overall model is significant.
B_{unstd}: unstandardized coefficient; B_{std}: standardized coefficient.

Table 4: Regression model results for DIFF in men and women.

Block	Variable	B_{unstd}	B_{std}	P	R^2 change	P (block)
			Men			
1	UPDRS	−0.001	−0.086	0.722	0.143	**0.006**
2	ABC	−0.001	−0.147	0.557	−0.016	0.635
3	GDS	−0.005	−0.184	0.411	0.073	0.066
	PDQ	−0.003	−0.296	0.265		
4	BEL	−0.010	−0.196	0.253	0.007	0.253
					Total $R^2 = 0.207^{*}$	
			Women			
1	UPDRS	−0.001	−0.254	0.366	0.162	**0.012**
2	ABC	0.001	0.279	0.271	0.045	0.107
3	GDS	0.001	0.006	0.974	−0.055	0.978
	PDQ	0.001	0.068	0.832		
4	BEL	−0.008	−0.197	0.285	0.006	0.285
					Total $R^2 = 0.158$	

$^{*}P < 0.05$ overall model is significant.
B_{unstd}: unstandardized coefficient; B_{std}: standardized coefficient.

Our model was able to explain about 2.5 times more variability in SELF and FAST compared to DIFF, indicating that DIFF may not be as clinically useful compared to SELF and FAST when assessing people with PD. Blocks 3–5 (ABC, mood/quality of life, attitudes about exercise) only contributed an additional 0.075 to the R^2 value in the DIFF model after controlling for age and disease severity, compared to 0.15 and 0.178 R^2 increases for the SELF and FAST models, respectively. It is possible that DIFF was actually measuring disease severity, meaning that lower DIFF represented a physical inability to increase speed, rather than a lack of internal drive. However, DIFF was weakly correlated with UPDRS scores ($r = -0.365$) compared to SELF ($r = -0.575$) or FAST ($r = -0.574$). Alternatively, some of the variance in DIFF could have resulted from an unidentified interaction of two or more variables, which if it occurred, would confound the relationship between nonmotor behavior and change in gait speed. Interestingly, the block representing mood/quality of life significantly contributed to the variation in FAST but not SELF gait speed (Block 4, Table 3); that is, those who have a greater maximum gait speed may have better mood and quality of life. We were limited in our ability to interpret this finding because we used the total PDQ-39 summary score and did not analyze each subsection (emotion, cognition, stigma, etc.). The scores of a certain sub-section may in fact have driven the differences, but subsection analysis was beyond the scope of this paper. Overall, the regression models did not reveal a major distinction in the characteristics of an individual based on his/her SELF and FAST walking speed. Future work should consider longitudinal analyses of gait speed given that gait speed predicts declines in attention and psychomotor abilities over time in older adults [32].

Research focusing on identifying fallers and predicting falls is important in order to reduce injury and prevent future falls in PD. Many groups have used a variety of gait and balance characteristics to predict fallers with much success [33–36]. Here we showed that, by themselves, SELF, FAST, and DIFF (in men only) were strongly associated with falling in people with PD. This finding is in contrast to Duncan and Earhart [37], who determined that SELF and FAST gait speeds were poor predictors of falling in a PD cohort compared to balance assessments. One major distinction between that

Table 5: AUC, specificity, sensitivity, and LR for ROC curve analyses of gait speeds.

Measure	AUC (95% CI)	Cut-off score (m/s)	Sensitivity	Specificity	LR+ (95% CI)	LR− (95% CI)
SELF	0.803 (0.704, 0.902)	0.980	0.800	0.717	2.827 (1.765, 4.528)	0.279 (0.125, 0.622)
FAST	0.811 (0.707, 0.916)	1.326	0.840	0.755	3.429 (2.072, 5.659)	0.212 (0.085, 0.527)
DIFF	0.703 (0.581, 0.826)	0.226	0.720	0.642	2.011 (1.300, 3.104)	0.436 (0.226, 0.845)
DIFF (male)	0.806 (0.659, 0.953)	0.356	0.813	0.828	4.727 (2.052, 10.822)	0.226 (0.806, 0.637)
DIFF (female)	0.569 (0.356, 0.783)	−0.067	0.667	0.583	1.600 (0.826, 3.100)	0.571 (0.214, 1.529)

work and the present study is that Duncan and Earhart measured participants off medication. We assessed participants on medication, which has been shown to improve self-selected gait speeds [38, 39]. Given that people are normally medicated during daily activities, assessments conducted on medication may be better at predicting fallers compared to off-medication assessments. In any case, our AUC values from SELF and FAST speeds were comparable to other balance and gait measures for fall prediction [34, 35].

Our ROC results were in line with Paul et al., who determined a self-selected gait speed cutoff of 1.1 m/s to help predict future fall risk [14]. Our cut-off value (0.98 m/s) was slightly more stringent. Despite this minor difference, together these findings supported the use of gait speed for screenings to predict future fallers. These screenings would complement existing evaluation tools such as multi-item balance assessments and 3-dimensional gait kinematics. Balance assessments require trained raters and longer evaluation times, while kinematic measurements need sophisticated equipment and analysis techniques [4, 5]. In contrast, gait speed can be quickly and accurately measured in any setting with only a stop-watch and measuring tape and a minimally trained rater.

Our data indicated that men increased their gait speed from SELF to FAST more than women, even when corrected for height. Consequently, we evaluated DIFF in men and women using a second hierarchal regression model and also determined if this speed differentially predicted falls in men and women. Our model explained only 5% more variability in DIFF in men compared to women. This marginal distinction between genders was primarily due to a 7% change from block 2 to 3, showing a contribution from the block representing mood/quality of life in men (Table 4). However, DIFF accurately identified male but not female fallers. This result lends some support for the value of DIFF when assessing male PD patients. However, DIFF does not provide additional information over SELF or FAST to predict male fallers, and thus its value in screening is not clear. While some work has investigated gender differences in PD disease severity and motor symptoms [40, 41], to date no one has shown any gait-related gender differences. Additional studies examining gender differences in gait characteristics may help define the relationship between gait speed and falling.

There are several limitations of our work that should be addressed. First, we examined this sample at only one time point, which may limit the relationships between gait speed, disease severity, and nonmotor behavior. A longitudinal analysis would allow us to detect individual changes in these variables over time and may help reduce intrasubject variability. Furthermore, we did not randomize the order of SELF and FAST which may have induced a priming effect on FAST speeds. Secondly, in our model selection, we tried to choose both statistically relevant and sensible predictors of gait speed. In doing so, we did not include terms that, while not significantly correlated with gait speed, may have added to our overall model potency. To add, many predictor variables were highly intercorrelated, and while our collinearity diagnostics for either model returned no major concerns, this may have influenced individual predictor strength and final model interpretation. Finally, we collected fall data via subject recall. Hannan et al. showed that older individuals may underestimate how many times they fell in the last three months when measured with self-report compared to tracking falls with a calendar [42]. As such, our study may

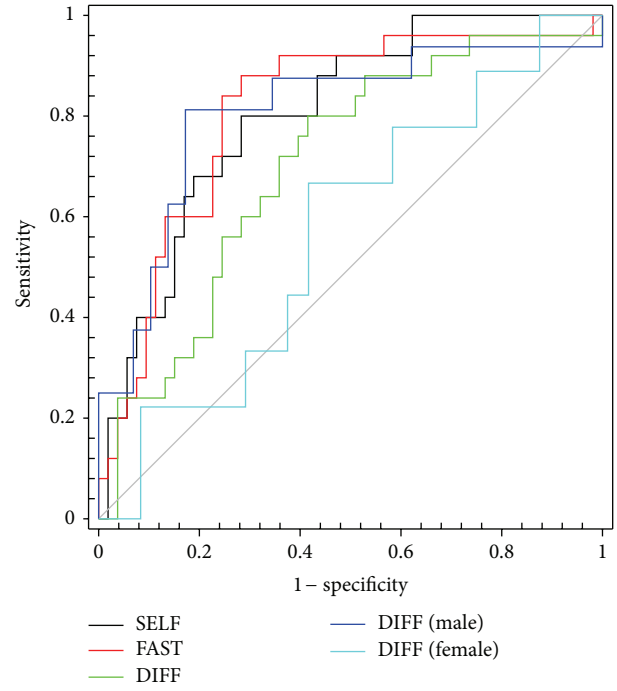

Figure 1: ROC curves for SELF (black), FAST (red), and DIFF (green) predicting fallers in the total sample. DIFF was also used to predict fallers, respectively, in men (blue) and women (cyan). SELF and FAST were strong predictors of fallers in the pooled sample. DIFF was a strong predictor of fallers in men but not women (see Table 5 for AUC, sensitivity, and specificity values).

have lacked sufficient power to discriminate fallers from nonfallers.

5. Conclusion

Using a blockwise linear regression model, we identified age, disease severity, and balance confidence to be strong predictors of comfortable and fast-as-possible gait speeds in a cohort of people with PD. SELF and FAST were also significantly related to fallers in our total sample, illustrating the potential utility of including gait speed as a screening measure for individuals with fall risk. The difference between SELF and FAST gait speeds was not well described by nonmotor behavior in the total sample. However, mean DIFF speed was larger and more associated with fallers in men than in women, suggesting that it may be a more informative measure in men.

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Clinical Study

Short- and Long-Term Efficacy of Intensive Rehabilitation Treatment on Balance and Gait in Parkinsonian Patients: A Preliminary Study with a 1-Year Followup

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Parkinson's disease (PD) is a neurodegenerative disease in which gait and balance disturbances are relevant symptoms that respond poorly to pharmacological treatment. The aim of this study was to investigate whether a 4-week inpatient multidisciplinary intensive rehabilitation treatment (MIRT) is effective in improving balance and gait and whether improvements persist at a one-year followup. We studied 20 PD inpatients (stage 3 Hoehn-Yahr) who underwent a MIRT. Outcome measures were UPDRS items for balance (30), falls (13), and walk (29), Berg Balance Scale, six-minute walking test, Timed Up and Go Test, and Comfortable-Fast gait speeds. Patients were evaluated at admission, at the end of the 4-week treatment, and at a 1-year followup. Pharmacological therapy was unchanged during MIRT and follow-up. All outcome measures improved significantly at the end of treatment. At 1-year follow-up control, UPDRS walk and Comfortable-Fast gait speeds still maintained better values with respect to admission ($P = 0.009$, $P = 0.03$, and $P = 0.02$, resp.), while the remaining scales did not differ significantly. Our results demonstrate that the MIRT was effective in improving balance and gait and that the improvement in gait performances was partially maintained also after 1 year.

1. Introduction

Parkinson's disease (PD) is a neurodegenerative disorder characterized by different motor symptoms (rigidity, akinesia, tremor, and impairment of balance and gait). Even though pharmacological treatment has changed the natural course of disease, gait and balance worsen over time and these disturbances progressively lead to major disability [1, 2].

Postural instability leads to falls: PD subjects often fall because they respond to a sudden loss of balance with abnormally short steps that are inadequate to recover equilibrium [3, 4].

Moreover, Parkinsonian patients present continuous gait disturbances (shorter stride length, reduced gait speed, increased variability of stride, and increased double support time) that, often associated with freezing and festination, lead to frequent falls [5, 6].

In the last five years, several studies have shown that physiotherapy strategies, including cueing techniques, treadmill training, and cognitive movement strategies, are useful in improving balance and gait in PD patients [7–10].

However, whether the effects of the rehabilitation on gait and balance persist over time and what the optimal content

of exercise intervention is (the kind of exercises, the intensity, and the duration of treatment) remain open questions [11].

It has been recently hypothesized that the best approach to rehabilitation in Parkinson disease is a multidisciplinary treatment [12].

There are very few multidisciplinary approaches in rehabilitation of Parkinson disease [13, 14].

Gait and balance disorders have a multifactorial aetiology and a multidisciplinary approach which might be more effective for the different components responsible for these symptoms.

In this context, we developed a 4-week inpatient multidisciplinary intensive rehabilitation treatment (MIRT) in which standard physical therapy techniques were associated with treadmill with auditory and visual cues (treadmill plus) and a stabilometric platform.

The present study was devised: (a) to test whether our protocol is effective in improving balance and gait during supervised multidisciplinary treatment; and (b) to verify whether improvements persist after one year of unsupervised treatment.

2. Methods

We enrolled 20 patients (7 males and 13 females) (Table 1) with a diagnosis of "clinically probable" idiopathic PD according to Gelb et al. [15], in Hoehn-Yahr stage 3, with the ability to walk without any assistance, who had fallen in the last year at least 2 times, with mini-mental state examination score ≥26, without any relevant comorbidity or vestibular/visual dysfunctions limiting locomotion or balance, and who had been assuming stable dopaminergic therapy in the last 4 weeks. patients were screened by a neurologist specialized in movement disorders, and eligible patients were admitted to the Rehabilitation Institute, for a 4-week rehabilitation treatment. The study was approved by the local Scientific Committee and Institutional Review Board (Fondazione S. Maugeri, IRCCS, Istituto Scientifico di Montescano). Written informed consent was obtained from all patients before participation.

The outcome measures were the Unified Parkinson's Disease Rating Scale (UPDRS) [16] items for balance and falls (UPDRS_30 and UPDRS_13, resp.) and the Berg Balance Scale (BBS) [17] for balance as well as the UPDRS items for walk (UPDRS_29), the six-minute walking test (6MWT) (the participant walked along a straight path), the Timed Up and Go Test (TUG), and the Comfortable (CGS) and Fast gait speeds (FGS) (10 meters straight path) for the gait [18, 19].

Patients were evaluated at the beginning and at the end of 4-week inpatient rehabilitation treatment and at a 1-year followup in the morning, one hour after the first dose of Levodopa, by a neurologist specialized in movement disorders, who was blinded to the study design.

2.1. Intervention. Patients were admitted to the Rehabilitation Institute where they underwent a MIRT: a 4-week cycle of physiotherapy that entailed three daily sessions (two in the morning and one in the afternoon, one hour each), 5 days a week. The MIRT involved different professionals: physiatrists, neurologists, physiotherapists, occupational therapists, nurses, psychologists, and nutritionists. The rehabilitation treatment was administered each day in different sessions. The first session comprised cardiovascular warm-up activities, relaxation exercises, muscle-stretching (scapular, hip flexor, hamstring, and gastrocnemius muscles), exercises to improve the range of motion of spinal, pelvic and scapular joints, and exercises to improve the functionality of abdominal muscles and postural changes in the supine position. The second session included exercises to improve balance and gait using a stabilometric platform with a visual cue and treadmill training associated with auditory and visual cues (treadmill plus). In brief, using the stabilometric platform, the patients were asked to follow a circular pathway on the screen by means of a cursor sensitive to the movements made by their feet on the platform. For treadmill training, the visual cue was a target, displayed on a screen, which the patient had to reach within a stride while the auditory cue consisted of musical beats, synchronized with the visual cues, with a frequency of 0.5 c/s [10]. All treadmill treatments were performed in an aerobic manner with a heart rate reserve ≤60% and a maximum speed of treadmill scrolling of 3.5 Km/h.

The last was an occupational therapy session with the aim of improving autonomy in daily living activities: transfers from sitting to standing, rolling from supine to sitting and from sitting to supine, dressing, use of tools, and exercises to improve hand functionality and skills (e.g., using screws and bolts). At the end of MIRT, the patients were instructed to continue a set of learned exercises in order to maintain functionality of the spine, scapular, and pelvic joints All patients received the same exercise program, that was part of the overall inpatient program. Patients were instructed to perform the exercises every day and to walk at least 30 minutes a day. The adherence to the exercise program and walking was not measured over this 11-month unsupervised period.

2.2. Sample Size Computation. Published studies report a standard error of measurement (SEM) equal to 30 m, 1.8, 0.59 s, 0.06 s, and 0.09 s for 6MWT, BBS, TUG, CGS, and FGS, respectively [20, 21]. We expected an effect size around 35 m, 4, 1.2 s, 0.12 s, and 0.15 s for the same variables. Hence, to detect a change with a two-tailed type I error of 0.05 and a power of 80%, the estimated sample size (the largest among all estimates) was 14 patients. We chose a conservative sample size of 20 patients.

2.3. Statistical Analysis. Descriptive statistics are given as mean ± SD. The Shapiro-Wilk statistic was used to test the normality of the distribution of all variables.

To investigate the primary and secondary end point, the time course of each functional variable considered was assessed by repeated measurements analysis of variance with three repeated measurements: admission, discharge, and 1-year followup. Pairwise comparisons (discharge versus admission and 1-year followup versus admission) were carried out by contrast analysis in repeated measurements analysis of variance. A P-value <0.05 was considered statistically

Table 1: Demographic data.

Age	Sex (M/F)	Years of disease	Hoehn-Yahr	UPDRS tot	UPDRS III	UPDRS II
71 ± 7	7/13	8.3 ± 2.1	3	34.74	18.18	14.48

Table 2: Functional characteristics of studied patients at admission, discharge, and at the 1-year followup.

	N	Admission	Discharge	*P*	1-year followup	*P*
UPDRS_13	20	0.7 ± 0.9	0.1 ± 0.4	0.012	0.7 ± 0.9	0.012
UPDRS_30	20	1.8 ± 0.5	1.1 ± 0.4	<0.0001	1.4 ± 0.6	0.77
BBS	20	45.1 ± 7.4	50.8 ± 6.8	<0.0001	45.4 ± 7.5	0.86
UPDRS_29	20	1.9 ± 0.9	1.1 ± 0.6	<0.0001	1.6 ± 0.9	0.009
sixMWT (m)	20	258.1 ± 86.1	322.7 ± 107.4	<0.0001	271.1 ± 82.5	0.098
TUG (s)	20	12.4 ± 3.0	9.6 ± 2.5	<0.0001	11.6 ± 2.8	0.31
CGS (m/s)	20	0.87 ± 0.18	1.00 ± 0.13	0.0002	0.96 ± 0.18	0.03
FGS (m/s)	20	1.07 ± 0.22	1.24 ± 0.19	0.0007	1.17 ± 0.20	0.02

significant. All analyses were carried out using the SAS/STAT statistical package, release 9.2 (SAS Institute Inc., Cary, NC, U.S.A.).

3. Results

All patients completed the MIRT (all patients attended the three daily sessions included in the program), and there were no dropouts at the end of study. Table 1 reports demographical characteristics of studied patients. During the MIRT and followup pharmacological therapy was unchanged. The functional characteristics of patients at admission, discharge, and at the 1-year followup are reported in Table 2. The *P* values for the comparison with the measurement performed at admission, taken as the control level against which successive measurements are compared by contrast analysis, are also reported.

All considered scales improved significantly at the end of the rehabilitation treatment ($P < 0.0001$ for UPDRS_29, UPDRS_30, 6MWT, BBS and TUG, $P = 0.012$, $P = 0.0002$, and $P = 0.0007$ for UPDRS_13, CGS, and FGS, resp.).

At the 1-year followup, UPDRS_29, CGS, and FGS still maintained better values with respect to admission ($P = 0.009$, $P = 0.03$, and $P = 0.02$, resp.), while the values of the remaining scales did not differ significantly.

4. Discussion

This study was aimed primarily to test the efficacy of MIRT on balance and gait and to investigate whether the beneficial effects persist after one year of unsupervised treatment. Our results demonstrate that the treatment was very effective in improving postural stability and gait during the inpatient treatment.

At the 1-year followup, most of the scales related to gait evaluation (UPDRS 29, CGS, and FGS) were still significantly improved with respect to the values observed at enrollment, and the other functional variables exhibited values close to those observed at admission. None of the patients had to increase the drug dosage during the followup and it is possible to exclude a pharmacological intervention on patients' outcome.

These results point out that, despite the degenerative nature of their illness, Parkinsonian patients could improve balance and gait during a multidisciplinary inpatient intensive treatment and partially maintain the result over time if they continue to make regular physical activity. It is well known that the natural history of Parkinson's disease leads to a progressive impairment of gait and balance and to a progressive increase in Levodopa dosage which is scarcely effective in improving these symptoms and brings about several side effects, such as dyskinesia and hallucinations [2, 22–24].

Moreover, balance and gait may not be related to dysfunctions of the dopamine systems [25–27].

These considerations push to develop new strategies for the treatment of these symptoms.

There is great interest in using exercise for gait and balance disorders, as exercise may have both symptomatic effects as well as disease-modifying effects [28].

Gait and balance disturbances are complex phenomena with multifactorial problems involving vestibular, proprioceptive, and musculoskeletal dysfunctions. Hence, a multidisciplinary approach, delivered by an efficient and well coordinated multidisciplinary team, is likely to be more effective for the different components responsible for these symptoms. Indeed, our multidisciplinary protocol was not designed as simply the sum of a set of interventions delivered to the patient independently, but each intervention was integrated into a streamlined team approach, aimed to the development of a tailored rehabilitation program.

Treadmill training is effective in reducing the variability of gait, enhancing gait speed, and reducing freezing of gait in PD, and several balance training programs have been developed by different groups which also demonstrated short-term efficacy [29–32].

It has also been suggested that the intensity of treatment is a key factor in achieving better results [31–34]. We hypothesize that the persistence of improved gait performance at the 1-year followup might be related to the peculiarity of

our rehabilitation strategy, which was developed taking into account all these aspects.

As far as the functional variables related to balance are concerned, one year after treatment their values were virtually the same as at first admission. We think this is an important result which can be better appreciated considering the chronic-degenerative nature of PD.

5. Study Limitation

The lack of a control group and the lack of a control over the execution and adherence of the exercises during followup are the most important limitations of the study. However based on the lack of drop-outs and the good motor performance of the patients at followup, we can hypothesize a good adherence to instructions given at discharge. This hypothesis is further supported by the fact that none of the patients had to increase the drug dosage during the study.

6. Conclusion

Our findings indicate that balance and gait disturbances can be effectively countered by a multidisciplinary intensive inpatient treatment. The promotion of physical activity should be considered a valid option to maintain a good motor performance and autonomy in daily activity and to delay the increase in drug dosage with related adverse effects, although this needs to be tested in future well-controlled trials.

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Research Article

The Dysarthria Impact Profile: A Preliminary French Experience with Parkinson's Disease

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This preliminary study aimed to adapt the Dysarthria Impact Profile (DIP) in French and to confirm its relevance for the assessment of the psychosocial impact of dysarthria in Parkinson's disease (PD). The DIP scale was administered to 10 people with PD and 10 age-matched control subjects. The DIP psychometric properties were calculated (discriminant validity, internal consistency, and concurrent validity), notably by using the Voice Handicap Index (VHI) for interscale comparisons. The French version of the DIP discriminated people with PD from control subjects (χ^2 test, $P < 0.05$). Good internal consistency was observed in both populations (Cronbach's $\alpha = 0.93$ for PD people and $\alpha = 0.76$ for control subjects). The DIP was highly correlated with the VHI (Spearman's $\rho = -0.70$, $P < 0.01$), confirming the external validity of the scale. There was no direct relationship between PD speech and quality of life as assessed by the Parkinson's Disease Questionnaire-39 (PDQ-39). Our preliminary data suggest that the French version of the DIP has the potential to make a useful contribution for the assessment and outcome management in acquired dysarthria for both clinicians and researchers.

1. Introduction

Improving quality of healthcare and encouraging clinicians to adopt a more holistic approach to the assessment and treatment of patients were significant contributions of the International Classification of Functioning Disability and Health (ICF), promoted by the World Health Organization (WHO) during the 2001 international conference in Geneva [1] to the field of speech sciences. Since the adoption of this framework, considering patients' personal feelings regarding physical, psychological, and social domains has received increasing interest over the last decade. Classical assessment procedures now aim at including evaluations of quality of life and well-being in populations with communication impairments [2]. However, the few tools available for the investigation of the psychological and social impact of oral communication deficits mainly focus on voice and speech production disorders [3–6].

Hypokinetic dysarthria in Parkinson's disease (PD) is a motor speech disorder that arises as a consequence of a neurodegenerative process. Around 70% of people with PD are affected to some degree by voice and speech impairment [7], leading one to consider that communication impairment is highly prevalent and debilitating in this population. Indeed, people with PD are less likely to participate in conversations, or to have confidence in social interactions [8]. Several studies suggest that as PD progression is associated with a growing discomfort in verbal communication, there is an important negative alteration to social life [9–11]. Capturing the impact of dysarthria on the person with PD is not straightforward. While there are many clinical and instrumental ways to evaluate dysarthria, the person's own experience of his/her communicative limitations has been long neglected. Even if dedicated self-reporting questionnaires for the assessment of voice and speech difficulties arising from dysarthria are available [12–14], scales examining the impact of such

difficulties on daily-living activities are scarce. To address this limitation, the Dysarthria Impact Profile (DIP) has been proposed as an alternative for the assessment of the psychosocial impact of dysarthria on speakers [15]. Whereas the gold standard dysarthria questionnaires mainly assess speech and/or voice parameters (e.g., acoustics, articulation), the original approach of the DIP is to focus on the impact of speech deficits', specifically the psychosocial impact of the speech disorder on the communicative participation from the speaker's perspective.

The term "psychosocial impact" is multidimensional [16, 17], defined as "*the psychological and social consequences of a motor speech disorders with quality of life, subjective well-being, and societal participation, viewed predominantly as consequence or factors that contribute to psychosocial impact*" [2]. The DIP scale was designed using data from in-depth interviews with people presenting with non-congenital dysarthria [18, 19], drawing also from earlier accounts from other researchers [18, 20–23] and personal accounts of individuals with dysarthric speech [24–26]. From these data, forty-eight items were drawn up and divided into five specific topic areas: (1) the effect of dysarthria on me as a speaker, (2) accepting my dysarthria, (3) how I feel others react to my speech, (4) how dysarthria affects my communication with others, and (5) dysarthria relative to other worries and concerns [15]. This scale has been used in studies examining the psychosocial impact of dysarthria from the speaker's perspective [23, 27, 28].

The DIP was devised in English and is used with English speaking populations. The main goal of this study was to translate the DIP into French and assess its relevance in French for the description of the psychosocial impact of dysarthria in PD. We explored the discriminant validity, (i.e., the comparison between the PD population scores with the scores from control subjects); the concurrent validity of the DIP, by calculating its correlation with other self-reporting questionnaires that aimed at evaluating associated constructs of voice handicap and quality of life; and the relationship between the negative impact of PD speech and negative quality of life.

2. Material and Methods

2.1. Participants. Ten people with PD (6 males and 4 females) and under medication participated in the study. They were recruited by a movement disorders' neurologist (F.V.) at the Neurology Department of the Aix-en-Provence Hospital (Centre Hospitalier du Pays d'Aix), where they attended outpatient clinics. The mean (±SD) age of the participant sample was 68.6 ± 12.3 years (age range: from 47 to 84 years). The mean (±SD) disease duration was 4.7 ± 3.6 years (range: from 4 months to 9 years). The selection criteria included patients diagnosed with idiopathic PD, no cognitive impairment, no history of hearing impairment, and no previous speech therapy rehabilitation. The patients recruited underwent an examination using part III of the Unified Parkinson's Disease Rating Scale, UPDRS [29], which assessed the global motor state of the patients. The mean (±SD) UPDRS III score *on* medication was 14.1 ± 7.2. The cognitive state of the patients was evaluated using either the Mattis Dementia Rating Scale [30] or the Mini-Mental State Examination [31]. None of the participants had evidence of any cognitive impairment.

Ten age-matched healthy control subjects (4 males and 6 females) were recruited from the experimenters' personal contacts to participate in the study. The mean (±SD) age of the control group was 72.4±3.9 years (age range: from 70 to 83 years). None of the control subjects had history of any hearing or cognitive impairment or other neurologic or psychiatric diseases. Demographics and characteristics of people with PD and control participants are summarized in Table 1.

2.2. Assessment Measures. Two valid and reliable assessment measures (the Voice Handicap Index, VHI, and the Parkinson's Disease Questionnaire, PDQ-39) were used along with the DIP. All the assessments were administered in one day. Regarding the people with PD, three participants completed the scales with the help of an experimenter (A.L.), since they presented with writing difficulties; the remainder completed the scales independently. All control participants completed the scales independently at home.

2.2.1. Dysarthria Impact Profile (DIP). Items from the original questionnaire were translated into French by A.L. & S.P. and compared with the original items by a bilingual linguistics researcher. The final translated version integrated all the translation adjustments. In the first 4 sections of the scale, the person with PD was asked to rate statements in each section using a five-point scale ("strongly agree," "agree," "not sure," "disagree," and "strongly disagree"). In order to test the responder reliability (i.e., the participant answer congruence or responder consistency), the DIP scale incorporated 2 similar statements in each section, differently formulated. The DIP uses positively and negatively worded statements. In the positively worded statements, "strongly agrees" answers receive a score of 5 and "strongly disagree" answers receive a score of 1. Reversely, in negatively worded statement, "strongly agrees" answers receive a score of 1 and "strongly disagree" answers receive a score of 5. In the fifth section, people were asked to list and rank (from 1 = most worry to 5 = least concern) their five main worries, including speech impairment. The DIP could be completed by the person him/herself or with assistance. All answers were added to obtain a global impact score; the lower the score, the higher the level of impact.

2.2.2. Voice Handicap Index (VHI). The VHI [3] is often considered as the *gold standard* for the evaluation of voice self-perception [32]. It includes 30 items split into three domains: physical, functional, and emotional. It has been previously translated into French and validated with a French population [33]. Each item is scored from 0 to 4 ("never," "almost never," "sometimes," "almost always," and "always"); the higher the score, the higher the degree of perceived handicap.

2.2.3. Parkinson's Disease Questionnaire (PDQ-39). The PDQ-39 [34] is a global and PD-specific quality of life

Table 1: Demographics and characteristics of people with PD and control participants.

People with PD[a]	Gender	Age (years)	Disease duration (years)	UPDRS score on medication	Controls[b]	Gender	Age (years)
P1	Male	55	1.5	11	C1	Female	70
P2	Female	76	6.6	8	C2	Female	70
P3	Male	75	2.0	15	C3	Female	72
P4	Male	56	6.8	25	C4	Male	72
P5	Female	78	9.0	20	C5	Female	72
P6	Female	72	8.0	4	C6	Male	74
P7	Female	84	9.3	Missing data	C7	Female	83
P8	Male	47	1.0	13	C8	Male	70
P9	Male	64	0.3	8	C9	Male	70
P10	Male	79	2.0	23	C10	Female	71
Mean ± SD		68.6 ± 12.3	4.7 ± 3.6	14.1 ± 7.2			72.4 ± 3.9

[a] The selection criteria included patients diagnosed with idiopathic PD, no cognitive impairment, no history of hearing impairment, and no previous speech therapy rehabilitation. The cognitive state of the patients was evaluated using either the Mattis Dementia Rating Scale [30] or the Mini-Mental State Examination [31]. None of the participants had any evidence of cognitive impairment. [b] None of the control subjects had any history of hearing or cognitive impairment or other neurologic or psychiatric disease.

questionnaire, also available in French [35]. The scale consists in 39 items allowing for the determination of an overall quality-of-life score examining 8 specific domains: mobility, activities of daily living, emotional well-being, stigma, social support, cognition, communication, and bodily discomfort. Each item is scored from 0 (normal) to 4 (maximum disturbance); the higher the score, the higher the impairment of quality of life.

2.3. Statistical Analyses. Statistical analyses (R Development Core Team, http://www.r-project.org/) were carried out in order to estimate the psychometric properties of the French version of the DIP in our preliminary set of data. Since the DIP scale is nominal, χ^2 test was used to evaluate the ability of distinguishing people with PD from controls (discriminant validity). Regarding the VHI, which is an ordinal scale, Wilcoxon ranked test was performed. Internal consistency of the DIP was assessed by calculating Cronbach's α coefficient for each population. Responder reliability was tested by measuring correlations between connected items within each of the first 4 sections (Spearman's ρ coefficient). Concurrent validity was assessed by correlating the DIP and VHI scores (Spearman's ρ coefficient).

3. Results and Discussion

3.1. DIP Main Effects and Discriminant Validity. As it can be seen in Table 2, the people with PD obtained lower scores on the DIP than control subjects, suggesting a high level of psychosocial impact of dysarthria in this population. The French version of the DIP was able to discriminate between control subjects and people with PD ($\chi^2 = 176.6$, df = 4, $P < 0.05$), as did the VHI total score (Wilcoxon $W = 78.5$, $P < 0.05$). In Section E of the DIP ("*Dysarthria relative to other worries and concerns*"), speech was the main concern for only 1 out of the 10 PD participants and an important worry for 5 of them (50%). The remaining four people with PD were slightly or least concerned about their speech.

3.2. Internal Consistency. Internal consistency, (i.e., how well all items in a scale correlate with each other and follow the same trend) was assessed using Cronbach's α coefficient. An adequate consistency is considered with a coefficient of at least 0.70. Thus, internal consistency was confirmed for the DIP total scores for both the PD ($\alpha = 0.93$) and control ($\alpha = 0.76$) populations. Internal consistencies were also confirmed for the DIP subsections A ($\alpha = 0.85$), B ($\alpha = 0.72$), C ($\alpha = 0.87$), and D ($\alpha = 0.83$) for the PD patients.

3.3. Responder Reliability. Responder reliability was tested by measuring correlations between 2 connected items within each subsection (Spearman's ρ correlation), sections A ("*The effect of dysarthria on me as a speaker*"), B ("*Accepting my dysarthria*"), and D ("*How dysarthria affects my communication with others* of the scale") displayed statistically significant correlations ($\rho = 0.76$, $\rho = 0.59$, and $\rho = 0.72$, resp., $P < 0.01$), whereas the connected items of section C ("*How I feel others react to my speech*") did not show any correlation ($\rho = 0.39$, $P = 0.08$).

3.4. Concurrent Validity of the DIP. Although the DIP, VHI, and PDQ-39 levels of measurements are different (nominal for the DIP, ordinal for the VHI and PDQ-39), we thought important to have an idea of the construct validity by testing, nevertheless, correlation analyses between the scales' total scores. As displayed in Figure 1, correlations between the DIP and the VHI were high for both the people with PD and the control subjects (Spearman's $\rho = -0.70$; $P < 0.01$). Furthermore, in the PD group, the total DIP score correlated significantly with the "Functional" sub-section (the impact of voice disorders on daily living activities) of the VHI scale ($\rho = -0.82$, $P < 0.01$). This was not the case with the PDQ-39 total score ($\rho = -0.41$, $P = 0.23$).

3.5. Discussion Points. Due to the small number of participants in the present study, our findings still have to be considered as preliminary. Despite that fact, our data were

Table 2: Total and mean scores from self-assessments.

People with PD	DIP[a] (score/225)	VHI[b] (score/120)	PDQ-39[b] (score/156)	Controls	DIP	VHI
P1	159	14	41	C1	166	69
P2	215	6	18	C2	189	5
P3	118	69	58	C3	200	9
P4	129	31	27	C4	192	13
P5	179	7	37	C5	201	5
P6	140	26	38	C6	204	17
P7	134	65	65	C7	190	1
P8	150	44	86	C8	197	8
P9	135	46	19	C9	203	10
P10	129	75	95	C10	199	13
Mean ± SD	148.8 ± 29.0	38.3 ± 25.6	48.4 ± 26.85		194.1 ± 11.1	15 ± 19.5

[a] The lower the score, the higher the impact; [b] the higher the score, the higher the impairment.

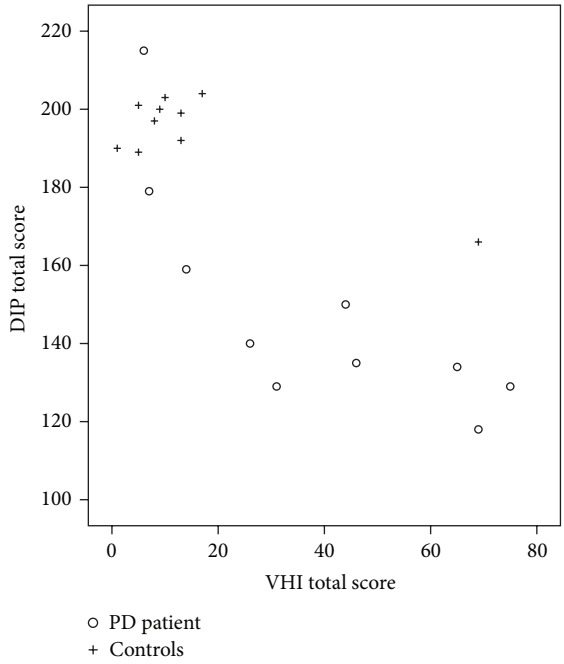

Figure 1: Voice Handicap Index (VHI) versus Dysarthria Impact Profile (DIP) total scores for the 20 participants (10 people with PD and 10 control subjects).

able to demonstrate that (1) the French DIP was able to discriminate people with PD from control subjects, (2) the DIP was highly correlated with the VHI, and (3) no direct relationship between the DIP and quality of life as assessed by the PDQ-39 was displayed. This last point should be expected as the DIP does not assess quality of life and the authors of the DIP view quality of life and psychosocial impact as separate constructs [19].

Speech and voice impairments are frequent in patients with PD. PD speech manifesting itself most typically as a hypokinetic dysarthria displays a combination of respiratory, laryngeal, resonance, and supralaryngeal articulatory deficits [36, 37]. Dysphonia in PD involves monotony of pitch and loudness, a breathy and harsh voice, which represents crucial parameters altering speech intelligibility and, as a consequence, communication ability. This might account for the strong correlation found between the DIP and VHI scales. Methodological constraints did not allow us to acquire neither any acoustical recordings nor any formal assessment of the speech disorder severity. Further experiments will need to take into account this aspect in order to explore the relationship between the DIP and the severity of the speech impairment. Moreover, this will be particularly of interest when assessing different types of dysarthria, as carried out, for example, regarding the validation of the French version of the Speech Handicap Index [14].

The original DIP questionnaire was administered to 31 people with dysarthria, 10 of whom had PD [15]. We performed the present exploratory study with the same number of people with PD. In our group, the mean DIP score was calculated to be 148.8 (cf. Table 2), which is similar to that provided in the original study (144.9). Both English and French versions of the DIP show good internal consistency, arguing a reasonable similarity of our French version with the original one. However, the lack of intraindividual congruence of the 2-connected answers in section C we found in the French version might result from the design of the DIP, particularly the alternation between positive and negative worded statements. In fact, this shift may also imply difficulties for both patients and control subjects when completing the scale, leading to possible incongruent responses. This was not the case with the original version, leading us to consider the need for some amendments in the French version of the scale. Additionally, the completion time of the DIP French version was rather long, more than 30 minutes on average for PD patients. Difficulties when answering might also be due to the visual form of the DIP. Changes are recommended in order to improve both reading and recording responses and in order to shorten the completion time for patients. These represent practical issues that will be taken into account in a further amended format of both English and French versions of the scale. Work on this is currently underway.

Some reliability and validity has been established with the French DIP used in the present experiment. However, further validation needs to be performed in order to confirm the psychometric properties demonstrated in our preliminary results. To do so, the amended version of the French DIP will need to be administered on a larger sample of people with dysarthria, covering a range of different aetiologies. Due to the fact that control subjects may also present with speech alteration associated with age, as suggested by the performance of one control (cf. Table 2 and Figure 1), a larger number of controls covering a range of ages will also be required. Test/reretest reliability and responsiveness to change will have to be considered as well. Work on these aspects is underway in the English version. Regarding specifically the French version, a back-to-back translation procedure should be planned for the updated version of the scale.

4. Conclusions

While some behavioural treatments for speech in PD might have predictable beneficial impacts [38], pharmacological and/or neurosurgical treatments have relatively limited and variable effects on PD speech [39]. There is a need to consider treatments beyond the level of impairment thereby justifying the use of a self-administered questionnaire to measure the psychosocial impact of dysarthria from the perspective of the speaker. This is particularly of interest since this kind of self-assessment may help the patient realise his/her difficulties and lead him/her to take part with the clinician in therapeutic work. The DIP is part of a range of new self-assessments, including the Speech Handicap Index [12, 14] and the French *Parole Handicap Index* [13], all aiming at producing "*a comprehensive picture of speech impairment*" [14]. Our preliminary data suggest that the French version of the DIP may have the potential to make a useful contribution to outcome management in acquired dysarthria for both clinicians and researchers.

Availability of the French Version of the DIP

In order to obtain a copy of the French version of the DIP used in the present study, interested parties should contact the corresponding author (serge.pinto@lpl-aix.fr) who will be pleased to send a copy of the material.

Conflict of Interests

The authors have declared no conflict of interests.

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Clinical Study

Repetitive Transcranial Magnetic Stimulation Improves Handwriting in Parkinson's Disease

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Background. Parkinson disease (PD) is characterized by hypometric movements resulting from loss of dopaminergic neurons in the substantia nigra. PD leads to decreased activation of the supplementary motor area (SMA); the net result of these changes is a poverty of movement. The present study determined the impact of 5 Hz repetitive transcranial magnetic stimulation (rTMS) over the SMA on a fine motor movement, handwriting (writing cursive "l"s), and on cortical excitability, in individuals with PD. *Methods*. In a cross-over design, ten individuals with PD were randomized to receive either 5 Hz or control stimulation over the SMA. Immediately following brain stimulation right handed writing was assessed. *Results*. 5 Hz stimulation increased vertical size of handwriting and diminished axial pressure. In addition, 5 Hz rTMS significantly decreased the threshold for excitability in the primary motor cortex. *Conclusions*. These data suggest that in the short term 5 Hz rTMS benefits functional fine motor task performance, perhaps by altering cortical excitability across a network of brain regions. Further, these data may provide the foundation for a larger investigation of the effects of noninvasive brain stimulation over the SMA in individuals with PD.

1. Introduction

Hypometric movements, resulting in diminution of letter size, reduced speed and slow acceleration, typically characterize handwriting in individuals with Parkinson disease (PD) [1–5]. Deficits in handwriting begin with hypometric movements and then may progress to micrographia as PD severity progresses. Specifically, hypometric movements may be related to the impaired ability to maintain adequate muscle force and to process concurrent and forthcoming movement information while writing. Given that individuals with PD suffer from hypometric handwriting [1], we selected this task to consider the effects of noninvasive brain stimulation on hand function.

Normally, the basal ganglia (BG) play a role in the kinematic scaling of movements [6], but in individuals with PD, suboptimal BG function due to dopamine depletion leads to widespread changes in interconnected brain regions that include decreased activity in the supplementary motor area (SMA) and reduced efferent feedback in the basal ganglia-thalamocortical motor loop [7]. Consequently, individuals with PD show altered activation patterns in the SMA [8–15] and overall less corticocortical excitability [8–10, 12]. Taken together, changes in activation patterns across a broad cortical network and sub-optimal BG function lead to hypometric movements associated with PD.

Located on medial aspect of the forebrain, the SMA plays a key role in motor selection in sequentially structured tasks such as handwriting. Data from healthy controls suggest that the cortical control of handwriting requires activity in the SMA, motor cortex, and BG in order to produce finely graded precision grip required by handwriting [6]. To generate movements in the absence of external cues, the SMA receives efferent information from the BG and then transmits information that likely helps to prepare movement [16] to M1. However, individuals with PD suffer from overactivation

Table 1: Participant Characteristics.

P	Sex	Age	MoCA	UPDRS-III	H&Y	DH	More affected side	Disease duration (years)	Medication (daily dose—mg)
1	M	52	25	9	1.5	R	L	4	Levodopa/Carbidopa 100/25 QID Entacapone 200 QID Pramipexole 1 QID
2	M	73	28	18	1.5	R	R	10	Levodopa/Carbidopa CR 200/50 QID Levodopa/Carbidopa/Entacapone 100/25/200 QID Levodopa/Carbidopa 120/25 TID
3	M	77	27	11	1.5	R	L	4	Levodopa/Carbidopa 250 QD
4	M	77	24	13	1.5	R	R	4	Levodopa/Carbidopa CR 100/25 QID Levodopa/Carbidopa 100/25 BID
5	M	71	29	7	1	R	R	8	Levodopa/Carbidopa CR 200-50 TID Rasagiline 1 QD
6	M	77	29	9	1.5	R	L (more axial)	3	Levodopa/Carbidopa CR 100/25 QID
7	M	72	26	7	1.5	R	R (more axial)	5	Levodopa/Carbidopa 200/50 q5H Pramipexole 1 TID
8	F	64	28	5	1.5	R	R (more axial)	6	Levodopa/Carbidopa CR 100/25 q5H Pramipexole 1 TID Rasagiline 0.5 QD
9	M	64	30	6	1.5	R	L	4	Levodopa/Carbidopa 100/25 QID Pramipexole 0.5 QID
10	M	78	29	9	1.5	R	R	3	Levodopa/Carbidopa CR 200/50 QID

P: participant, Age: years, F: female, M: male, R: right; L: Left, MoCA: Montreal Cognitive Assessment, UPDRS-III: Unified Parkinson's Disease Rating Scale-motor section, H&Y: Hoehn and Yahr's stages, DH: dominant hand, CR: controlled release, QD: one/day, BID: two times/day, TID: three/day, QID: Four/day, q5H: Five/day.

of internal segment of Globus Pallidus internus (GPi) in BG that leads to inhibition of thalamic neurons to cortex, especially to SMA [1–4, 13–15, 17]. Consequently, individuals with PD have decreased activity in SMA owing to diminished efferent feedback from BG-thalamocortical motor loop. Due to poor BG and SMA functions, individuals with PD suffer from a reduced ability to process concurrent and forthcoming information about movement; in the case of handwriting, progressive micrographia results [18].

Repetitive transcranial magnetic stimulation (rTMS) is a non-invasive technique that allows cortical excitability to be altered; when delivered at frequencies ≥5 Hz rTMS cortical excitability may be increased. Past work suggests that rTMS over motor and prefrontal cortex induces a dopamine release in the striatum in people with PD [19–21]. However, this work did not consider whether the application of rTMS might impact functional motor skill performance. Thus, the main aim of the present study was to consider whether the delivery of excitatory rTMS could impact handwriting performance. We targeted the SMA with rTMS based on its known role in handwriting performance [6] in combination with previous reports of altered SMA function in individuals with PD [8, 9]. Past kinematic studies of handwriting [1, 4] suggest it is an ideal task for the study of motor skill function in individuals with PD.

Given that rTMS over the SMA may shift cortical excitability both locally and in linked cortical areas, we hypothesized that following 5 Hz rTMS individuals with PD would demonstrate improved speed and amplitude of handwriting movements. Tuelings et al. [22] reported that individuals with PD show greater disfluency in writing tasks involving wrist flexion than in the tasks involving wrist extension. Therefore, we predicted that individuals with PD would demonstrate more improvement in the downstroke as compared to the upstroke following 5 Hz rTMS. Finally, given the strong cortico-cortico connections between SMA and M1 we also hypothesized 5 Hz rTMS over SMA would also affect the excitability of M1. To our knowledge, the present study is the first study to assess the effect of rTMS over SMA on a functional motor skill, handwriting, in individuals with PD.

2. Materials and Methods

Ten individuals with PD (mean age: 70.5 years) participated (Table 1). To characterize disease status, the motor section of the Unified Parkinson's Disease Rating Scale (UPDRS-III) and Hoehn and Yahr's (H&Y) scores were determined by a physiotherapist prior to the first session of testing while individuals were on medication. Exclusion criteria included (1) age above 80; (2) cognitive dysfunction (i.e., Montreal Cognitive Assessment < 24); (3) history of psychiatric disturbances; (4) any neuromuscular, skeletal, cardiovascular conditions that might interfere in participating in the study; (5) history of seizures/epilepsy, substance abuse or head trauma, stroke, tumor; or (6) severe PD (H&Y stage > 3).

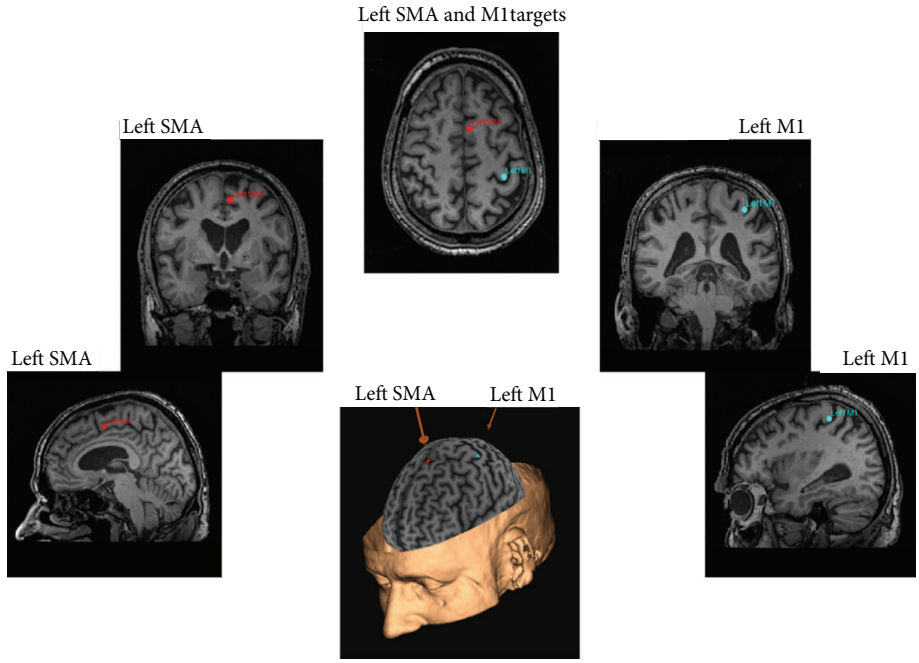

Figure 1: Stereotaxic system for coil placement. Brainsight was used to locate left SMA (as per Talairach coordinates) and left M1; markers were placed to ensure accuracy of coil placement within and across stimulation sessions.

Additional exclusion criteria for functional magnetic resonance imaging (fMRI) anatomical scanning and TMS mapping included pacemaker, pregnancy, metallic objects in the body, or claustrophobia. None of the participants presented with significant tremors.

Participants were tested while on their regular medication schedule; interviews confirmed that medication status did not change during the period of study participation. To control for medication-induced fluctuations in function, all participants were tested at the same time of day for each of the two sessions, two hours before their next medication dosage. That is, the testing was done during second (declining) phase of medication cycle, to capture the maximum add-on effect of rTMS. All participants gave informed, written consent for their participation in the study and all procedures were institutionally and ethically approved. To control variability in participants, all participants were tested using their right hand to write; rTMS was delivered over the left hemisphere for SMA and M1. This study had cross-over design, all participants received 5 Hz and control rTMS over left SMA one week apart. The order of type of stimulation was randomly allocated.

2.1. TMS Protocol. A Magstim Super Rapid stimulator (Magstim Company, Ltd.) was used to deliver the whole TMS, in conjunction with a 70 mm figure-of-eight air-cooled coil. During TMS participants were seated in a semireclined dental chair with arms bent and supported. For the whole stimulation session, over both M1 to determine resting motor threshold (RMT) and SMA for rTMS, the TMS coil was oriented tangentially to the scalp with the handle pointing back and away from midline at 45 degrees. The magnetic stimulus had a biphasic waveform with a pulse width of 400 us. On a separate day, prior to the start of the experiment, each participant had an anatomical MRI scan at the University of British Columbia (UBC) 3T MRI Centre (T1 images TE = 5 ms, TR = 24 ms, 40° flip angle, NEX = 1, thickness = 1.2 mm, FOV = 256 mm). These images were imported into Brainsight TMS neuronavigation software (Rogue Research Inc.) to allow for stereotaxic registration of the participant's brain with the TMS coil for online control of the trajectory of stimulation and to ensure consistency of stimulation location across experimental days. Each participant's brain was transformed into standard Talairach space using Brainsight software. This enabled standardization of rTMS delivery over known Talairach coordinates for the SMA: −5, −3, 52 [23, 24] (Figure 1).

Motor evoked potentials (MEPs) were used to determine the coil position that evoked the maximal response (i.e., the "hot spot") in the right flexor carpi radialis (FCR). MEP amplitude was monitored by surface electromyography (EMG) over participant's right FCR using the evoked potential unit of the Super Rapid^2 control unit (Magstim Super Rapid^2, Magstim Company, Ltd.). Once the location and trajectory of the coil were determined for this hot-spot it was marked using Brainsight to minimize variability. The motor cortical hot-spot was verified at the beginning of each experimental session, as well as before and after rTMS. Following determination of the motor cortical hot spot, RMT was established as the percentage of stimulator output intensity that elicited an MEP > 50 μV in 5 out of 10 trials. To determine the impact of stimulation conditions

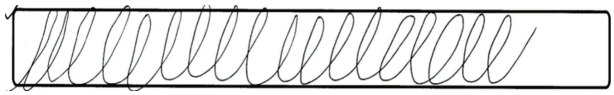

Figure 2: Example of raw data from handwriting task from an individual trial showing a rectangular box of 0.79 by 8 inches; participants were instructed to match the height of their loops to the size of the box.

(5 Hz and control rTMS over SMA) on the excitability of the primary motor cortex we repeated our assessment of RMT on left M1 following 5 Hz stimulation over the SMA. Figure 1 shows the site of stimulation as recorded in Brainsight for left M1 and left SMA.

All participants were naïve to TMS and were blinded to group assignment. 1200 pulses of rTMS stimuli were delivered at 110% of RMT at a frequency of 5 Hz over the SMA [16] (approximately 6 minutes of stimulation). The same protocol was followed for the control, sham stimulation. Control stimulation over SMA was delivered by using an identical custom sham coil that had same look and sound as an active coil but did not induce any current in the underlying cortex. One participant reported scalp discomfort at 110% intensity and thus was stimulated at 100% RMT. All stimulation parameters were in accordance with published safety standards [25].

2.2. Handwriting. Handwriting assessments were performed while participants sat at a table adjusted for height to allow the right arm to be comfortably placed with the elbow below the shoulder. Participants were asked to write repetitive cursive loops or "l"s in their everyday style and preferred speed using an ink pen on an 8.5 by 11-inch paper placed on top of a digitizing tablet (WACOM Intuos3 tablet 9X12). The paper contained rectangular boxes of 0.79 by 8 inches and participants were instructed to match the height of their loops to the size of the box (Figure 2). Before starting the experiment, all participants were allowed to practice a trial. Two trials of 15 seconds each were recorded. For each condition (5 Hz versus control rTMS), data was collected twice—prior to rTMS and after rTMS on the same day.

2.3. Data Analyses. Kinematic variables of handwriting were quantified using ScriptAlyzer software (NeuroScript, LLC; Tempe, AZ, USA). ScriptAlyzer was used to record position data (X-Y coordinates) and then calculate the kinematic parameters of interest at a frequency of 200 Hz with a spatial resolution of 0.002 cm. For each loop, the software used the zero velocity crossing to identify two segments, an upstroke and a downstroke. The software automatically eliminated the first loop (up- and downstroke) from each trial. For any trials where freezing or hand repositioning events occurred, the software identified the segment immediately before and after the event and eliminated those segments and the data within that event. After software elimination, stroke segments were visually inspected to verify data. On average, 20 segments were analyzed per subject per test session.

Finally, for each trial, ScriptAlyzer used the averaged segment data to calculate the following kinematic parameters: (1) vertical size (cm); (2) peak vertical velocity (cm/sec); (3) average pen pressure (z coordinate). We analyzed parameters of the complete loop as well as separated segments (up- and downstrokes).

2.4. Statistical Analysis. For each of the above dependent variables, a 2 (session: 5 Hz, control rTMS) by 2 (Time: before and after stimulation) ANOVA with repeated measures corrections was performed. The mean of each variable was the dependent measure; SPSS software (v.14) was used for each analysis. Significant interactions (session by time) were decomposed with follow-up t-tests. The same statistical test was employed with RMT as the dependent measure to index cortical excitability. Threshold for significance was set to $P \leq 0.05$.

3. Results

3.1. Complete Loops. (a) *Vertical size*: a significant session by time interaction ($F(1, 9) = 5.59$, $P = 0.04$; Table 2; Figure 3(a)) resulted from increased global vertical size for the 5 Hz group at the posttest as compared to control group.

(b) *Peak vertical velocity*: a significant main effect of time was noted for peak vertical velocity ($F(1, 9) = 10.67$, $P = 0.01$). This suggests that both groups wrote faster at the posttest, regardless of stimulation type. Neither the session nor time interaction was significant (Table 2).

(c) *Average pen pressure*: there were no significant effects of rTMS on pen pressure.

3.2. Up- and Downstrokes. (a) *Vertical size:* there was significant Session by Time interaction for vertical upstroke size ($F(1, 9) = 9.62$, $P = 0.01$). Upstrokes were larger following 5 Hz rTMS (Table 2; Figure 3(b)). No interaction was observed for downstrokes.

(b) *Peak vertical velocity*: a significant main effect of Time on downstrokes resulted from increased peak vertical velocity ($F(1, 9) = 8.69$, $P = 0.02$; Table 2).

(c) *Average pen pressure*: there was significant Session by Time interaction for upstrokes ($F(1, 9) = 4.93$, $P = 0.05$). This was due to the decreased pen pressure following 5 Hz rTMS (Table 2; Figure 3(c)). No interaction was observed for downstrokes.

3.3. Motor Cortical Excitability. A Session by Time interaction was noted for RMT ($F(1, 9) = 5.25$, $P = 0.05$). This was the result of lower RMT over M1 following 5 Hz rTMS ($P = 0.02$; Table 3). This was not the case following control rTMS.

4. Discussion

This is the first study to demonstrate short-term changes in functional fine motor task performance following 5 Hz rTMS over SMA in individuals with PD. Specifically, we noted that 5 Hz rTMS over SMA increased the global size

Table 2: Average means (SD) before and after rTMS for each group and P values for all segments, upstrokes and downstrokes.

Variable	All segments			Upstroke			Downstroke		
	5 Hz	Control	P value	5 Hz	Control	P value	5 Hz	Control	P value
Vertical size (cm)									
Before	1.87 (0.09)	1.85 (0.12)	0.04*2	1.88 (0.09)	1.87 (0.12)	0.01*2	1.86 (0.09)	1.84 (0.12)	NS
After	1.92 (0.10)	1.84 (0.16)		1.94 (0.09)	1.85 (0.17)		1.90 (0.12)	1.84 (0.16)	
Peak Vertical velocity (cm/sec)									
Before	6.97 (1.72)	7.54 (1.08)	0.01*1	7.41 (1.48)	8.11 (1.31)	NS	6.55 (2.07)	7.06 (1.38)	0.02*1
After	7.99 (1.90)	7.98 (1.62)		8.34 (1.89)	8.48 (1.62)		7.72 (2.06)	7.59 (1.86)	
Average pen Beforessure									
Before	658.94 (209.10)	546.43 (204.47)	NS	675.30 (211.95)	566.43 (195.68)	0.05*2	642.39 (211.93)	536.50 (207.25)	NS
After	564.64 (154.47)	550.07 (254.76)		581.09 (161.34)	570.02 (254.05)		543.31 (150.10)	528.36 (259.84)	

NS: not significant; *1significant main effect of time; *2significant session by time interaction.

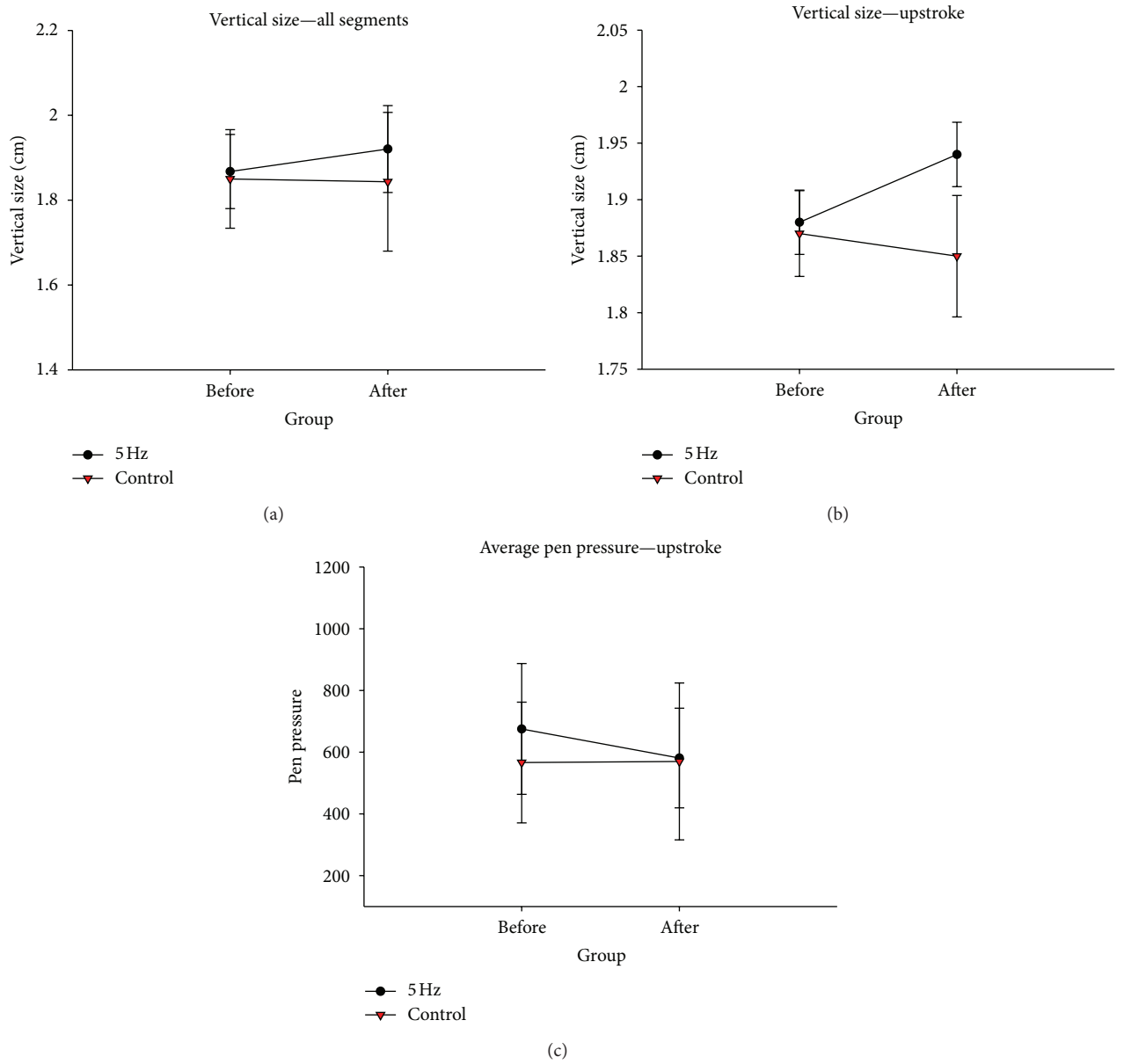

Figure 3: Significant interactions in behavioural data from handwriting task for (a) vertical size, (b) upstroke size, and (c) average pen pressure. Error bars are standard error of the mean (SEM).

Table 3: Average means (SD) before and after rTMS for each group, and *P* values for RMT.

Variable	TMS		*P* value
	Active	Sham	
RMT			
Before	63.1 (10.55)	62.3 (8.08)	0.05*
After	60.2 (9.14)	61.2 (8.59)	

*Significant SESSION by TIME interaction.

of handwriting as shown by larger "l"s, specifically upstroke height increased and pen pressure decreased following rTMS over SMA. Van Gemmert et al. [26] reported that individuals with PD undershoot when asked to match their letter height to a target box. In the present study, we show that 5 Hz rTMS countered the undershooting of letter height, at least in the short term. We speculate that 5 Hz rTMS over SMA may alter corticostriatal and corticocortical connectivity perhaps by exciting an otherwise hypoactive SMA and its projections to the BG, M1, and other motor areas. The BG play an important role in motor behavior. According to a hypothetical model, the putamen controls GPi, both directly and indirectly. In PD, the balance between putamen and GPi and globus pallidus-externus (GPe) is altered due to loss of dopamine. The SMA acts with the basal ganglia reciprocally to prepare movements [27–31], forming a corticosubcortical loop. The SMA also sends information to M1 for final output [17]. Our data

suggest that 5 Hz rTMS over SMA helped to compensate for corticostriatal imbalance by imposing an efferent influence on BG output and enhanced cortico-cortical connections, thus enabling participants to generate a larger vertical letters following stimulation.

5 Hz rTMS also led to decrease in the amount of pen tip pressure, during the now larger upstroke. Other work suggests that PD leads to an inefficient recruitment of muscle force, deficits in amplitude and/or velocity scaling, and rigidity in muscle groups [7, 32], resulting in jerky movements [22]. The M1 is well known to encode the force requirements of movement [33]. Importantly, we noted lower motor thresholds for M1 following 5 Hz rTMS over the SMA [34, 35]. Given the strong cortico-cortico linkages between the SMA and M1 this result is not surprising. Taken together, the decrease in pen pressure and reduction in the threshold for stimulation of M1 following 5 Hz rTMS suggest that non-invasive brain stimulation facilitated the cortical control of force perhaps by moving M1 towards a more excitable state. To better understand the mechanism(s) of these improvements, future studies should attempt to quantify dopamine release in different areas of the brain, but especially in the BG, after 5 Hz rTMS over SMA in individuals with PD.

In addition, we noted that participants improved significantly in writing size for upstrokes as compared to downstrokes after 5 Hz rTMS over SMA. This is contrary to our hypothesis and may be attributed to the fact that individuals with PD have more tonic activation of flexor muscles and reduced control of wrist flexion [22]. Writing curved loops involve finger and wrist extension for upstrokes and finger/wrist flexion for downstrokes. Therefore, rTMS may have facilitated the easier movement of wrist extension (required by upstrokes). Alternatively, it is possible that faster downstrokes resulted from the larger amplitude of movement upward. Future studies should endeavor to use of EMG over the wrist flexors and extensors to directly assess the impact of 5 Hz rTMS over SMA on muscle activity. However, our handwriting data do indicate that participants were able to generate larger letters at their preferred speed following 5 Hz rTMS over SMA as compared to after control rTMS. It is possible that improved handwriting was attributable to better overall muscular control following stimulation.

We also revealed main effects of time for peak vertical velocity. Since both groups improved, the possibility of a placebo effect cannot be excluded [20]. In fact, placebo effects have been noted to induce an endogenous dopamine release in the BG [36]. However, it is also possible that these effects were attributable to a practice effect. Given that each individual in the present study was in the declining phase of his or her medication cycle, demonstration of improved performance associated with a repetition of the handwriting task is not trivial. The possibility that skilled motor practice improved handwriting provides support for future motor learning and rehabilitation trials of this function in people with PD.

A limitation of the present study was that all participants were stimulated on medication. However, we did control for medication cycle effects by testing individuals in the same relative phase two hours before their next medication dosage for each session. Secondly, small sample size may have limited our findings. To control for variability in the sample we employed a cross-over design and all participants were both right handed and tested using their right hand. All participants were naïve to rTMS. In addition, none of the past work has assessed the impact of rTMS on motor function, therefore, it was difficult to calculate adequate sample size and run corrections for multicomparisons. Thirdly, we applied rTMS over Talairach coordinates for SMA, which may have altered our ability to impact both flexion and extension of wrist. Future studies may aim for more disperse delivery of rTMS for more global effects. Other methodological limitations may include the heterogeneity of participants in terms of age and gender bias.

5. Conclusions

Taken together, results of the present study reveal that 5 Hz rTMS over the SMA can influence several key aspects of handwriting including vertical size and axial pressure in individuals with PD, at least in the short term. Although the current study cannot elucidate the exact mechanism by which 5 Hz rTMS induced these effects, our data suggest that brain stimulation over SMA altered excitability within the BG-SMA-M1 loop, which led to greater M1 excitability and improved handwriting function. The data reported here represent a first step in determining the potential therapeutic utility of rTMS over the SMA in individuals with PD. In future, rTMS can be combined with other therapeutic modalities for rehabilitation in individuals with PD. Given our promising early results, future work should attempt to elucidate the mechanism(s) associated with the changes in function reported here and examine the cumulative impact of repeated sessions of 5 Hz rTMS over SMA on motor function in individuals with PD.

Acknowledgments

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Research Article

Exploring Outcome Measures for Exercise Intervention in People with Parkinson's Disease

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Background. It is widely believed that exercise improves mobility in people with Parkinson's disease (PD). However, it is difficult to determine whether a specific type of exercise is the most effective. The purpose of this study was to determine which outcome measures were sensitive to exercise intervention and to explore the effects of two different exercise programs for improving mobility in patients with PD. *Methods*. Participants were randomized into either the Agility Boot Camp (ABC) or treadmill training; 4x/week for 4 weeks. Outcome measures were grouped by the International Classification of Function/Disability (ICF). To determine the responsiveness to exercise, we calculated the standardized response means. t-tests were used to compare the relative benefits of each exercise program. *Results*. Four of five variables at the structure/function level changed after exercise: turn duration ($P = 0.03$), stride velocity ($P = 0.001$), peak arm speed ($P = 0.001$), and horizontal trunk ROM during gait ($P = 0.02$). Most measures improved similarly for both interventions. The only variable that detected a difference between groups was postural sway in ABC group ($F = 4.95$; $P = 0.03$). *Conclusion*. Outcome measures at ICF body structure/function level were most effective at detecting change after exercise and revealing differences in improvement between interventions.

1. Introduction

The progression of Parkinson's disease (PD) inevitably results in problems of balance, contributing to injuries, loss of mobility, increased health costs, and decline in quality of life. Delaying and minimizing these inevitable complications of PD with physical therapy exercise would have a major impact on patients and their families' quality of life, healthcare systems, and possibly even the course of disease progression.

Exercise has received much attention in the past decade as a way to delay the onset of mobility disability and there are a steadily increasing number of randomized controlled trials demonstrating that varying types of exercise improve some aspects of balance or gait [1–12]. However, it is difficult to determine whether a specific type of exercise program is more effective than another. One recurring obstacle, which makes it difficult to compare treatment approaches, is that studies use different types of outcome measures [13]. In addition, exercise studies almost always compare their favored type of intervention with a placebo or no intervention, rather than a head-to-head comparison of different types of exercise programs. The difficulty in comparing 2 potentially effective rehabilitation interventions is the need for very sensitive tests of change and a large number of subjects to differentiate exercise programs.

Although there is evidence from the animal literature that different exercise protocols result in different effects on synaptic and structural proteins in the brain, differentiating functional improvements in humans after different types of exercise has been more difficult to demonstrate [14]. For example, studies in rodents made Parkinsonian from 6-hydroxydopamine show that aerobic exercise on a treadmill results in increased angiogenesis whereas agility exercise that provides a mental challenge results in more synaptic plasticity [15]. However, a recent meta-analysis of human exercise studies could not distinguish relative benefits among the

different types of exercise on clinical balance outcomes in patients with PD [16]. They found 15 randomized and quasi-randomized controlled trials of at least moderate quality in which the primary outcome measure was balance activity performance and found improved balance activity performance (Hedges' g, 0.33; 95% confidence interval, 0.11–0.55; $P = 0.003$). Although the pooled estimate of the effect of exercise was significant, the difference in effect size among different types of exercise intervention was not statistically significant ($P = 0.166$). A more recent Cochrane review that examined the effectiveness of physical therapy intervention for people with PD found similar results [17]. These authors found 33 trials with 1,518 participants that compared physical therapy with no intervention. They found evidence that most clinical measures improved after intervention (gait velocity, Timed Up and Go, Functional Reach, Berg Balance Scale, and Unified PD Rating Scale). However, they did not find any evidence of a difference in treatment effects across types of intervention. While no difference was noted between exercise interventions in both of these review papers, the outcome measures, except for gait velocity, were all clinical measures of performance or participation, which are often insensitive, subjective, and prone to ceiling effects, in contrast to objective measures of balance and gait [18, 19]. Therefore, exercise-specific differences in efficacy may have been overlooked.

A recent review paper synthesized the effects of balance rehabilitation across the spectrum of PD disability [5]. This review systematically examined the impact of exercise interventions on balance outcomes on categories of disability defined by the World Health Organization in the International Classification of Functioning, Disability, and Health (ICF) model [20]. The ICF model categorizes outcomes according to 3 levels of human function: (1) "participation" includes problems an individual may experience in involvement in life situations (i.e., quality of life or falls) (2) "activity" is the execution of a task or action by an individual (i.e., performance during balance activities), and (3) "body structure and function" describes the physiologic function of various body systems (i.e., postural sway analysis). These authors found moderate evidence that exercise was effective for improving postural instability but only for the activity and body structure and function outcomes. They found limited evidence that exercise results in improvements in the participation level of function, such as quality of life measures or fall events.

While most clinicians believe that exercise improves function at all ICF levels in people with PD, there are many pressing questions remaining such as what are the most sensitive outcome measures at each ICF level for rehabilitation? What is the most effective type of exercise? For any of these questions to be satisfactorily and definitively addressed, it is critical that clinicians and researchers use sensitive outcome measures to adequately power a study and quantify change.

The purpose of this study was (1) to determine which ICF outcome measures were most sensitive to exercise intervention and (2) to explore the effects of two different therapeutic exercise programs for improving mobility in PD. This exploratory aim will be used to determine the number of subjects needed to directly compare exercise programs in a future trial. To this end, we compared 2 published programs: (1) an Agility Boot Camp program (ABC) [21] versus (2) an aerobic treadmill (TT) approach [8]. Both exercise programs were customized and progressive and carried out at the same frequency and intensity by a physical therapist. Both exercise programs were selected to be efficacious for gait mobility, but only the ABC approach focused specifically on balance-related mobility. We hypothesized that objective measures of mobility at the body structure/function level would be more sensitive than clinical measures of mobility activity and participation to distinguish efficacy between the two approaches.

Table 1: Participant characteristics.

Variables	Intervention groups		P value
	ABC	TT	
Age (yr)	65.7 ± 8.3	65.1 ± 7.3	0.70
Height (cm)	172.1 ± 8.0	175.0 ± 10.5	0.97
Weight (kg)	75.5 ± 16.3	81.8 ± 16.2	1.3
Gender	8 (F); 12 (M)	6 (F); 13 (M)	NA
UPDRS motor	33.4 ± 16.6	32.3 ± 13.8	0.72
H&Y	2.5 ± 0.8	2.4 ± 0.6	0.23

2. Methods

2.1. Design Overview. This study was a randomized, single-blinded intervention study for people with PD. Participants were randomized into one of two different exercise programs, ABC or TT. This trial was prospectively registered (NCT00982709) at http://clinicaltrials.gov/.

All participants came into outpatient physical therapy at Oregon Health & Science University for two baseline pretest visits (four weeks apart) then participated in an intensive progressive exercise program under the direct supervision of a physical therapist, followed by a posttest visit after the completion of the exercise program. Insurance was billed for exercise visits and participants were partially compensated for testing to help offset copayments. The same outcome measures were collected at all three testing sessions by examiners blinded to group assignment. All pre- and posttesting sessions were performed in the same order and rest breaks were given as needed to avoid fatigue. All participants took their PD medication as normally indicated and were tested in the on state at the same time of day before and after intervention.

2.2. Participants. Thirty-nine participants with idiopathic PD participated in the intervention with 20 randomized to ABC and 19 to TT intervention (Table 1). Participants were recruited from OHSU's Movement Disorders Clinic. Inclusion criteria included a diagnosis of idiopathic PD by a movement disorders neurologist, treatments with levodopa, between the ages of 45 and 85, and willing and able to come to the clinic 4 times per week for 4 weeks. Individuals were excluded from enrollment in the study if they were unable to ambulate unassisted, had other neurologic, cardiovascular, or orthopedic problems which could impact mobility, or had cognitive impairments that would limit participation in

the intervention. Participants agreed not to alter their current medications or independent exercise habits during the study, as able. 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).

2.3. Randomization and Intervention. The randomized group assignment was computer generated by an engineer in our laboratory, not associated with recruitment, study design, or implementation. All participants were assigned the same number of sessions (16 in total) for the same amount of time (75 minutes each session). These sessions took place four times per week for four consecutive weeks, under the direct instruction of one of four specially trained physical therapists. Fidelity of the intervention was maintained by unannounced observations and by having physical therapists document progression levels of training. Two of the physical therapists were trained in the ABC program and 2 were trained in the TT program. Analysis was done on intent-to-treat model.

2.4. Agility Boot Camp (ABC) Program. The theoretical basis for a novel, sensorimotor ABC exercise program is based on research from our laboratory and others that identified the primary neurophysiological constraints that limit balance and mobility in PD [21]. The exercises are designed as a circuit with 6 types of sports skill activities focused on improving basic postural systems: (1) pre-Pilates (2) kayaking to improve biomechanical constraints on joint flexibility, muscle strength, and postural alignment, (3) tai chi to improve kinesthesia and increase functional limits of stability, (4) boxing to improve anticipatory postural adjustments prior to stepping in multiple directions, (5) lunges to improve the speed and size of automatic stepping for postural correction, and (6) agility course to improve stability and coordination during gait challenged by quick changes in direction, avoiding or overcoming obstacles and simultaneously performing a secondary cognitive or motor task.

Each activity was engaged for 10 minutes with rest periods and systematically progressed from beginning to intermediate to advanced levels by challenging (1) sensory integration (altering vision and/or surface conditions), (2) adding a secondary, cognitive task, (3) limiting external cues, and (3) increasing speed and resistance. Cool-down activities at the completion of the circuit included adapted floor Pilates: stretching of flexors and rotators, strengthening of extensors, and practice of transitional activities such as rising from a chair, getting onto the floor, rolling, and coming to stand from the floor [22]. This program and levels of progression are detailed in a previous publication [21].

2.5. Treadmill Training (TT) Program. The TT followed a previously published exercise protocol that demonstrated improved measures of gait, mobility, and quality in life in individuals with PD [8]. This program consisted of fast walking on a treadmill for up to 30–45 min as tolerated per session, with an additional 10 minutes of warm-up and cool-down adapted Pilates, that was the same as the ABC arm. Treadmill intensity was started at 80% of each participant's natural, overground, gait velocity and was increased to 90% after a week. Natural gait velocity was measured at the beginning of each week with a stopwatch prior to each treadmill training by asking participants to walk 25 feet. From the third week of training, the treadmill speed was gradually increased to reach a goal of 5% to 10% above that week's overground walking speed. Participants were allowed to hold onto the railing to focus on gait training. Therapists encouraged participants to increase stride length and height and to keep their upper body erect during the training period but were not allowed to work with the patient on any direct aspects of balance, beyond that used for walking on a treadmill. Safety harnesses were worn at the discretion of the physical therapist and none of the participants used a body weight support harness.

All participants were instructed to take their anti-PD medications as normal during the exercise program. All participants were instructed not to change their anti-PD medications during the study if possible.

2.6. Outcome Measures. Outcome measures were classified at 3 levels (participation, activity, and body structure and function) according to the International Classification of Function and Disability (ICF) model.

2.6.1. Level 1 of ICF: Participation. To assess changes at the participation level, we used the Parkinson's Disease Questionnaire (PDQ-39) [23] for quality of life, the Activities of Balance Confidence Scale (ABC) [24], and the Activities of Daily Living from the Unified Parkinson's Disease Rating Scale (UPDRS Part II) [25]. The PDQ-39 is a frequently used, validated questionnaire that was designed as a tool for determining treatment effect on eight different domains in individuals with PD: mobility, activities of daily living, emotional well-being, stigma, social support, cognition, communication, and bodily discomfort. Each of the eight sections has a separate total score, on a scale of 0 (perfect health) to a maximum score of 100% (worse health). This scale has been found to be a valid and reliable way in which to measure quality of life for individuals with PD [26, 27]. The ABC is a reliable method for detecting loss of balance confidence in an aging population and for those with PD [28]. The test is comprised of sixteen questions that are averaged for one total score. A score of less than 68% indicates low mobility [24]. The UPDRS Activities of Daily Living is a 13-item questionnaire focusing on the effects of PD on activities of daily living [25].

2.6.2. Level 2 of ICF: Activity. To characterize changes at the activity level, we measured overall changes in balance, mobility function, and disease severity using the Mini-BESTest, Berg Balance Scale, and the UPDRS Part III. The Mini-BESTest test is a 14-item test that focuses on dynamic balance; specifically, anticipatory transitions, postural responses, sensory orientation, and dynamic gait. Each item is scored from 0 to 2; a score of 0 indicates that a person is unable to perform the task while a score of 2 is normal. The highest score, indicating no impairment, is 28 [29]. Berg Balance Scale is a 14-item clinical test that measures balance by assessing performance on specific functional tasks [30]. Each task

is scored from 0 to 4 (0: unable to 4: normal), for a maximum best score of 56 points. Scoring is based on criterion that is specific to each task. The UPDRS III [25] is a motor examination used to assess disease severity. This test has a maximum score of 108; each item is scored from 0 (not affected) to 4 (most severely affected). These clinical scales were categorized at the "activity" level because though they measure subcomponents on the impairment level (i.e., tremor, rigidity), it is not a physiologic assessment and the overall score is based on the execution of a task or action by an individual.

2.6.3. Level 3 of ICF: Body Structure and Function. To characterize body structure and function, we objectively measured gait and turning using the Instrumented Timed Up and Go (ITUG) [31] and balance during quiet standing with the Instrumented Sway (ISway) [32]. The participants wore a portable data-receiver (X-Bus) connected with wires to 6 MTX XSens sensors (49A33G15, XSens, Enschede, The Netherlands) positioned on (1) the posterior trunk at the level of L5, near the body center of mass, (2) one on the anterior shank of each leg, (3) one on the dorsum side of each arm, and (4) the sternum. The sensor recorded 3D accelerations and angular velocity while the controller wirelessly streamed data to a laptop via Bluetooth. A custom MATLAB [33] graphical interface was used to acquire and store data. Later, data were automatically analyzed using Mobility Lab software (APDM Inc., Portland, OR, USA) [34].

The ITUG involved instructing participants to stand up, walk over a tape on the ground 7 meters away, turn around, walk back, and sit down. ITUG uses automatic analysis algorithms from APDM's Mobility Lab to objectively calculate temporal and spatial gait metrics during straight ahead gait as well as turning metrics. In the present study, we calculated the median of 3 ITUG trials of the following metrics: stride velocity, peak arm speed, horizontal trunk range of motion, and turn duration [31]. These measures were chosen because previous studies suggest that they are sensitive to early PD [31] and they comprehensively characterize commonly impaired aspects of PD (slowed gait, slowed turns, decreased arm swing, and decreased trunk rotation during gait).

The ISway [32] involved instructing participants to stand with arms at their sides and looking straight ahead at an art poster for 30 seconds across 3 trials. The size of participants' stance was fixed and made consistent with a spacer block momentarily placed between the feet. ISway uses automatic analysis algorithms from APDM's Mobility Lab to objectively calculate amplitude, velocity, and frequency of sway during quiet standing. In the present study, we calculated the median of 3 ISway trials for the bidirectional range of sway.

2.7. Statistical Analysis. Subject characteristics between the two exercise groups were summarized with group means and compared with t-test to investigate any group differences. Stability of outcome measures during the two baseline measures 4 weeks apart was compared using intraclass correlation (ICC type (1, 1)). To determine the most sensitive outcome measures after exercise intervention, we calculated the standardized response mean (SRM) for each measure as well as paired t-tests to determine if statistical change occurred

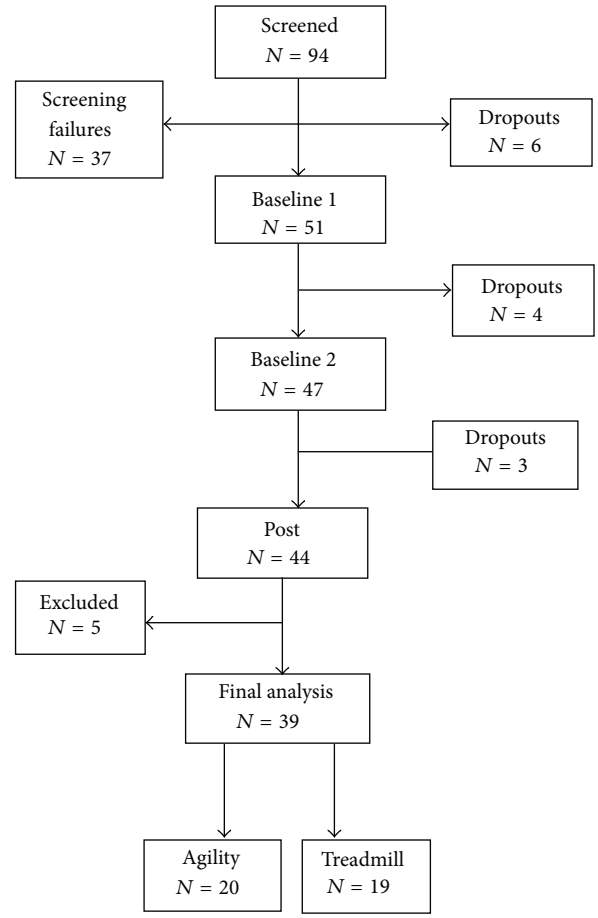


Figure 1: Consort diagram of recruitment and participation.

before and after intervention. SRM is the mean change (d) reported in units of standard deviation of change (SD_{diff}), $SRM = d/SD_{diff}$. For SRM, a value of 0.20 represents a small change, of 0.50 a moderate, and 0.80 represents a large change [35]. To compare the effects of the ABC versus the TT intervention, we used t-tests to evaluate the benefit of exercise (post minus pre exercise value) between the 2 programs. To determine the necessary number of subjects needed to distinguish benefits from the different exercise programs, we used the "pwr" package in R program for a power and sample size analysis. For power analysis a significance level of $\alpha = 0.05$ and a power $= 1 - \beta = 0.80$ were assumed.

3. Results

Of the 94 people recruited for the study, 37 did not meet inclusion criteria and were not scheduled for a study visit (Figure 1). Six people dropped out before the study began for reasons of convenience, distance to travel, or costs associated with participation. Seven more people dropped out during the course of the study for similar reasons. At the end of the study, 44 people completed the study. Five of these people were excluded from the analysis for the following reasons: one person was subsequently diagnosed with multiple systems atrophy with significant cognitive decline, 2 people had surgery

Table 2: Baseline stability of outcome measures.

Variables	ICC	Real difference ± SD
Participation		
PDQ-39	0.794	−4.6 ± 13.8
ABC	0.767	4.2 ± 11.3
UPDRS-ADL	0.914	−0.3 ± 2.6
Activity		
Mini-BESTest	0.879	0.9 ± 3.2
Berg Balance Scale	0.951	−0.3 ± 3.0
UPDRS motor	0.917	−0.9 ± 6.1
Body structure and function		
Turn duration	0.827	−0.1 ± 0.4
Stride velocity	0.886	0.03 ± 5.1
Peak arm speed	0.802	4.5 ± 40.1
ROM trunk horizontal	0.889	−0.2 ± 0.9
Sway range	0.695	−0.01 ± 0.17

during the course of the study, 1 person was unable to ambulate without her walker during the pretest, and 1 person had a medication change during the course of the study. The target number of visits for this intervention was 16 exercise sessions over the course of four weeks. However, due to the logistics of coordinating with rehabilitation services, standard-of-care, and insurance policies, the average number of intervention visits prior to posttesting was 16 ± 1 visits.

Adverse events: no soreness or musculoskeletal complaints were reported. One participant fell during lateral stepping during an ABC training session but no injury occurred. No other adverse events were reported.

Baseline characteristics of the participants are shown in Table 1. No statistical differences were found in baseline characteristics between the 2 intervention groups.

4. Stability of Outcome Measures over 4 Weeks without Intervention

All of the outcome measures were stable prior to intervention. The ICCs between two baseline measures taken 4 weeks apart were all above 0.7 and there was no significant difference between baseline measures. Table 2 provides ICC values for each outcome measure for the 2 baseline tests. Each section of PDQ39 is detailed in Table 4.

5. Responsiveness of Outcome Measures to Exercise

To determine which measures were most responsive to intense exercise intervention, we initially grouped all subjects together, regardless of exercise intervention assignment, to obtain a higher power. We found that 4 out of 5 measures in the body structure and function ICF level improved, 2 of 3 measures in the activity level improved, and just 1 of 3 measures in the participation level improved after 4 weeks of exercise (Table 3).

6. Which Measures Distinguish between ABC and TT Intervention?

Both groups improved in numerous measures similarly but only one measure, at the body structure and function ICF level (sway range, Figure 2), showed a significant interaction effect for the different outcomes of the exercise programs ($F = 4.95$; $P = 0.03$).

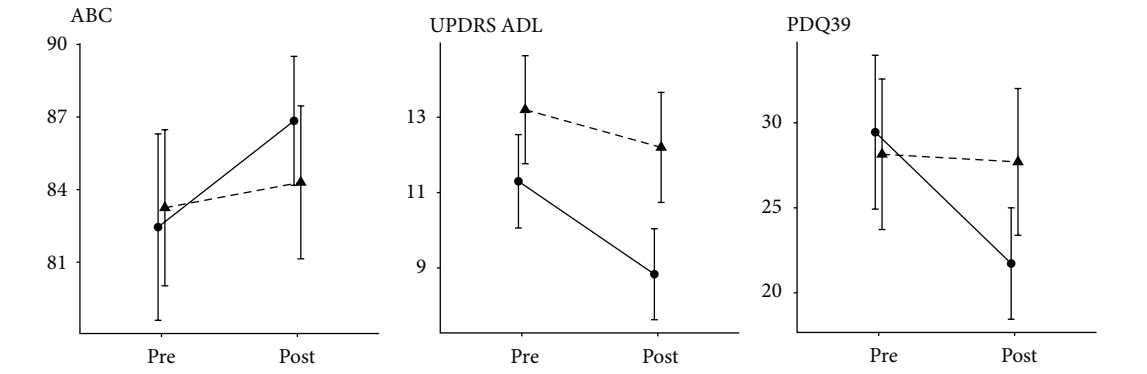
Though this study was not powered to detect a difference in outcomes between the two short exercise intervention programs, we saw trends suggesting that the ABC program may result in greater improvement for many outcomes (Figure 2). t-tests were performed on the groups separately. The ABC group significantly improved in balance (Mini-BESTest $t = -3.1$; $P = 0.007$), gait (stride velocity $t = -2.27$; $P = 0.04$), peak arm speed ($t = -3.31$; $P = 0.004$), and ROM of trunk during gait ($t = -2.48$; $P = 0.02$). The TT group improved in balance (Mini-BESTest $t = -2.7$; $P = 0.01$), gait (stride velocity $t = -2.97$; $P = 0.01$), and peak arm speed ($t = -3.25$; $P = 0.005$).

6.1. Power Analysis Depends on Outcome Measure. In our study, the 3 outcome measures that showed the most promising ability to detect a change between the ABC and the TT program were (1) range of postural sway, (2) the Mini-BESTest, and (3) ROM of the trunk during gait. A power analysis revealed that to detect program differences, one would need 33 people when using sway as an outcome measure for balance, 273 people when using ROM of the trunk during gait, and 283 people if using the Mini-BESTest. All other outcome measures required greater than 1000 people to detect a programmatic difference due to small effect sizes.

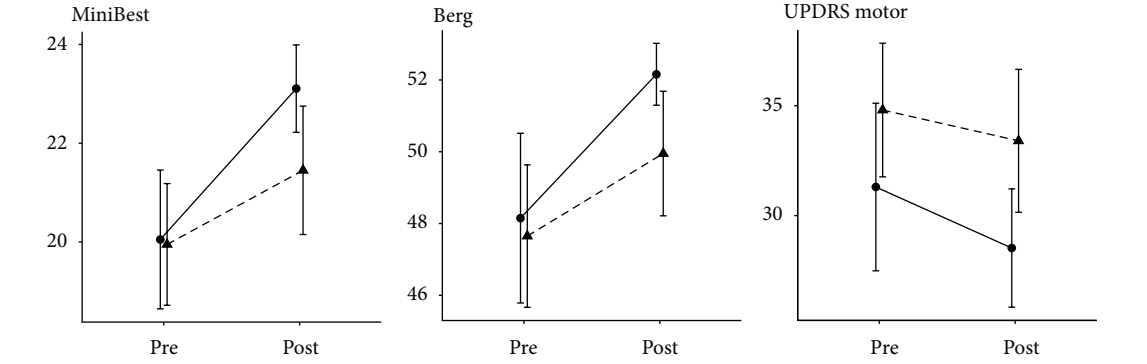
7. Discussion

The main finding of this study is that improvement after exercise intervention was most readily measured at the body structure and function level of the ICF. Only sway range during quiet stance differentiated outcomes for the 2 short-term, high-frequency mobility intervention programs. Despite different rehabilitation focus, aimed at either dynamic balance for agility (ABC intervention) or aerobic treadmill training (TT intervention), people with PD showed similar improvements on many clinical measures.

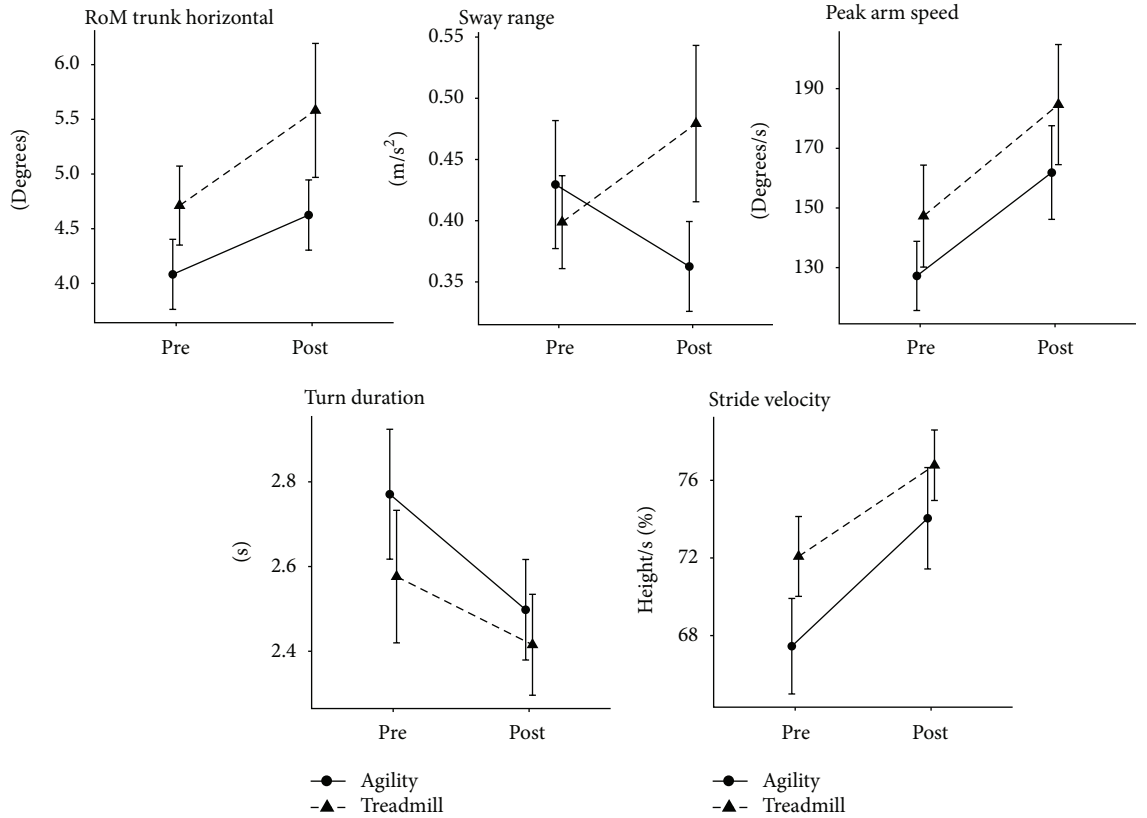
The importance of sensitive, specific outcome measures for clinical trials and clinical practice cannot be underestimated. Though this study was underpowered to see differences between programs with a direct comparison, our results showed trends suggesting that a greater number of outcome measures improved after ABC exercise than treadmill. The only measures with an interaction effect was postural sway which decreased after ABC exercise. Postural sway is considered a sensitive measure of balance and though increased sway is associated with falls in the literature, it is not a measure typically assessed in the clinic. The findings from our study suggest that an important reason for a lack of obvious difference between different types of rehabilitation program effectiveness, both in our study and in the literature, may be



(a) Participation



(b) Activity



(c) Body structure and function

Figure 2: Pre- to Postintervention plots for each exercise group, Agility Boot Camp and treadmill intervention, for each variable according to International Classification of Function and Disability.

Table 3: The effects of exercise intervention for each category of ICF.

Variables	Pre- mean (SD)	Post- mean (SD)	SRM	*P* value
		Participation		
PDQ-39	28.8 ± 19.8	24.9 ± 17.0	−0.331	0.127
ABC	82.9 ± 15.7	85.5 ± 12.9	0.319	0.152
UPDRS-ADL	12.3 ± 6.00	10.6 ± 6.07	−0.531	**0.021***
		Activity		
Mini-BESTest	20.0 ± 5.83	22.3 ± 4.97	0.814	**0.001*****
Berg Balance Scale	47.9 ± 9.64	51.0 ± 6.17	0.649	**0.004****
UPDRS motor	33.1 ± 15.3	31.1 ± 13.3	−0.304	0.255
		Body structure and function		
Turn duration	2.68 ± 0.66	2.46 ± 0.50	−0.609	**0.030***
Stride velocity	69.6 ± 9.88	75.3 ± 9.71	0.772	**0.001*****
Peak Arm Speed	137 ± 60.7	173 ± 75.4	0.986	**0.001*****
ROM trunk horizontal	4.38 ± 1.45	5.07 ± 2.04	0.523	**0.019****
Sway range	0.41 ± 0.19	0.42 ± 0.23	0.051	0.406

*Significance at the 0.05 level.
**Significance at the 0.01 level.
***Significance at the 0.001 level.

Table 4: Effects of exercise on the PDQ-39 subsections.

Variables	Pre- mean (SD)	Post- mean (SD)	SRM	*P* value
PDQ-39 total	28.8 ± 19.8	24.9 ± 17.0	−0.33	0.127
PDQ mobility	8.05 ± 8.06	6.31 ± 6.47	−0.37	**0.09**
PDQ ADL	5.28 ± 4.44	3.92 ± 3.77	−0.49	**0.01****
PDQ emotional	4.18 ± 3.54	4.13 ± 3.53	−0.02	0.85
PDQ stigma	2.23 ± 2.33	2.08 ± 2.15	−0.05	0.72
PDQ social	0.88 ± 1.14	0.87 ± 1.17	−0.01	0.44
PDQ cognitive	2.88 ± 2.37	2.71 ± 2.13	−0.09	0.78
PDQ communication	2.30 ± 2.15	2.03 ± 1.90	−0.15	0.49
PDQ discomfort	3.03 ± 2.27	2.82 ± 2.12	−0.12	0.51

**Significance at the 0.01 level.

due to insensitive outcome measures, underpowered studies, or both.

Most exercise intervention studies do not find differences in outcomes when comparing two potentially efficacious physical therapy interventions. For example, both the SCILTS and the LEAPS trials found that conventional, overground walking in rehabilitation of people with spinal cord injury (SCILT) and conventional, home-based exercise for people with stroke (LEAPS) produced similar results compared to people using advanced technology involving the bodyweight supported treadmill training [36, 37]. Dobkin and Duncan [38] published a review of robotic-assisted stepping devices and bodyweight-supported treadmill and revealed little solid evidence that such approaches are more beneficial than standard of care in physical therapy [38]. The primary outcome measures for these studies were primarily standard noninstrumented scales used in the clinic such as the Berg Balance Scale, Functional Independence Measures, and overground walking speed with a stopwatch. These clinical measures may not be sensitive enough to detect differences between types of intervention. Further analysis revealed that more than 1000 people would be needed to possibly show a difference between the interventions in the SCILT trial [38].

Also of note is that the UPDRS did not change in either our ABC or TT group after exercise. While this was not surprising since one would not expect 4 weeks of exercise to significantly change many motor signs measured in the UPDRS (hand movements, tremor, speech, and facial expression), it is important since many studies of exercise intervention for PD use the UPDRS as an outcome measure [2, 6, 7]. However, a very long duration, 12-month, 2 times per week agility intervention based on therapeutic tango lessons, showed a significant improvement in the UPDRS in the off state [39]. The on levodopa state was not tested.

The main focus of the ABC program was practicing to control body center of mass during a variety of tasks with a moving base of support and under a variety of sensory and cognitive challenges. For example, the ABC group practiced lunges with big steps and progressed to lunging without visual feedback or while performing a dual task. This group did not specifically practice walking or sway during quiet stance. Therefore, our results suggest that the participants in the ABC group were able to control their center of mass

more efficiently; even in conditions they did not practice, indicating a carryover of skills to new tasks. Similarly, the TT group improved in balance scores that were not specifically practiced during gait training. It can be argued, however, that walking on a treadmill, especially without use of handrails as they progressed, required balance control so this group may have had dynamic balance training as well. The results may represent a specificity of training effect since the ABC program was designed to target underlying impairments, perhaps similar to what is tested at the function/structure level. Similarly, perhaps there was no difference between groups at the activity level because both groups addressed some aspects of balance and gait leading to improvements in these areas across both groups.

One limitation of this study is that the study design prevented us from calculating the minimal detectable change for our measurements. The time between repeated measures before intervention was too long to reliably measure the minimal detectable change. This information would be valuable in future studies, particularly for the new, instrumented measures that have not been documented. Though the exercise sessions were frequent and for longer duration per session than traditional physical therapy sessions, the overall timeline of exercise intervention was relatively short (4 weeks). The design of our study included people who were coming in for therapy, billing to insurance. This may have biased our sample since people without insurance or certain types of insurance could not participate. Similarly, our participants came in for exercise 4 times per week for 75 min, precluding those people with very poor endurance or who had difficulty leaving their homes to travel to the clinic. This frequency was chosen in the design in order to maximize improvements in a short duration since we were unable to carry out a long-term study. Our participants were relatively of high-level functioning so it may be more difficult to detect change after exercise compared to people with less mobility. Because each person participating had to pay a copayment each visit, it was an expensive way to administer an intense exercise program. Future studies should investigate less expensive group classes.

8. Conclusions

This study suggests that future randomized clinical trials of mobility intervention should include objective measures of balance and gait at the body structure and function level of the ICF to distinguish between two types of physical therapy intervention with reasonable size groups. Physical therapists in the clinic, however, should consider using responsive, objective outcomes at each of the ICF levels to help direct their intervention and document change. Outcome measures should be used strategically to help therapists understand what is and what is not changing after intervention and appropriate outcomes with frequent measures can help guide therapeutic intervention.

Disclosure

OHSU, Dr. F. Horak, and Dr. A. Salarian have a significant financial interest in APDM, a company that may have a commercial interest in the results of this research and technology. This potential institutional and individual conflict has been reviewed and managed by OHSU.

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Research Article

Housing and Health: Very Old People with Self-Reported Parkinson's Disease versus Controls

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Objectives. To explore whether aspects of housing and health among very old people with self-reported Parkinson's disease (PD) differ from matched controls. *Methods.* Data from the ENABLE-AGE Survey Study were used to identify people with self-reported PD ($n = 20$) and three matched controls/individual ($n = 60$). The matching criteria were age (mean = 82 years), sex, country, and type of housing. The analyses targeted problems in activities of daily living, objective and perceived aspects of housing, for example, number of environmental barriers, accessibility (i.e., person-environment fit), and usability. *Results.* The number of physical environmental barriers did not differ ($P = 0.727$) between the samples. The PD sample had more ($P < 0.001$) accessibility problems than controls and perceived their homes as less ($P = 0.003$) usable in relation to activities. They were less independent and had more functional limitations (median 5 versus 2; $P < 0.001$), and 70% experienced loss of stamina or poor balance. *Conclusions.* Due to the fact that they have more functional limitations than very old people in general, those with self-reported PD live in housing with more accessibility problems. This explorative study has implications for rehabilitation as well as societal planning, but larger studies including people with a confirmed PD diagnosis are needed.

1. Introduction

An increasing proportion of very old people remain living in their ordinary homes despite declines in health. With an increased life expectancy for the general population and for those living with chronic diseases, this poses major challenges to rehabilitation as well as societal planning and housing development [1, 2]. Although Parkinson's disease (PD) is typical for old age, older people with PD are often excluded in research [3]. The knowledge on the life situation of those ageing with PD is therefore insufficient, and little is known about their housing and health situation. In order to develop more efficient rehabilitation strategies for those living with a chronic disease during many years, such knowledge is needed.

In PD research, most studies are based on hospital-based samples excluding old and very old people [3], with attention mainly to disease-specific outcomes. Using such selected samples with no consideration to contextual factors is quite insufficient. According to the International Classification of Functioning, Disability, and Health (ICF) [4], environmental factors influence activity and participation. Examples of physical environmental barriers in the housing environment and in its close exterior surroundings are high thresholds; wall-mounted kitchen cupboards and shelves placed extremely high, and no/too few seating places along walking paths. Environmental barriers constitute one of the two components of accessibility, a relative concept implying that accessibility problems should be expressed as a person-environment (P-E) relationship [5]. In other words, accessibility is the encounter between the functional capacity of the individual (personal component) and the design and demands of the physical environment (environmental component). Most important, the environmental component of accessibility refers to compliance with official standards for design of the built environment. Thus, accessibility is an objective concept [5]. To enable participation in life situations, the recently published World Disability Report stresses

the need for focusing on accessibility issues and environmental barriers [6]. Turning to the concept of usability, it implies that a person should be able to use, that is, to move around, be in, and use, the environment on equal terms with other citizens [5]. Accessibility is a necessary precondition for usability, which takes user perceptions into account. Usability is thus mainly subjective in nature. Most important, there is a third component distinguishing usability from accessibility, that is, the activity component [5]. In order to deliver efficient interventions, rehabilitation approaches that take contextual factors into account are imperative. The majority of PD studies have addressed body functions in contrast to activity, participation, and contextual factors. Consequently, little is known about the relationship between contextual factors and activity, participation, and health factors in people with PD.

Major gerontology studies are often based on population samples applying perspectives and methodologies quite different from those of neuroscience and rehabilitation. When it comes to theoretical foundations, the model most often referred to is Lawton's ecological theory of ageing (ETA) [7, 8] in which the person is defined in terms of a set of competencies and the environment is defined in terms of press. Thus, person-environment fit (P-E fit) comprises two interactive components: the personal component and the environmental component. In the ETA, P-E fit is a prerequisite for the matching between the personal component and environmental component, denoted "adaptation." Manifested in real life situations, performance of activities of daily living (ADL) is one important aspect of adaptation [9]. When health declines in very old age, the environmental pressure often exceeds the personal capacities, resulting in more P-E fit problems and negative health outcomes. Based on the notion of P-E fit, research on housing and health in old age considers contextual factors such as objective and perceived aspects of housing [10–12]. Besides usability, perceived aspects of housing such as housing satisfaction, meaning of home, and housing-related control beliefs are related to health in very old age [10–12]. Targeting such aspects represents a quite novel approach for PD research, and the knowledge of the situation of very old people with PD in comparison with very old people in general is virtually nonexisting. Consequently, this study aimed at exploring aspects of housing and health in ordinary housing among very old people with self-reported PD as compared to matched controls. The following general hypotheses guided the study.

(i) Since ordinary housing displays great diversity in design, there is no reason to believe that very old people with PD live in dwellings with a different number of environmental barriers than very old people in general.

(ii) There is reason to assume that very old people with PD have more functional limitations and use mobility devices to a greater extent than very old people in general, resulting in more housing accessibility problems.

(iii) Since usability considers activity performance, it might be rated lower by very old people with PD than by very old people in general. As to other perceived aspects of housing, there is less reason to assume that very old people with PD differ from others.

Table 1: Sample characteristics: very old people reporting having Parkinson's disease (PD) ($n = 20$) and controls not reporting having PD ($n = 60$).

Variable	PD, $n = 20$	Controls, $n = 60$
Age, mean (SD, min–max)[a]	82 (3.6, 76–90)	82 (3.6, 76–91)
Sex, n women/men (% women)[a]	15/5 (75)	45/15 (75)
Country, n (%)[a]		
Germany	4 (20)	12 (20)
Hungary	7 (35)	21 (35)
Latvia	4 (20)	12 (20)
Sweden	1 (5)	3 (5)
United Kingdom	4 (20)	12 (20)
Type of housing, n (%)[a]		
Multidwelling block	16 (80)	48 (80)
One-family house	2 (10)	6 (10)
Semidetached/two-family house	1 (5)	3 (5)
Other	1 (5)	3 (5)

[a]Matching variable.

2. Participants and Methods

2.1. Project Context. This study is based on data from the ENABLE-AGE Survey Study [10], gathered in Sweden, Germany, the United Kingdom, Hungary, and Latvia. The target sample in each country was very old people (75–89 years), living in single-person households in urban areas. The total sample included 1,918 participants (78% women). The study was conducted in accordance with the Declaration of Helsinki; all participants were enrolled after informed consent, following the ethical guidelines of each country. After training, interviewers collected data at home visits [13]. Details on the ENABLE-AGE have been published elsewhere (see, e.g., [10, 12]).

2.2. Study Samples. The present study is a cross-sectional comparison between two subsamples retrieved from the ENABLE-AGE database; one sample of individuals, responding to structured questions based on the ICD-10, reported having PD (PD sample) versus a matched control sample (for characteristics see Table 1). Twenty-one individuals with self-reported PD were identified, but one Hungarian woman was excluded due to extensive missing data. The final PD sample consisted of 20 individuals (15 women and 5 men; mean age 82 years).

Each individual reporting having PD was individually matched with three controls [14] from the ENABLE-AGE database. The matching criteria were sex, country, age (± one year), and type of housing (Table 1). By means of the software R version 2.12.1 (R Development Core Team, 2010), the three controls were randomly selected among all individuals fulfilling the matching criteria [14]. The matched control

sample included 60 individuals (45 women and 15 men; mean age 82 years).

2.3. Instruments. All included instruments fulfilled basic criteria for reliability and validity (for details, see publications referred to below). For project-specific instruments, an inter-rater reliability study [15] and psychometric analyses were accomplished [16].

2.4. Aspects of Housing. Objective housing was operationalized as the number of environmental barriers in the home and the magnitude of accessibility problems, assessed using the Housing Enabler (HE) [17]. With this instrument, accessibility is assessed by professionals, based on the notion of P-E fit [7]. The administration of the HE contains three steps.

Step 1. Representing the personal component of P-E fit: Interview and observation of a profile of functional limitations (13 items) and dependence on mobility devices (2 items: dependence on walking devices and/or wheelchair), all dichotomously assessed (no/yes). The 13 items that target functional limitations are difficulty in interpreting information; visual impairment; blindness; loss of hearing; poor balance; incoordination; limitations of stamina; difficulties in moving head; reduced upper extremity function; reduced fine motor skill; loss of upper extremity skills; reduced spine and/or lower extremity function; extremes of size and weight.

Step 2. Representing the environmental component of P-E fit: Observation and dichotomous assessment (no/yes) of 188 physical environmental barriers in the home and the immediate outdoor environment. Step 2 generates the variable "number of environmental barriers."

Step 3. Representing the facet of P-E fit denoted accessibility: Based on the assessments in Steps 1 and 2, by means of a complex matrix procedure with predefined 0–4 scores, a total accessibility score is computed by means of special software (for details, see [17]). Thus, the variable accessibility is operationalized as the magnitude of accessibility (P-E fit) problems caused by the case-specific combination of functional limitations/dependence on mobility devices and environmental barriers; higher scores = more accessibility problems. In cases with no functional limitations/dependence on mobility devices, the accessibility score is 0.

Perceived aspects of housing were captured by means of the four-domain model of perceived housing [16], based on self-ratings. The four domains include housing satisfaction (i.e., in relation to physical housing conditions), usability in the home, the meaning of home, and housing-related control beliefs. Housing satisfaction was assessed by using the single item: "Are you happy with the condition of your home?" with response options ranging from 1 ("definitely not") to 5 ("yes, definitely"). With the Usability in My Home Questionnaire (UIMH), the participant evaluates the degree to which the physical housing environment supports activity performance at home. In the present study, the subscales "activity aspects" (4 items) and "physical environmental aspects" (6 items) were used. Items are rated from 0 ("not at all") to 5 ("fully agree"); higher scores denote higher usability. The Meaning of Home Questionnaire was used to rate the physical (7 items), behavioral (6 items), and cognitive/emotional (10 items) aspects of bonding/attachment to the home. Each statement is rated from 0 ("strongly agree") to 10 ("strongly disagree"); higher scores mirror a stronger bonding/attachment. Finally, we used the combined external control subscale (16 items, rated from 1 = "not at all" to 5 = "very much") of the Housing-related Control Beliefs Questionnaire. External control means either that some other person, luck, chance, or fate are responsible for events or things that happen. For further details and original references to the specific instruments, see [16].

2.5. Aspects of Health. Representing the outcome of adaptation as manifested in real life situations [9], ADL problems were captured and assessed by professionals as well as by means of self-ratings. Independence in daily activities was assessed by professionals through interview and observation using the ADL Staircase [18]. This instrument comprises five personal ADL (P-ADL: feeding, transferring, going to the toilet, dressing, and bathing) and four instrumental ADL (I-ADL: cooking, transportation, shopping, and cleaning). The assessment captures dependence on assistance from another person during activity performance (rated as independent/partly dependent/dependent). For all ADL items scored as "independent," the interviewer also asked a project-specific dichotomous (Yes/No) question: "Even if you manage on your own, do you experience any difficulty when performing. . .?" The nine items were dichotomized as follows: dependent, partly dependent or having difficulties (1)/independent, and with no difficulties (0). Perceived independence in daily activities was captured by a single item: "All in all, how would you evaluate your own independence, that is, in performing activities of daily living?" [16]. The response options range from 0 ("completely dependent") to 10 ("completely independent").

The variables number of functional limitations and use of mobility devices (Yes/No) were retrieved from Step 1 of the HE [17]. Self-perceived health was rated using the global item from the SF-36 [19]: "In general would you say your health is. . .?", rated from 1 ("excellent") to 5 ("poor"). Depressive symptoms were dichotomously assessed with the 15-item version of the Geriatric Depression Scale (GDS) [20].

2.6. Data Analysis. Internal missing was treated in the following way. If there was a missing value for one of the individuals reporting PD, all the controls belonging to that individual were also excluded from that particular analysis. If there was a missing value for one or two of the controls, the individual reporting PD and the remaining controls were included in the analysis. Missing data are reported in Tables 2 and 3.

All dichotomous variables were compared using the Mantel-Haenszel test, with continuity correction, which takes the matching with multiple controls into account. These tests were performed using SPSS Statistics 18 for Windows (IBM Corporation, Somers, NY, USA). For ordinal scores, we

Table 2: Comparison of aspects of housing between very old people reporting having Parkinson's disease (PD) (n = 20) and controls not reporting having PD (n = 60).

Variable	PD, n = 20		Controls, n = 60		
	Median	q1–q3	Median	q1–q3	P value[a]
Number of environmental barriers, (HE)	48	36–61	52	34–63	0.727
Accessibility, (HE)	192	112–232	63	14–128	<0.001
Usability (UIMH)					
(i) Activity aspects[b,c]	3.8	3-5	5	4.3–5	0.003
(ii) Physical environmental aspects[b]	4.1	3.4–4.8	4.3	3.6–5	0.600
Meaning of home (MOH)					
(i) Physical bonding[b,c]	7	5.3–8.9	8.6	6.9–8.9	0.018
(ii) Behavioral bonding[c]	7	4.8–8.6	8.8	7.3–10	<0.001
(iii) Cognitive, emotional bonding[b,c]	8	7.1–9.4	8.2	7.4–9	0.444
External housing-related control beliefs (HCQ)[b,c]	2.7	2.1–3.4	2.8	2.1–3.2	0.867
Housing satisfaction[c]	5	4-5	5	4-5	0.114

Decimals are only given when rounding was needed.
[a]A version of Wilcoxon signed rank test extended to include multiple controls was used.
[b]For these variables the PD sample had missing values (for 1 to 2 participants); the number of controls was reduced accordingly.
[c]For these variables some of the controls had missing values (for 1 to 4 participants).
HE: Housing Enabler; higher accessibility scores mean more accessibility (person-environment fit) problems (range 0 to >2000; theoretically but never reached in reality). UIMH: Usability In My Home; higher scores are positive. MOH: Meaning of Home Questionnaire; higher scores mean stronger attachment to the home. HCQ: Housing-Related Control Beliefs Questionnaire; higher scores indicate more external control. Housing satisfaction is rated from 1 (no, definitely not) to 5 (yes, definitely).

Table 3: Comparison of aspects of health between very old people reporting having Parkinson's disease (PD) (n = 20) and controls not reporting having PD (n = 60).

	PD, n = 20		Controls, n = 60		
	n	%	n	%	P value[a]
ADL Staircase item[b]					
(1) Feeding	7/20	35	2/60	3	0.001
(2) Transfer	10/20	50	13/60	22	0.047
(3) Toileting	7/20	35	3/60	5	0.003
(4) Dressing	10/20	50	15/60	25	0.074
(5) Bathing	14/20	70	23/60	38	0.017
(6) Cooking	12/20	60	15/60	25	0.017
(7) Transportation	14/18	78	21/53	40	0.017
(8) Shopping	16/19	84	29/57	51	0.035
(9) Cleaning	17/19	90	41/57	72	0.206
Personal ADL (items 1–5)[b,c]	6/20	30	0/60	0	<0.001
Instrumental ADL (items 6–9)[b,c]	9/18	50	9/53	17	0.011
Dependence on walking aids (HE)	10/20	50	12/60	20	0.018
	Median (q1–q3)		Median (q1–q3)		
Self-rated functional independence[d]	5 (5–7)		8 (7–10)		<0.001
Number of functional limitations (HE)[e]	5 (4–7)		2 (1–4)		<0.001
Depression (GDS)[f]	6.5 (3.1–9.8)		4 (2.1–6.9)		0.048

[a]Dichotomous variables were compared using the Mantel-Haenszel test, with continuity correction. Sum-scores/ordinal variables were compared using a version of Wilcoxon signed rank test extended to include multiple controls.
[b]Assessed as dependent or partly dependent, or reporting having difficulties.
[c]The results refer to being dependent or reporting having difficulties in all personal or instrumental ADLs, respectively.
[d]Higher scores are "better," that is, more independent.
[e]In both samples, the three most common functional limitations were reduced spine and/or lower extremity function, loss of stamina, and prevalence of poor balance.
[f]Higher scores are "worse," that is, more depression.
ADL: Activities of Daily Living; HE: Housing Enabler; GDS: Geriatric Depression Scale.

applied a version of Wilcoxon signed rank test extended to include the multiple controls [21]. For these tests, P values were obtained using Monte Carlo simulations in the R-programming environment, version 2.12.1. Given the exploratory nature of this study, no correction for multiple tests was applied; that is, results with P values <0.05 were considered statistically significant.

3. Results

3.1. Aspects of Housing. Regarding objective aspects of housing (Table 2), the number of environmental barriers in the home did not differ significantly ($P = 0.727$) between the two samples. Turning to accessibility (P-E fit) problems, the participants in the PD sample had significantly ($P < 0.001$) more problems than the controls; that is, the median (q1–q3) scores were 192 (112–232) versus 63 (14–28).

Regarding perceived aspects of housing (Table 2), the participants in the PD sample reported their home as less usable in relation to activities ($P = 0.003$), but the two samples did not differ ($P = 0.600$) regarding physical environmental aspects of usability. The participants in the PD sample were less attached to their home in relation to physical ($P = 0.018$) and behavioural ($P < 0.001$) aspects of meaning of home than the controls, while there was no difference ($P = 0.444$) regarding cognitive/emotional aspects (Table 2). External housing-related control beliefs ($P = 0.867$) and housing satisfaction ($P = 0.114$) showed no significant differences between the two samples (Table 2).

3.2. Aspects of Health. The participants with self-reported PD were more ($P = 0.018$) dependent on walking aids than the controls (Table 3), that is, 10/20 (50%) versus 12/60 (20%). Their total number of functional limitations was also significantly ($P < 0.001$) higher (Table 3). In the PD sample, the three most common functional limitations were reduced spine and/or lower extremity function (18 out of 20; 90% versus 67% in controls), poor balance (14/20; 70% versus 28% in controls), and loss of stamina (14/20; 70% versus 47% in controls); see also footnote in Table 3. In the PD sample, the vast majority of those having reduced spine and/or lower extremity function also had loss of stamina (13/18; 72%) and poor balance (12/18; 67%).

For six out of the nine ADLs, there were statistically significant differences between the two samples (Table 3) with the PD sample demonstrating more ADL problems; that is, they were more dependent or reported having more difficulties. In the activities transfer, dressing and cleaning, there were no statistically significant differences. More participants in the PD sample were dependent in all four I-ADLs ($P = 0.011$) and in all five P-ADLs, $P < 0.001$ (Table 3). Self-ratings of functional independence showed that those in the PD sample perceived themselves as less ($P < 0.001$) independent than the controls (Table 3).

In both samples, the participants rated in median their general health as "fair" (i.e., 4: $P = 0.190$), and q1–q3 were 3–5 ("good"–"poor") for the PD sample and 3-4 ("good"-"fair") for the control sample. The participants in the PD sample reported significantly ($P = 0.048$) more depression symptoms than the controls (Table 3).

4. Discussion

As stated in the general hypothesis that guided the present study, the main results indicate that very old people with self-reported PD live in housing with more accessibility problems and experience less usability of their home than matched controls. At the same time, they seem to be less attached to their home although housing satisfaction and perceived control over their housing situation do not statistically differ. Even if this exploratory study is based on a small sample of participants with self-reported PD, it rests on solid methodology [10, 12, 16, 17], well acknowledged in research on ageing. Since this type of research has yet not been seen in PD, the knowledge contribution of this explorative study is substantive.

Although the present study shows that very old people with self-reported PD live in housing situations with more accessibility (P-E fit) problems, there was no statistically significant difference between the PD sample and the controls regarding number of environmental barriers (Table 2). This highlights the fact that the accessibility (P-E fit) problems were generated by the higher number of functional limitations and more use of walking aids in the PD sample (Table 3). This is in line with previous studies (see, e.g., [12, 22]), and supports the basic notion of P-E fit as described in the ETA [7].

While seldom at target in PD research, in rehabilitation research and clinical settings an explicit attention to contextual factors is imperative; that is, focusing on accessibility issues and environmental barriers is imperative in order to enable activity and participation [6]. For example, by means of reduction of accessibility problems (i.e., by strengthening of the functional capacity of the individual or/and by removing environmental barriers), the usability of the home, manifested in self-perceived reduction of ADL problems, might be improved. In order to reduce accessibility problems among very old people with PD, our results suggest that rehabilitation primarily should target independence in walking, reduced spine and lower extremity function, limitations of stamina, and balance problems. A recent Cochrane review concluded that physical therapy significantly improves outcomes of walking, mobility, and balance as compared with no intervention [23]. The treatment effects were, however, generally small and the majority of studies had a short follow-up period. It should be noted that there is a lack of rehabilitation studies that target very old people with PD. This is highly warranted due to the increased life expectancy of the general population and for those living with chronic diseases, but also since older people with PD are often excluded in research [3].

Our finding that very old people with self-reported PD live in housing with more accessibility problems should be seriously considered, not the least since people with PD have an increased risk for falls even at a younger age [24]. Thus, the P-E fit perspective is highly relevant for research and

fall prevention in PD. According to a previous study [22], accessibility (P-E fit) problems are more common among very old people who fall than among nonfallers, and also a stronger predictor for falls than the number of environmental barriers per se. This suggests that fall prevention in the home should target P-E fit and not only environmental barriers, with a specific attention on strengthening the functional capacity of the individual, that is, the personal component of P-E fit. A prior study showed that the most common functional limitations in very old people were reduced spine and/or lower extremity function, limitations of stamina, and poor balance [25]. Although the same top three functional limitations were identified for the PD sample, the prevalence was higher among very old people with self-reported PD than for matched controls (e.g., poor balance: 70% versus 28%). Consequently, individualized approaches might be more efficient than removing environmental barriers based on traditional fall risk hazard checklists; that is, based on a decomposition of the individual accessibility (P-E fit) score generated by the HE [17], fall risks could be eliminated by a case-specific, targeted elimination of the environmental barriers that in relation to the individual profile of functional limitations generate the most severe accessibility (P-E fit) problems. Such an analysis is easily accomplished by means of the HE software. However, it should be noted that based on the definition of accessibility (P-E fit) [7] that underpins the HE [17], physical environmental barriers are assessed based on standards and guidelines for housing design. Removing barriers based on these might not be sufficient from the individual perspective; that is, the housing design features specified in the existing standards and guidelines may nevertheless generate problems for individuals with more complex profiles of functional limitations [26]. Therefore, more research is needed on housing accessibility among people with neurological disorders.

Further, the present results suggest that very old people with PD are less attached to their home in physical and behavioural aspects than very old people in general. Earlier studies show that a strong bonding to home facilitates coping with ADL difficulties [16], whereas a weak bonding relates to a higher magnitude of accessibility problems [27]. In other words, in the present study those reporting having PD were probably less attached to their home due to having more accessibility problems [27]. If reducing the accessibility problems in their housing situation, it may be speculated that a stronger bonding to home could strengthen their ability to cope with ADL difficulties [16].

Regarding aspects of health, the results are as could be expected, and thus in line with what we hypothesized; that is, very old people with self-reported PD are less independent, have more functional limitations, and are more dependent on walking aids (Table 3). This is not surprising since gait and balance problems (including falls and fear of falling) are common among people with PD [24, 28, 29], and ADLs are affected already in de novo PD [30]. Demonstrating the relevance of studying aspect of housing and health among people with PD, it should be noted that dependence on others for ADL has been shown to be a predictor of relocation to assisted living [31]. This is of specific importance since people with PD are more likely to be placed in assisted living, causing high costs to society [1].

There are study limitations and challenges that need to be kept in mind when interpreting our results. First of all, the population-based sample was based on self-reported PD, and, consequently, we lack clinical data describing PD severity and disease-specific problems. We do, however, have data on functional limitations, serving as an indirect indicator of disease severity. Since PD-specific factors may negatively influence P-E fit, these ought to be addressed in future studies. The individuals that reported having a PD diagnosis (mean age 82 years) constituted about 1% of the original cross-national database ($n = 1{,}918$). For this age group, this PD prevalence is low [32]. Since people with PD are admitted to assisted living at an earlier age than the general population [1], the low prevalence rate probably reflects the inclusion criteria of the original study (i.e., single living in ordinary housing in urban areas) [10]. There were some prevalence differences among the national samples, ranging from one (Sweden) to seven individuals (Hungary). Since the ENABLE-AGE Project targeted ordinary housing, a plausible explanation may be cultural or societal differences among the countries, for example, differences in the availability of housing options such as assisted living facilities. These are mere speculations but highlights one type of challenges in cross-national research [13]. Cautious interpretation is needed since there were few individuals with self-reported PD in each of the national samples. The original sampling imposes some additional concerns for the external validity of our findings. It targeted a selected portion of people in very old age and does not represent the population in general, but rather a healthier segment in a European context. Furthermore, reflecting the dominance of women in the very old population, it consisted of 78% women explaining the female preponderance in the present study, despite that PD is more common among men [32]. Another important consideration is that, due to the exploratory nature of the study, we did not correct for multiple comparisons. This calls for cautious interpretation of our findings, especially so for results not showing highly significant P values such as for depression ($P = 0.048$) and some of the results regarding ADL, for example, transfer ($P = 0.047$) and shopping ($P = 0.035$) (Table 3). Turning to a strength of the study, due to the large scale study database available, we were able to apply a strong design by selecting three randomized matched controls per case [14]. Notwithstanding the limitations discussed, this study demonstrates that important knowledge can be gained by fusing different strands of research traditions. The findings can be used as a starting point for larger prospective studies, with optimized validity for those ageing with PD. Future prospective studies that target accessibility problems in PD should preferably also include variables that tap PD-specific problems and symptoms, for example, gait problems and freezing of gait. In addition, future PD studies ought to investigate which environmental barriers that account for the most accessibility problems.

5. Conclusions

The results of this explorative study suggest that despite similar housing environments in terms of number of environmental barriers, very old people with self-reported PD live in housing with more accessibility (P-E fit) problems than very old people in general. The accessibility problems are generated by their higher number of functional limitations and more use of walking aids. As a consequence, very old people with self-reported PD also have more ADL problems. Since they perceive their homes as less usable in relation to activities and seem to be less attached to their home, the results are relevant for issues such as fall prevention and relocation counselling. This study demonstrates that research on housing and health among people with self-reported PD has potential to generate knowledge of importance for the development of rehabilitation and societal planning for this patient group. Larger prospective studies including people with a confirmed PD diagnosis are, however, needed to support or refute the present findings.

Conflict of Interests

In terms of financial interests, one author (S. Iwarsson) is a copyright holder and owner of the Housing Enabler (HE) instrument, provided as a commercial product (see http://www.enabler.nu/). The other authors have no competing interests.

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