UPPER-LIMB BIMANUAL COORDINATION IN INDIVIDUALS WITH PARKINSON'S DISEASE

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By

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Foreword

This thesis has been written in a format suitable for publication. The two sections of the thesis each contain a different experiment that is being submitted separately. The title of the paper in Section I is: "Bimanual Coordination Deficits with Parkinson's disease: The Influence of Movement Speed and External Cueing." Section II contains a paper titled: "Bimanual Coordination and Freezing in Parkinson's disease: The Influence of an Intentional Shift During Movement".

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What would a Master degree be without fishing? – thanks Neil!

Table of Contents

Introduction

Parkinson's disease (PD) is a progressive neurological disorder that affects the ability to execute functional movements in older adults (Marsden, 1994). There are four trademark symptoms of Parkinson's disease: akinesia (difficulties with the initiation of movement); bradykinesia (slowness in the execution of movement); rigidity (resistance to passive muscle stretch); and tremor (5-6Hz trembling of limbs, at rest) (Stelmach & Phillips, 1991). Recent evidence has also supported "freezing" or the temporary interruption during on-going voluntary movement as a fifth cardinal symptom of PD, because of its relation to higher cortical areas of the brain in addition to typical basal ganglia dysfunction (Giladi, Kao, & Fahn, 1997).

Many of these motor control problems are associated with movement execution, which refers to the time between initial onset of movement and an eventual termination of the movement at a target location. Execution impairments have been suggested to be the result of attention deficits (Cunnington, Iansek, & Bradshaw, 1999), improper force generation (Cornack & Winstein, 1997), and/or increased need for external sensory cueing (Dibble & Nicholson, 1997). These difficulties often arise during complex coordinated movements and may be associated with a loss of independent functioning as the disease progresses. For this reason, the execution of coordinated movements between the upper limbs is the focus of this investigation.

Understanding the motor control impairments is the first step in creating a basis for effective therapeutic intervention, and the eventual goal of this research is to develop rehabilitation techniques that optimize the independent functioning of individuals with

PD. A closer look at some of the specific motor control problems will help identify the importance of studying movement coordination in individuals with PD.

Motor Control Deficits with Parkinson's Disease

Motor control deficits, as they relate to coordination in individuals with PD may be better understood if movement is subdivided into two of its components: initiation/preparation, and execution. This approach permits the examination of movement along a continuum, and hence relates the underlying motor control limitations to trademark symptoms of Parkinson's disease.

A common variable reflective of movement initiation and preparation is reaction time. It is generally accepted that reaction time is representative of the time required to recognize a stimulus and prepare an executable motor response (Henry & Rogers, 1960). Reaction time studies are commonly used to determine whether movement planning in selected populations is slower than healthy control subjects when given the opportunity to plan movements, choose among response alternatives, and use advance information. Healthy individuals commonly show an increase in reaction time as complexity of a movement task is increased (Henry & Rogers, 1960), although they are able to use advance information in order to plan and hence improve reaction time. This however, is not the case with PD. A comparison of simple versus complex reaction time (SRT vs. CRT) indicates that unlike healthy populations, there is an average 120 ms delay unrelated to CRT paradigms (Evarts, Teravainen & Calne, 1981; Stelmach, Worringham & Strand, 1986). That is, compared to healthy individuals, those individuals with PD reveal the same deficit in reaction time regardless of whether a choice is required before

response initiation suggesting that individuals with PD are unable to benefit from the opportunity to prepare for a known response. However, studies have also shown that advance information such as warning stimuli or direction of movement information can be used in pre-cued situations to enhance reaction time (Stelmach et al, 1986), suggesting that movement planning in itself is not impaired in individuals with PD. Researchers that have been unable to confirm the use of advance information in individuals with PD have suggested a possible deficit in storing the correct response through the time period just prior to stimulus presentation (Bloxham, Mindel, & Frith, 1984). Other research has speculated that problems in generating an initial force, overall slowness to PD movement, and cognitive processing deficits such as internal regulation of attention may also contribute to motor initiation impairments. This uncertainty has prompted further investigations into movement execution. Although it may not identify the underlying process, it is important to note that reaction time, because of its relation to movement preparation and initiation may be a useful index of akinesia.

Movement execution can be represented by variables such as movement time and various kinematic measures. These measurements can yield information about impairments that may occur between initiation and termination of movement, and hence may also be useful in distinguishing motor control deficits associated with PD. It is well documented that individuals with PD experience bradykinesia or slowness of movement (Benecke, Rothwell, Dick, Day & Marsden, 1987; Berardelli, Rothwell & Dick, 1986; Mak & Cole, 1991). However, it is difficult to decipher whether bradykinesia is a problem with ongoing planning of sequential movement, with force modulation or with

cognitive issues such as attention-sharing capabilities between movement tasks.

As previously mentioned, some researchers examining movement execution have focused on the impaired ability to shift attention as a central cognitive issue in Parkinson's disease. Robertson and Flowers (1990) determined that individuals with PD exhibit an inability to separate plans of action, which is presumably related to visual attention shifts that occur when transferring between motor tasks (Horstink, Berger, van Spaendonck, van den Bercken, & Cools, 1990). Interestingly, impairments during the on-going execution of movement may also be clinically evident as freezing. Clinical evaluations have revealed that 14% of impairments associated with freezing phenomena occur during movement execution rather than more common initiation problems (Giladi, McMahon, Przedborski, Flaster, Guillory, Kostic & Fahn, 1992). Each example described in the study indicates an attentional shift resulting in an interruption and subsequent hesitation, before the movement pattern is completed. Examples include difficulty changing between a climbing and normal gait when reaching the last step of a staircase; continuing gait into an elevator before the door suddenly closes; maintenance of a consistent gait pattern over a change in floor texture and, difficulty switching from forward motion to side-ways motion. Common to these cases of severe movement impairment is the requirement for coordination between the limbs (albeit the lower limbs), which provides a rationale for an examination into movement coordination in individuals with PD. Further, investigation of upper limb coordination allows us to determine if freezing impairments occur in other interlimb coordination tasks, or if these problems are specific to coordination of the lower limbs.

Bimanual Coordination

Coordination of sequential and simultaneous movement between the upper limbs is essential for many activities of daily living. Washing dishes, driving a car, and indeed, typing these words are all examples of coordinated movement. The execution of such coordinated limb movements is known as bimanual coordination and has been the focus of recent research in healthy young and older adult populations (Pacaud & Welford, 1989; Stelmach, 1982; Stelmach, Goggin & Amrhein, 1988). Results of this work indicate that certain coordinated movement patterns are inherent to human motor capabilities (Kelso, 1984; Turvey, 1990; 1994; Yamanishi, Kawato & Suzuki, 1980). These studies and others (Lee, Blandin & Proteau, 1996) support the tenet that some movement patterns, termed in-phase (simultaneous symmetric contraction of homologous muscle groups) and anti-phase (simultaneous contraction of opposite muscle groups) movements may be considered automatic because of the wide range of situations in which they occur without the need for practice (Baldissera, Cavallari, Marini & Tassone, 1991).

Kelso (1995) describes bimanual coordination as a process that develops over time and as a function of numerous factors that influence the motor system. One such factor is the temporal or speed component of movement, as defined by frequency of the limbs passing through a specified point (Kelso, 1984, 1986; Yamanishi et al, 1980). In these studies movements were made in parallel to the body and demonstrated that in-phase (no relative phase difference between the limbs - 0° relative phase) and anti-phase (180° relative phase difference between the limbs) movement patterns are performed with

tremendous accuracy and stability. Furthermore, as movement frequency is increased, the in-phase movements tend to be performed with greater accuracy and consistency than anti-phase movements (for review see Lee, Blandin & Proteau, 1996). Collectively, the findings of this work indicate that there are two preferred, stable states of coordination and that there is greater attraction for the in-phase as compared to anti-phase movements.

Movement Coordination with Parkinson's disease

Generally research suggests that movement execution deficits observed with PD become more pronounced when they involve coordinated sequential and simultaneous limb actions (Benecke et al, 1987). In a study involving a two-segmented movement, individuals with PD displayed a marked delay between movement segments, although movement kinematics were similar to those of healthy control participants (Weiss, Stelmach & Hefter, 1997). The interpretation of these results is that individuals with PD have difficulty switching between the sequential steps of a motor program. In a similar study Roy, Saint-Cyr and Taylor (1993), observed a marked hesitation during movement when participants with PD were required to produce different sequences of movements, as opposed to repeating the same sequence of movement repetitively. This finding would suggest that the difficulty making transitions between motor steps are accentuated in situations where different actions are involved in the movement sequence. Curra, Berardelli, Rocco, Modugno, Puorger, Accornero and Manfredi (1997) argue that individuals with PD may encounter delays in movement execution when required to process a greater quantity of information per unit of time. In their sequential line drawing task, Parkinson's patients encountered more difficulty than controls in completing a full

drawing sequence. In contrast, when a step-wise cueing of each segment of the drawing sequence was provided, PD patients were able to improve their performance. The results of these studies support the notion that individuals with PD may not adequately divide attention when selecting the appropriate motor steps required for executing a movement sequence (Brown, Jahanshahi, & Marsden 1993; Jones, Bradshaw, Phillips, Iansek, Mattingley & Bradshaw, 1994; Robertson & Flowers, 1990).

Sequencing difficulties of individuals with PD have also been documented in bimanual situations. As early as 1954, Schwab, Chafetz and Walker described the inability to maintain two concurrent voluntary motor activities. These observations were made using an ergogram-squeezing task with one hand while connecting points on a triangle with the other hand. Results of this study indicated that the PD participants could do each task very well in isolation, but were unable to maintain the attention to perform both tasks at the same time. Horstink et al. (1990) used a similar apparatus with kinematic measures. In this experiment, participants were asked to visually focus their attention on only one of the squeezing or drawing tasks. The results supported previous unimanual and bimanual findings that individuals with PD have difficulty with internal regulation of attention. In a study involving isotonic contraction of one arm while maintaining an isometric contraction with the other, individuals with PD divided attention very differently than healthy controls (Lazarus & Stelmach, 1992). In comparison to unimanual conditions, healthy individuals tended to improve their movement times and peak velocities in bimanual conditions. The authors suggested that healthy individuals use bilateral outflow to temporally couple and synchronize the limbs, hence improving

movement time and velocity. In contrast, individuals with PD treated each limb as a separate unit and as a result showed slower movement times and peak velocities in the bimanual condition. Although consistent in their findings, these studies have focussed on the coordination of different tasks with each limb. Furthermore, these results were not replicated in a coincident tapping and Purdue pegboard task (Brown et al., 1993). In this experiment, proportionality of movement slowness was compared in unimanual and bimanual conditions. The study found that although typical bradykinesia was present, individuals with PD were not proportionally slower than controls in bimanual situations.

When the movement task for each limb is related, results again do not support the notion that individuals with PD are unable to execute two simultaneous motor activities. Stelmach and Worringham (1988) used a discrete bimanual targeting task in in-phase and anti-phase conditions of varying distances. Unlike the findings of studies with different motor tasks for each limb, their results indicated that individuals with PD did program bimanual movements as a single unit, and that deficits beyond typical bradykinesia were only present for asymmetrical movements. Furthermore, a recent study involving sequential in-phase keypad pressing was unable to find any differences in bimanual performance between controls and individuals with PD (Samuel, Ceballos-Baumann, Blin, Uema, Boecker, Passingham, & Brooks, 1997). Hence, the circumstances under which bimanually coordinated movements become difficult for individuals with Parkinson's disease is unclear. It does seem plausible however, that the attention demands of preparing simultaneous movement sequences may be implicated.

It has yet to be determined how PD influences automatic tendencies toward certain coordination patterns. The overall purpose of this research is to investigate impairments in executing in-phase and anti-phase (i.e. symmetric and asymmetric) movements, when the motor system is challenged by speed and different attention demanding conditions. Findings from this research will help us to identify variables that facilitate coordinated movement in individuals with PD.

The first study will compare the intrinsic coordination tendencies in individuals with PD to a healthy age-matched population, where movement frequency and attention demands were modulated by the provision of an external auditory timing mechanism (Experiment 1). The second experiment will compare the stability of bimanual coordination in these same populations when they are asked to intentionally switch from one coordination pattern to another during the course of the trial (e.g. in-phase to anti-phase) (Experiment 2).

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Section I

Bimanual Coordination Deficits with Parkinson's Disease: The Influence of Movement Speed and External Cueing

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Abstract

Individuals with Parkinson's disease (PD) are typically impaired in the execution of sequential and simultaneous limb movements. In healthy adults, stable patterns of movement coordination have been identified that provide a basis for bimanual coordination. The present study investigates the stability of intrinsic patterns of coordination and the role of external timing cues for individuals with Parkinson's disease and healthy age- and gender-matched control subjects. Participants performed in-phase and anti-phase movements at one of three pacing speeds (0.75, 1.25 & 1.75Hz), and in two different cueing conditions. Individuals with Parkinson's disease performed in-phase movements with the same accuracy and stability of the healthy control group, while anti-phase movements were performed with greater mean error and variability. PD difficulties with the anti-phase task were also reflected by freezing (8.1% of anti-phase trials) and hypometric deficits (5.1% of anti-phase trials) during movement. None of these Parkinson's disease impairments occurred during in-phase trials. The overall accuracy or stability of movement coordination was not improved with the provision of external cues, suggesting that although execution impairments of individuals with PD are dramatically influenced by the attention demands of coordinated movement, external cueing does not necessarily improve movement performance.

Bimanual Coordination Deficits with Parkinson's disease: The Influence of Movement Speed and External Cueing

Coordinated control of sequential and simultaneous upper limb movements is essential for many activities of daily living, and represents an area of concern for individuals with Parkinson's disease (PD). More commonly referred to as bimanual coordination, this research has been focused primarily on healthy adult populations (1-3). Results of this work indicate that certain coordinated movement patterns termed in-phase (simultaneous symmetric contraction of homologous muscle groups) and anti-phase (simultaneous contraction of opposite muscle groups) are intrinsically preferred over other coordinated movements (4,5). Examination of the temporal or speed component of movement coordination reveals that in-phase coordination tends to be performed with greater accuracy and consistency than anti-phase movements as required movement frequency is increased (6). Although both patterns are stable and dominant states of coordination, there is a greater attraction for in-phase as compared to anti-phase movements. Similar results are seen in older adult populations, in that the in-phase pattern of coordination is more stable and is relatively unaffected by increasing the speed of the movement. Anti-phase movements are also relatively stable but are more affected by speed than the in-phase movements (7,8).

Generally research suggests that movement execution deficits observed with Parkinson's Disease become more pronounced when the coordination of long sequences and/or simultaneous limb actions is involved (9,10). Unimanual studies involving sequential movement suggest that individuals with Parkinson's disease experience

marked hesitations between segments of movement (9,11), and in performance of complex drawing movements that have not been separated into a cued series of events (12). However, in similar studies it has also been noted that movement hesitations may disappear when individuals with PD are asked to perform the same sequence of movement repetitively, as opposed to producing varied movement sequences (13). These findings would suggest that the difficulty in transition between motor steps is accentuated in situations where different actions are sequentially required.

Sequencing difficulties of individuals with PD have also been documented in bimanual situations. As early as 1954, researchers described the inability to maintain two voluntary motor activities (14). Observations were made using an ergogram- squeezing task with one hand while connecting points on a triangle with the other. Results indicated that individuals with PD are able to perform each task very well in isolation, but they experience extreme difficulty when required to divide their attention in order to perform both tasks simultaneously (14,15). In a similar study involving isotonic contractions of one arm while maintaining an isometric contraction with the other, individuals with PD were shown to divide attention very differently than healthy controls (16). In comparison to unimanual findings, healthy participants tended to improve movement times and peak velocities in the bimanual conditions. The authors concluded that healthy individuals are capable of a spatio-temporal coupling between the limbs, and hence use "bilateral outflow" to synchronize the limbs and thereby improve performance. In contrast, individuals with PD treated each limb as a separate unit and as a result showed slower movement times and peak velocities in the bimanual condition.

Although findings from these studies are fairly conclusive, it is important to note that they have been focused on the performance of different tasks for each of the limbs, and in fact have not been replicated in bimanual situations involving similar movement goals for both limbs. For example, Stelmach and Worringham (17) used a discrete bimanual targeting task for in-phase and anti-phase conditions of varying distance. Their results indicated that individuals with PD were able to program bimanual movements as a single unit, and that deficits beyond typical bradykinesia were only present for asymmetrical movements. Furthermore, a study involving unimanual versus bimanual in-phase sequential keypad pressing did not yield any differences in bimanual coordination performance between healthy controls and individuals with PD (18). Hence, the circumstance under which interlimb coordination becomes difficult for individuals with PD is unclear. In theory, it does seem plausible however that difficulty may be due to the attention required to prepare the simultaneous movement of each limb. The aim of the present study was to further evaluate differences in in-phase and anti-phase coordination performance using a task that involved similar movements and a common goal for both limbs. To increase demands on the motor system when performing these tasks, we employed the same movement frequency manipulations as previous research (6-8).

Attention impairments and the inability to internally control movement execution have been a recent focus of research in Parkinson's disease. The use of external amplitude and/or timing cues has been suggested to improve the focus of attention and to assist individuals with PD. This strategy has proved to be useful in studying movements

that involve continuous and/or sequential coordination (15,19,20) such as walking (21) and writing (22-24) in individuals with PD. In the present experiment, the use of internal versus external attention strategies in Parkinson's disease was examined by manipulating the presence of an external pacing device during coordinated in-phase and anti-phase movements. The overall purpose of this research was to investigate the execution impairments of repetitive coordinated movement involving the same task for both limbs, and to evaluate the effect of external timing cues. By manipulating the speed of in-phase and anti-phase movements, it was also possible to determine if coordination tendencies are similar to healthy populations. Further, it can be determined if movement strategies of individuals with PD are similar to that of elderly age-matched participants.

Methods

Participants. Thirteen (6 male and 7 female) patients with Parkinson's disease involved in rehabilitation at a regional health center for older adults (mean age = 68.1 years, range = 58-82 years), and 13 gender- and age-matched healthy control subjects recruited from the community (mean age = 67.9 years, range = 52-81 years) participated in the experiment. Clinical characteristics of individuals with idiopathic Parkinson's disease were assessed while on their medications, using the Hoehn and Yahr scale (25) and selected sections of the motor examination section of the Unified Parkinson's Disease Rating Scale (UPDRS) (26), as are shown in Table 1. Data for patients scoring higher than 3 using the Hoehn & Yar scale were not included in the analyses. All subjects were assessed for working memory capacity using the Digit Span Test (27) and were screened

for dementia as defined by, and using the Mini-Mental State Examination (28). Participants scoring 23 or less on the Mini-Mental State Examination were excluded from the study. All participants were confirmed by self-report to be right-handed, with normal to corrected vision in both eyes, and were free of shoulder injuries that might influence their ability to complete the necessary arm movements.

Apparatus. Participants were seated on a height-adjustable chair such that their forearms were parallel to a table-mounted sliding mechanism. The sliding devices consisted of two 9 x 13cm metal blocks, with an 8cm plastic molded handgrip bolted vertically to the surface of each block. The blocks were attached with low-friction rollers to a metal track, which restricted motion to a linear plane. Two clearly defined and symmetrical 16cm regions were marked on the base of the apparatus, one per hand, serving as visual cues for the boundaries of the required movements that were to take place. Linear potentiometers (BEI Electronics Company, model 612R12KL.08) were attached in parallel to the sliding device to encode displacement (Figure 1).

An 80486 microprocessor was used to sample data at a frequency of 200HZ. The computer controlled the start and stop of each trial, as well as the sounding of the auditory metronome (Lafayette Instrument Co. 58025) and the recording of data.

A computer monitor provided visual feedback during each trial in the form of a Lissajous figure. These figures were continuous; 2-dimensional plots of the relative motions of the two limbs. Right arm displacement followed the abscissa, while the left arm displacement followed the ordinate. An in-phase (0°) movement produced a diagonal straight line from the bottom left to top right of the computer screen, while an anti-phase

(180°) movement produced the exact opposite diagonal (bottom right to top left).

Procedure. Participants were verbally instructed to coordinate simultaneous and continuous displacements of the two linear sliding devices toward and away from the midline of the body, and in a plane parallel to the body. Forty-eight trials were administered, half of which were in-phase movements (defined as symmetric movements toward and away from the midline), while the other half were anti-phase (both limbs moving in the same direction). A full cycle of movement was to be performed for each auditory signal, at the pace determined by the metronome, and using the 16cm marked amplitude regions on the sliding device. Each successive 20s trial progressed in order from slowest to fastest trial (0.75, 1.25 and 1.75 Hz). In half of the trials, subjects were warned that the tone of the metronome would stop halfway (10s) into the trial, and that they were to do their best to maintain the pace previously dictated by the metronome, and until the end of the trial. All trials for a particular phase and tone combination were performed at the three speeds before subjects moved to the next combination. Participants were given one practice block consisting of a trial in each combination of phase, speed, and tone condition before data was recorded for the remaining three blocks. Participants were encouraged to produce the appropriate movement phase as much as possible, and to intervene with continuous movements, if necessary. Participants were instructed that it was most important to move continuously (without stopping) within each 20s trial.

Data Analysis. Data were prepared for analysis using the DADiSP Software program.

Data from each trial of limb movements were calibrated to the real amplitude of movements, in engineering units and passed through a low-pass Butterworth filter at 10Hz. The last 10 s of each trial was then extracted and analyzed, in order to compare the portion of the waveform in which the external timing device was or was not present. Interaction between the limbs was quantified by a continuous and instantaneous measure of relative phase. Relative phase was determined by the position of the left limb with respect to the right limb, using the formula proposed by Kelso et al. (29) to compute the relative phase:

$$\theta = \tan^{-1} [(dX_R/dt)/X_R]$$

where θ is the relative phase between limbs at each sample, X is the position of each limb within a cycle rescaled to the magnitude [-1,1], (dX_R/dt) refers to the normalized and continuous instantaneous velocity. The mean of these relative phase angles over the number of cycles provided a measure of average relative phase for each trial, where in-phase would be quantified by a relative phase of 0° and anti-phase would be represented by 180° of relative phase. Accuracy of relative phasing performance was subsequently calculated from the absolute difference between the average relative phase and the intended movement phase. The mean of the within-trial standard deviation provided a measure of stability for the 10 s of trial analyzed.

Measures of movement frequency and their within-trial standard deviations were based on the average of the cycle-by-cycle interval of both the positive and negative peaks completed per 10s trial segment. Additionally, the average of the absolute positive-to-negative peak movement amplitudes and their within-trial standard deviations

were calculated for each limb.

Relative phase data were analyzed using a 4-factor mixed ANOVA, in which all variables were within-subject variables except for group. The design involved four factors: 2 (Group: Parkinson's, control) x 2 (Tone: present, absent) x 2 (Phase: in-phase, anti-phase) x 3 (Speed 0.75, 1.25, 1.75 Hz) mixed analysis. The analysis of frequency and amplitude data involved a 5-factor mixed ANOVA, where group was again the only between-subject variable. The design was a 2 (Group: Parkinson's, control) x 2 (Hand: left, right) x 2 (Tone: present, absent) x 2 (Phase: in-phase, anti-phase) x 3 Speed: (0.75, 1.25, 1.75 Hz) mixed analysis. Tukey's HSD posthoc contrasts were performed on all significant effects and interactions.

Percentages of trials in which freezing and hypometric movements occurred were calculated by the number of trials in which the particular situation occurred divided by the total number of trials. Freezing is clinically described as a breakdown of repetitive voluntary movements (30), which is commonly characterized by "sudden, short-lasting episodes of breaks in motion" (31). In this experiment, we employed a strict interpretation of freezing based on any 1 s period within a trial, in which no change in movement amplitude was observed in either one or both of the limbs. Although hypokinesia is clinically described as a significant decrease or low movement amplitude (15), it also falls within the clinical description of freezing (30). However, for the purposes of this study, hypometric limb movements were further defined and distinguished as a minimum 40% decrease in average amplitude maintained for a period greater than 5 s, when compared to the initial 10 s of the trial.

Results

Impairments of Coordination Performance. Figure 2 illustrates a representative anti-phase trial from a control participant, as well as a sample anti-phase freezing and hypometric trial observed in a participant with PD. It is important to note that freezing and hypometric deficits were not observed during in-phase or anti-phase movement trials performed by control participants. Table 2 quantifies the percentage of PD group trials in which these deficits occurred during the anti-phase task. The results indicate freezing was experienced in 8.1% of all anti-phase trials, while hypometria was evident in 5.1% of trials. Overall, the results indicate that only the anti-phase task was prone to freezing and hypometric impairments.

Relative Phase. Figure 3 illustrates overall differences in performance accuracy (absolute mean error) between PD and control participants for the both in-phase and anti-phase tasks. Differences in performance were confirmed by a significant main effect for both group $F(1,24) = 6.38$, $p < .05$, and phase $F(1,24) = 25.85$, $p < .0001$. These results were superceded by a group by phase interaction, $F(1,24) = 9.41$, $p < .01$, indicating that participants with PD experienced difficulty in producing the anti-phase but not the in-phase coordination task relative to controls, although both groups coordinated anti-phase less accurately than in-phase movements overall. Post hoc results indicated that the poorer anti-phase performance of the control group was not significantly different than their in-phase movements. In addition, there was a main effect for speed, $F(2,48) = 6.38$,

$p < .0001$, indicating that both groups performed less accurately as the required movement speed increased.

Figure 4 illustrates that PD patients were more variable during the anti-phase but not the in-phase task when compared to controls. This finding is confirmed by a significant two-way interaction between group and phase, $F(1,24) = 13.64$, $p < .01$. Results for standard deviation also revealed a significant main effect for group, $F(1,24) = 13.55$, $p < .01$, and phase, $F(1,24) = 40.40$, $p < .00001$. Although controls appear to be more stable during in-phase compared to anti-phase movements (as portrayed in Figure 4), posthoc tests indicate that this difference narrowly missed significance ($p=.05$). A main effect for speed, $F(2,48) = 4.06$, $p < .05$ was also found indicating that an overall loss of stability was associated with the demands of increasing the required movement speed.

Unexpectedly, neither of these performance measures indicated any influence of the external timing device. Both absolute mean error and standard deviation of relative phase failed to reveal any significant main effects or interactions associated with the availability of tone.

Amplitude. Across all speed and tone conditions, participants with PD performed movements with proportionally smaller average amplitudes than healthy controls. This observation is supported by a main effect for group, $F(1,24) = 7.86$, $p < .01$. Two-way interactions for group by phase, $F(1,24) = 8.76$, $p < .01$, group by speed, $F(2,48) = 5.66$, $p < .01$ and a three-way interaction for group by phase by speed, $F(2,48) = 15.08$, $p < .0001$ were also significant, suggesting that movement amplitude remained relatively constant

for both groups during the in-phase task, but that each increment in anti-phase movement speed was related to a substantial decrease in amplitude for the participants with PD while control participants increased their amplitudes (Figure 5). Further posthoc tests revealed that only the amplitude decrements of the participants with PD were significant. Also, a significant two-way interaction was evident for tone by phase, $F(1,24) = 9.24$, $p < .01$, which indicated that only anti-phase movement amplitudes decreased significantly when the external timer was not available, whereas in-phase movements were not affected by the presence or absence of tone. There was, however, no differential effect of tone on group; hence we are unable to confirm that external timing devices can aid in the maintenance of movement amplitude for individuals with PD. Unexpectedly, a three-way interaction between group, hand, and tone, $F(1,24) = 5.75$, $p < .05$ was also significant and is shown in Figure 6. The figure illustrates (as confirmed by posthoc tests) that participants with PD performed movements with similar amplitudes to controls except when the tone was present for the left hand, and when the tone was absent for the right hand. In these two situations, participants with PD showed a significant decrease in amplitude.

To determine if the group with PD was more variable in their movements, standard deviation of amplitude was calculated. Although there was no difference between groups, main effects for phase, $F(1,24) = 28.19$, $p < .0001$ and speed, $F(2,48) = 3.36$, $p < .05$ revealed that, overall, participants became more variable in their movement amplitude when performing the anti-phase movements and when speed was increased. A significant two-way interaction between tone and hand, $F(1,24) = 20.40$, $p < .0001$

provided evidence for a similar finding to the mean amplitude data. In all participants, the left hands' amplitude variability did not depend on tone (as confirmed by posthoc tests) while the right hand displayed greater variability in amplitude only when tone was absent but not when it was present. Finally, a three-way tone by phase by speed interaction, $F(2,48) = 3.56$, $p < .05$ was also significant. The interaction revealed that amplitude variability did not differ for the in-phase pattern, regardless of the designated movement speed or availability of external timer. Anti-phase movements, in contrast, showed a greater amplitude variability and were very much dependent on tone. Amplitude variability substantially increased with each increment in speed, provided that the tone was available. Without the tone, variability remained constant regardless of speed increments, which was similar to the in-phase movement task (Figure 7).

Movement Frequency. The target frequencies for all participants were 0.75, 1.25 and 1.75 Hz. Figure 8 illustrates that participants with PD were unable to coordinate their limb movements to achieve the goal speeds as well as control participants. This finding was substantiated by a significant main effect for group, $F(1,24) = 12.68$, $p < .01$, for speed, $F(2,48) = 155.15$, $p < .00001$, and a significant two-way interaction between group and speed, $F(2,48) = 26.43$, $p < .00001$. Post-hoc results indicated that the difference between groups narrowly missed significance at 1.25 Hz, and was significant at 1.75 Hz ($p<.05$). Also significant was the typical main effect for phase, $F(1,24) = 55.32$, $p < .00001$ and a two-way interaction for phase and speed, $F(2,48) = 11.60$, $p < .0001$; suggesting that participants experienced more difficulty in maintaining anti-phase movements at the required speeds, in comparison to in-phase movements.

Variability of frequency data did not reveal any significant effects for group. Similar to frequency data, main effects were significant for phase, $F(1,24) = 7.07$, $p < .05$, and speed, $F(2,48) = 12.14$, $p < .0001$. As well, the two-way interaction between phase and speed, $F(2,48) = 3.64$, $p < .05$ was significant, indicating that subjects were more variable in movement frequency when performing the anti-phase task.

Discussion

Previous research has shown that individuals with Parkinson's disease experience difficulty when asked to perform sequential and/or separate simultaneous tasks (9-12, 14-16). Common to these studies is the fact that the simultaneous tasks employed have always involved a different goal and movement for each limb. Movements involving the same task for both limbs, or tasks that are repetitive in nature (13) do not follow these same trends. In fact, researchers fail to find Parkinsonian deficits in tasks that involve in-phase coordination, despite their occurrence during asymmetric movements (17,18). One of the goals of the present study was to determine if deficits in coordinating in-phase and anti-phase movement would become more apparent as the demands of movement speed were increased. We based our hypothesis on the premise that individuals with PD are unable to appropriately divide attention between two simultaneous movements. If this were the case, in-phase coordination might be less difficult because a common goal and movement pattern is shared between the limbs, and further because of the highly repetitive nature of the movements. Previous research has suggested that in-phase modes of coordination may permit limb synchronization in which 'bilateral outflow' (16) makes

the task easier to perform. The results of the present study support this explanation, in that participants with PD coordinated the in-phase but not the anti-phase movements with the accuracy and stability of controls (as reflected by absolute mean error and standard deviation of relative phase). Furthermore, although the PD group produced amplitudes that were significantly smaller than controls, they were able to maintain constant amplitudes for the in-phase task despite the increased demands imposed by movement speed. In contrast, the difficulty with anti-phase coordination was brought to light by a significant amplitude deficit for each increase in movement speed.

Perhaps the strongest evidence in support of PD difficulties with anti-phase coordination was the occurrence of freezing and hypometric impairments during 8.1% and 5.1% respectively, of the anti-phase trials, but never during in-phase trials. To our knowledge, this is the first report of freezing during an upper limb bimanual coordination task. In fact, coordination of gait results in the most common occurrence of freezing (31), and may be the only other continuous coordination task (although specific to lower limbs) that has been associated with such extreme movement impairments. The only impairments identified in upper-limb sequential tasks have required very small movement amplitudes such as writing, key pressing, and simultaneous lip movement and tapping combinations (20,22-24,33). The present study is unique in that it utilizes considerably larger movement amplitudes (16 cm) than previous tasks. Overall, this study provides evidence for the previously described 'assimilation' effect (17,34), which predicts that in-phase movements may have a tendency to be controlled synchronously and hence are easier to perform, when compared to other simultaneous movements.

Movement frequency results replicated recent findings of Swinnen et al. (32). Although participants with PD performed movements with significantly slower movement frequencies and with decreased movement amplitudes, performance of the anti-phase coordination pattern remained poor. Swinnen et al. were unable to detect significant differences between upper limb in-phase and anti-phase movements using a movement speed of 1Hz. The present study contributes to this picture by using three speeds, two of which were faster than the previous work (1.25, 1.75 Hz). Hence it is likely that the demands of speed produced difficulties associated with the anti-phase coordination mode.

It has been suggested that attention, and hence movement performance, can be improved with the provision of external cues. The external cue manipulated in this study was the presence of an auditory metronome, which signaled the required movement pace. Several studies have argued that individuals with PD have an impaired ability to internally regulate movement (12,13,15), especially movements that involve a timing component (19,20,24). Based on the most recent of these studies (24) we predicted that PD movement performance would be superior in the 'tone present' condition, and that these effects might be exemplified in measures that assess timing (relative phase). This was not the case however; our results showed no main effects for tone in any of our outcome measures suggesting that external cues may not always be helpful to individuals who experience movement difficulties.

For amplitude, the unexpected 3-way interaction between group, hand, and tone seems to suggest that the dominant right limb of participants with PD was able to produce

the appropriate movement amplitude in the presence of tone only, whereas the left limb demonstrated the exact opposite. This finding may in fact support the notion of Jones et al (37) that sequencing deficits associated with PD may be reflected in a strategy involving a lack of dominance for the right hand in simpler tasks. They documented poorer performance in a unimanual right hand condition when compared to bimanual sequential key presses. Their results indicated that individuals with PD tend to divert attention away from the right hand during unimanual and shorter sequence conditions. In our 'tone present' situation, participants with PD may have focussed on the right hand thereby allowing the appropriate amplitude to be produced, while the ignored left hand revealed deficits in amplitude. Accordingly when the tone was absent, participants may have thought it easier to attend to both hands, which resulted in improved performance for the left hand and a consequent deficit displayed for the right.

Alternatively, coordination researchers have also suggested that bimanual upper limb movements that are spatially or temporally related may become uncoupled with age (8). These findings imply that declines in ability to perform coordinated movements may be due to an age-related reduction in left-handed skills for right-handed individuals. Our results support this logic, in that, hand by tone interactions were significant for both amplitude and amplitude variability. This effect suggests that participants used the external signal as an anchor for dominant right hand movements (leading to a decrement in left-hand performance), while they focussed on their weaker left hand when the tone was not available to define movement end-points. Overall, the external cue did not directly improve movement coordination and performance. It is important to note that

amplitude is but one of many variables that describe movement, and thus it should not be the entire basis for judging improvements in movement performance. Moreover, our results suggest that the use of an external signal may influence each hand by independent processes.

In conclusion, our results re-affirm the position that individuals with PD are able to coordinate in-phase movements as well as healthy age-matched adults, although they have particular difficulty with anti-phase (i.e. asymmetric) modes of coordination. The use of an external timing device did not generate any significant improvement in movement performance, despite its influence on each limb independently. As previously suggested (33) the provision of external cues does not always have a beneficial influence on movement performance, although it is possible that participants were able to use the sliding of the hand-grips as an external cue. The results of this study would suggest that coordination of anti-phase movements may be an important focal point in the creation of rehabilitation programs for individuals with PD. The relationship between anti-phase movements and PD execution impairments may help identify the underlying processes associated with freezing, and merits further investigation.

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Table 1.
Parkinson's Disease Participant Characteristics Including Age, Gender, Clinical Evaluation and Medications

Case	Age (Yrs)	Sex	Hoehn & Yahr	UPDRS (III.21)	UPDRS (III.22)	UPDRS (III.31)	Side Affected	Medications
1	74	M	1	1	0	0	L	Sinemet, Selegiline, Bromocriptine
2	69	M	1.5	1	1	1	R>L	Sinemet
3	77	F	2	1	1	1	R	Sinemet
4	61	F	2.5	2	2	0	R=L	Sinemet CR, Sinemet, Requip
5	73	F	1	0	0	1	R	Sinemet, Selegiline
6	63	F	2	0	0	1	R	Sinemet, Requip
7	61	F	2	1	2	2	R	Requip, Trihexyphenidyl
8	82	M	2.5	2	2	2	L	Sinemet
9	58	M	2	3	2	1	L	Sinemet
10	59	M	2	1	0	1	L	Sinemet CR, Trihexyphenidyl
11	71	F	1.5	0	1	1	L>R	Mirapex, Sinemet CR
12	64	M	1.5	1	2	1	L	Sinemet
13	73	M	2.5	1	2	3	L	Sinemet, Selegiline, Permax

Note. UPDRS refers to the Unified Parkinson's Disease Rating Scale, section III reflects the motor examination scale where item 21 = tremor, item 22 = rigidity, and item 31 = overall bradykinesia and hypokinesia (on a scale of 0 to 4).

Table 2.
Movement Impairment Trials in Participants with Parkinson's disease

	Number of Trials - Frozen	Number of Trials - Hypometric
	19	12
% of Trials	8.1	5.1

Note. Percentage of trials is based on the total number of anti-phase trials performed by all PD patients (234 trials).

Figure Captions

Figure 1: Illustration of Apparatus.

Figure 2: Examples of Coordination Performance.

Figure 3: Absolute mean error performance in relative phase for the control and PD participants as a function of in-phase or anti-phase coordination pattern.

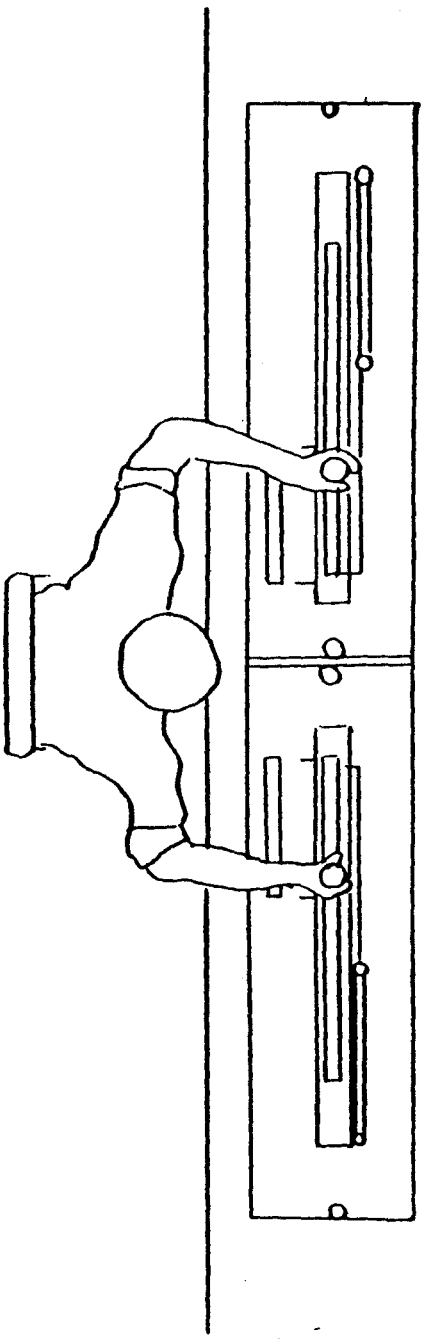
Figure 4: Standard deviation of relative phase for the control and PD participants as a function of in-phase or anti-phase coordination pattern.

Figure 5: Movement Amplitude for the control and PD participants as a function of required movement frequency and coordination pattern.

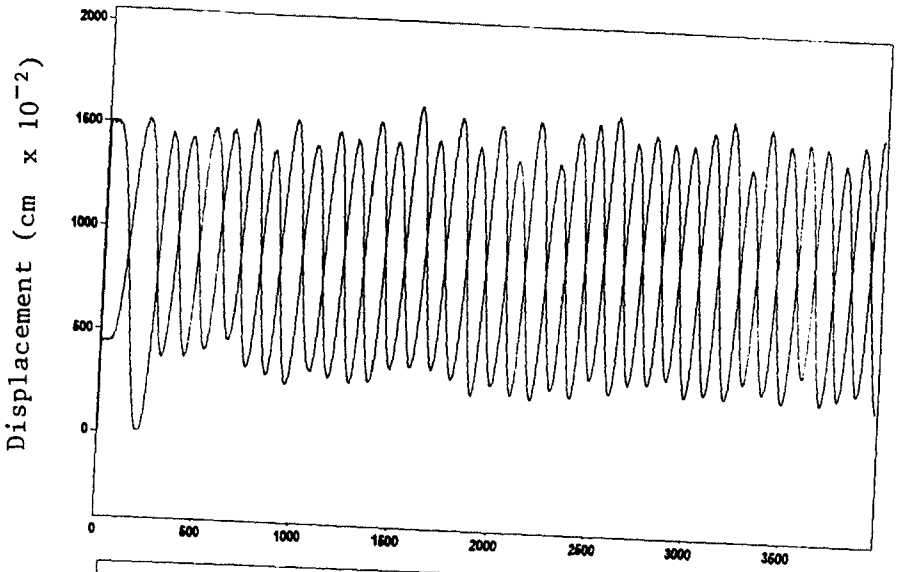
Figure 6: Movement Amplitude for the control and PD participants as a function of presence of external tone and hand.

Figure 7: Standard deviation of Amplitude for the control and PD participants as a function required movement frequency and coordination pattern.

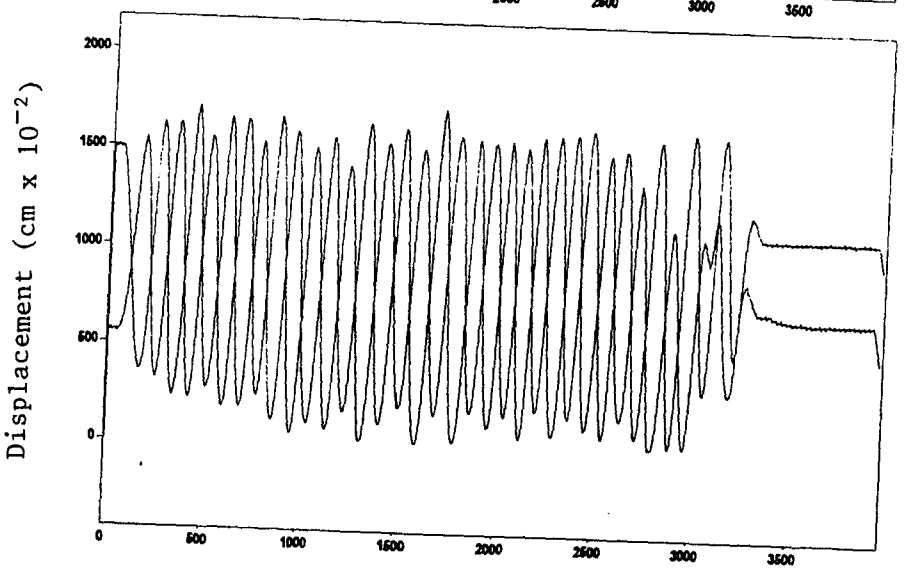
Figure 8: Actual Movement Frequency for the control and PD participants as a function of required movement frequency.



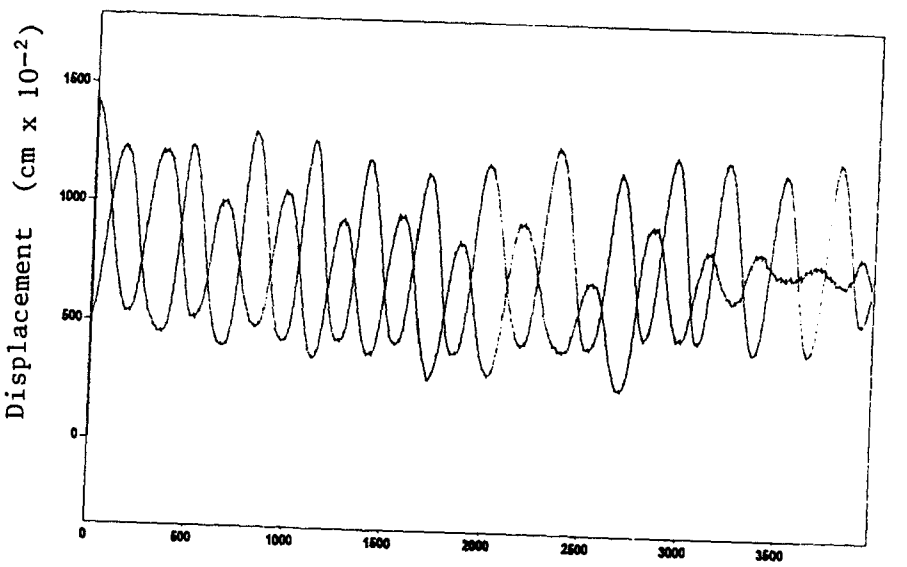
A. Healthy Control

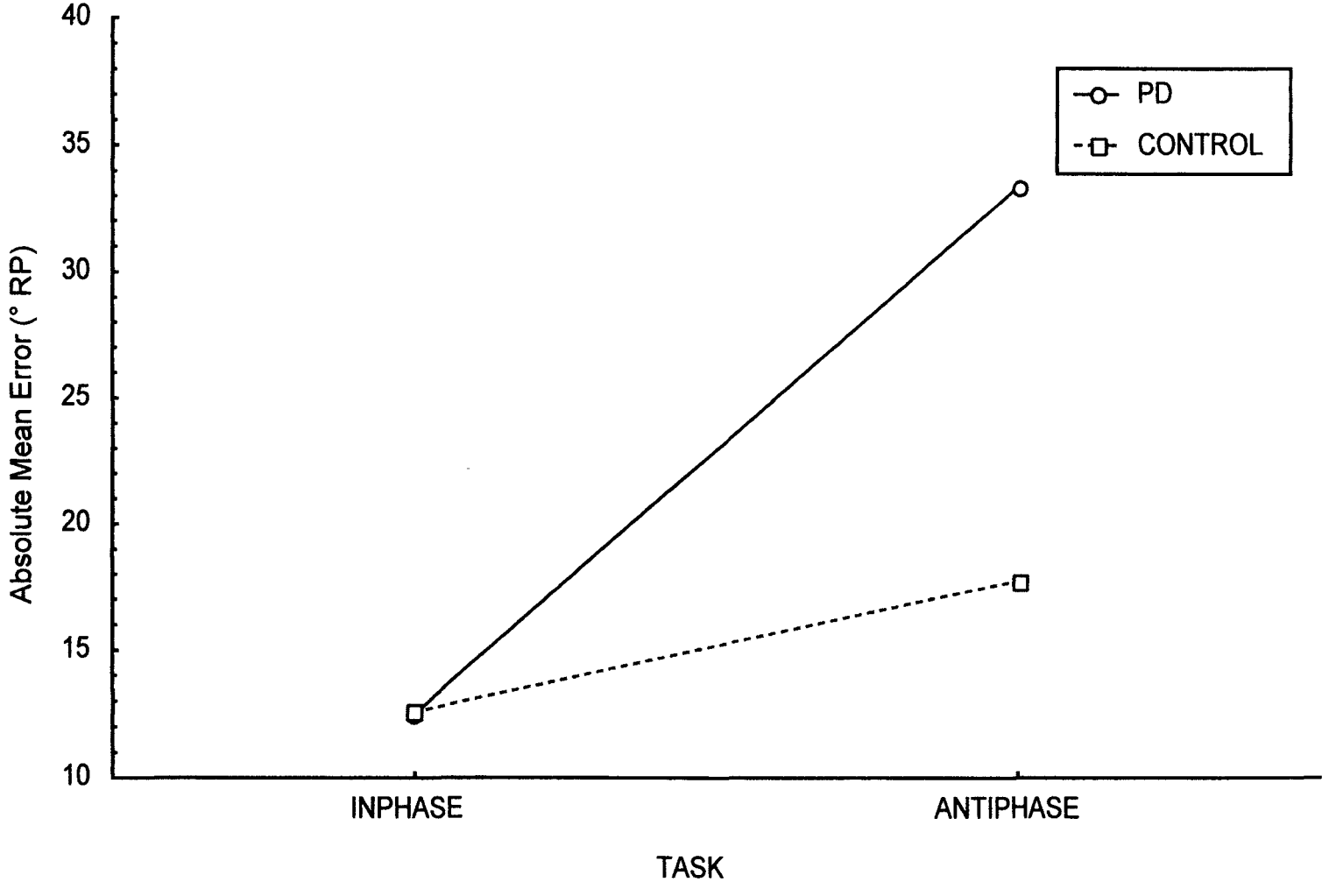


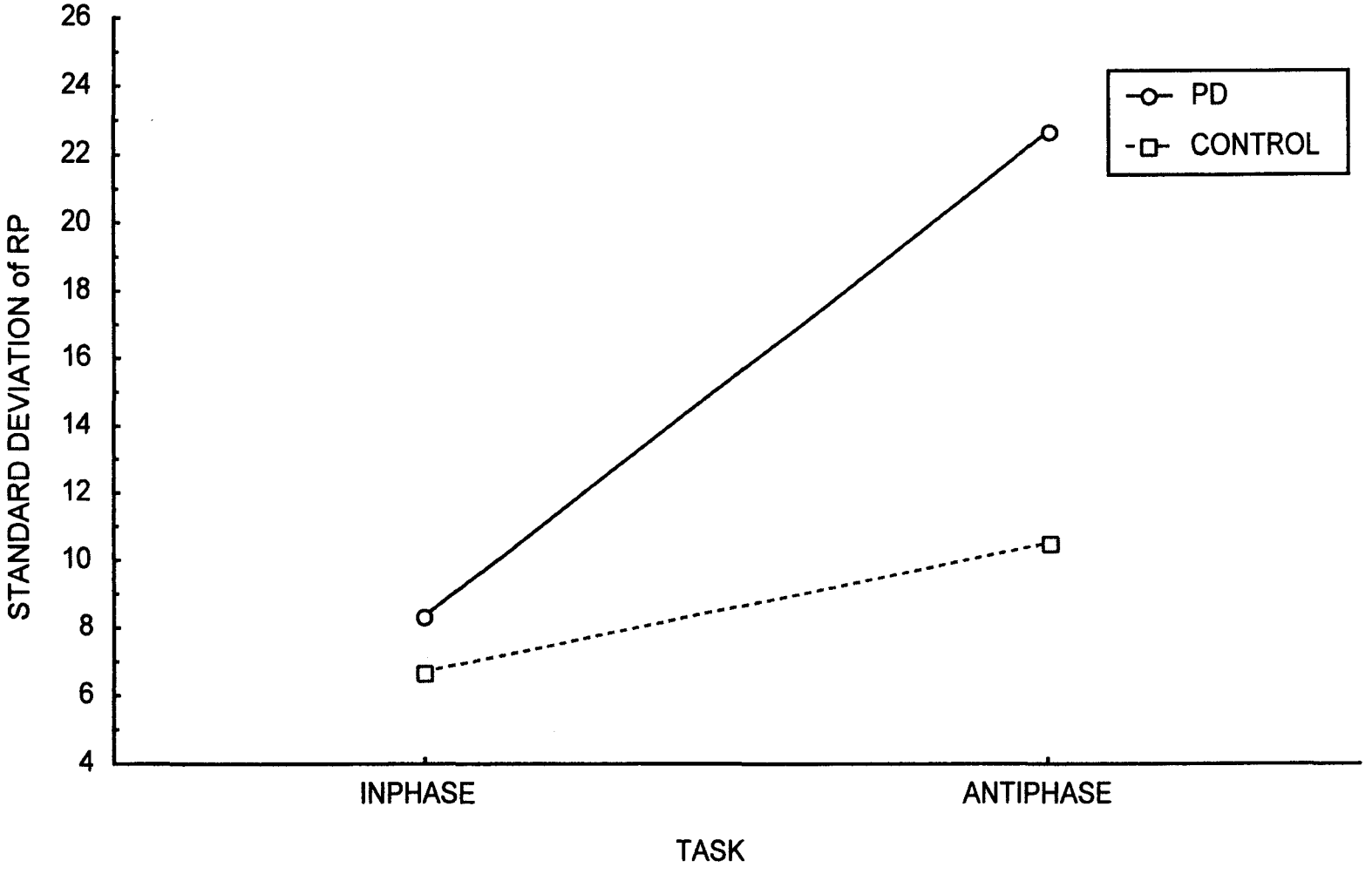
B. Freezing with PD



C. Hypometria with PD




40
35
30
25
20
15
10
Absolute Mean Error (° RP)
PD
CONTROL
INPHASE
ANTIPHASE
TASK


26
24
22
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18
16
14
12
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8
6
4
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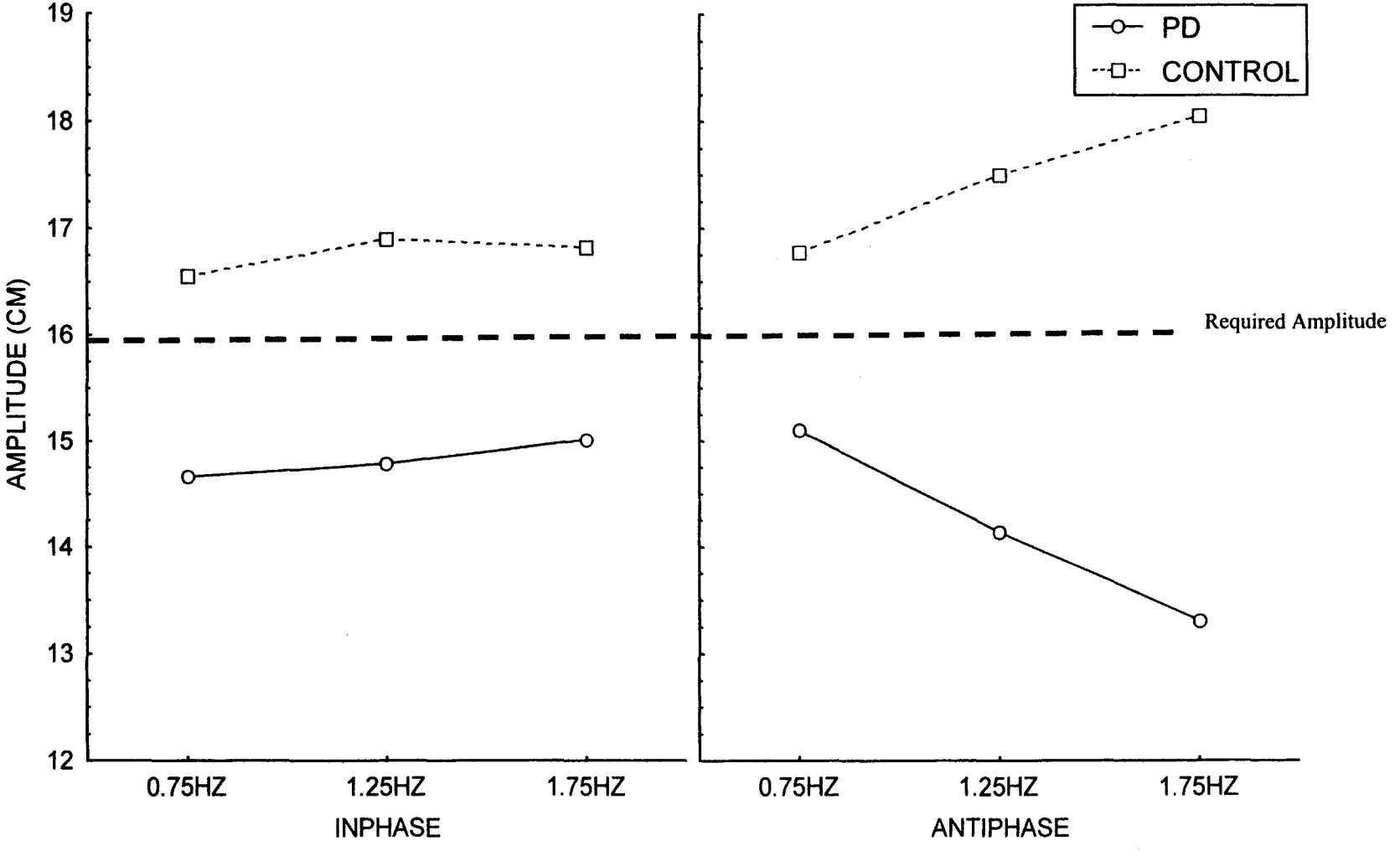
PD
CONTROL
INPHASE
ANTIPHASE
TASK


PD
CONTROL
Required Amplitude
AMPLITUDE (CM)
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18
17
16
15
14
13
12
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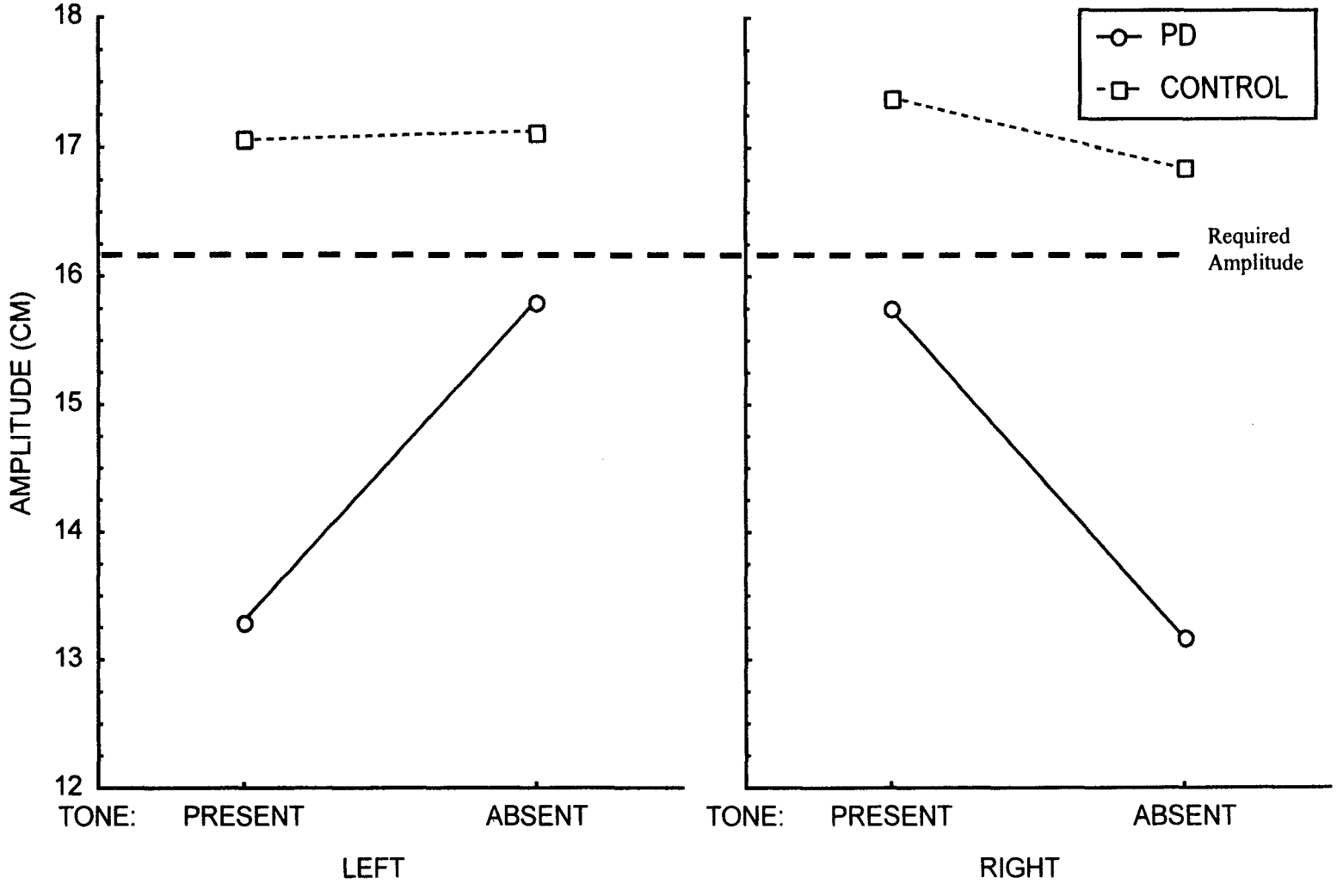
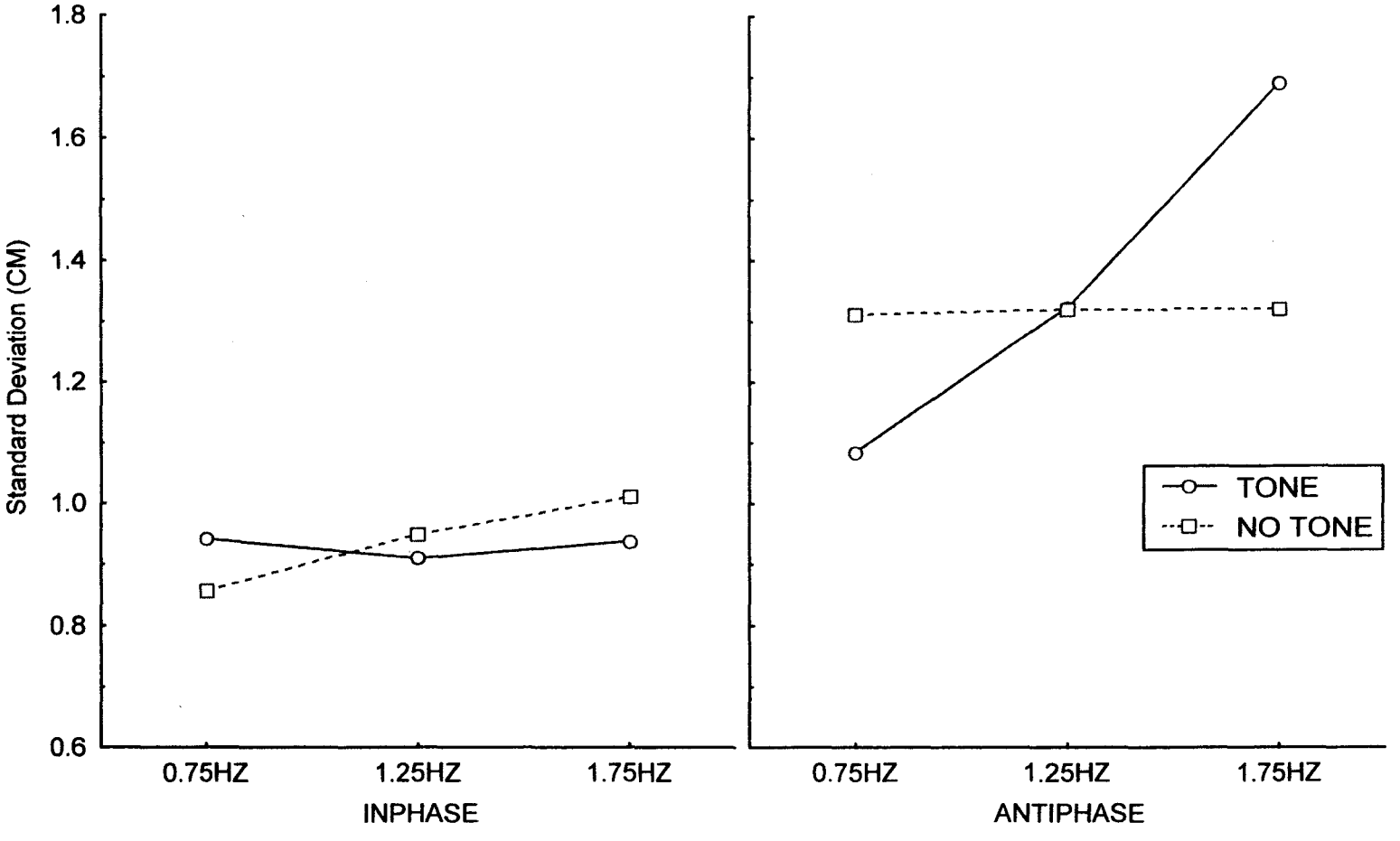
1.25HZ
1.75HZ
INPHASE
0.75HZ
1.25HZ
1.75HZ
ANTIPHASE


18
17
16
15
14
13
12
AMPLITUDE (CM)
PD
CONTROL
Required
Amplitude
TONE: PRESENT ABSENT
LEFT
TONE: PRESENT ABSENT
RIGHT


Standard Deviation (CM)
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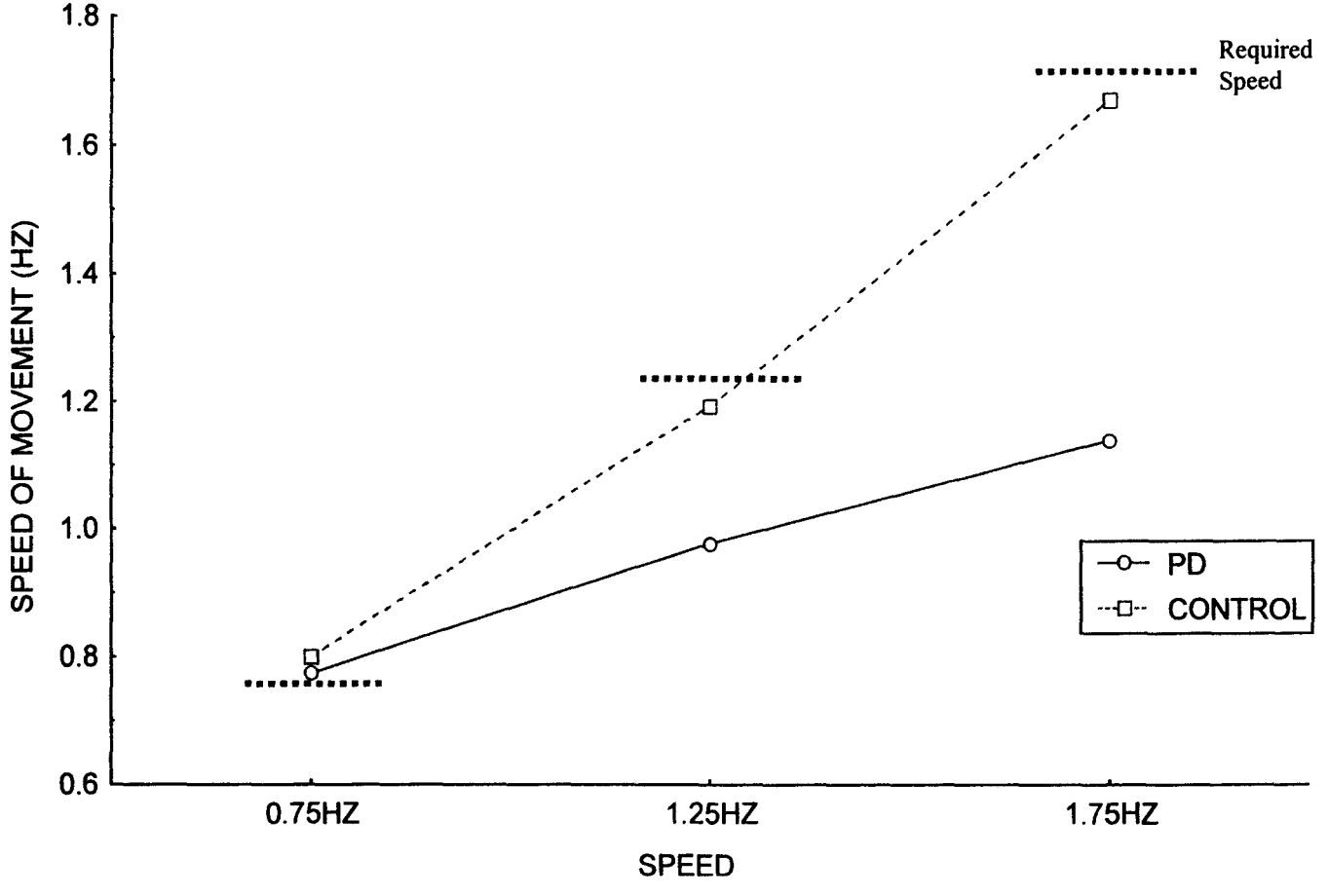
1.6
1.4
1.2
1.0
0.8
0.6
0.75HZ
1.25HZ
1.75HZ
INPHASE
0.75HZ
1.25HZ
1.75HZ
ANTIPHASE
TONE
NO TONE


1.8
1.6
1.4
1.2
1.0
0.8
0.6
SPEED OF MOVEMENT (HZ)
Required Speed
PD
CONTROL
0.75HZ
1.25HZ
1.75HZ
SPEED

Section II

Bimanual Coordination and Freezing in Parkinson's disease: The Influence of an Intentional Shift during Movement

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Abstract

A temporary and involuntary stoppage of movement or 'freezing' has been identified in the execution phase of writing, walking, and turning movements in individuals with Parkinson's disease (PD). Research has suggested that PD may limit the ability to effectively divide attention, making the execution of sequential and/or simultaneous limb movements particularly difficult for individuals with PD. The present study compared a PD and age-matched control group in their ability to coordinate continuous and simultaneous limb movements involving a two-component sequence. A trial involved participants performing either in-phase or anti-phase movements and then voluntarily switching to the opposite pattern upon hearing an auditory signal. Participants performed in-phase to anti-phase, and anti-phase to in-phase switches while paced by an auditory metronome at one of three movement speeds (0.75, 1.25, 1.75 Hz). Measures of timing coordination indicate that overall, participants with PD required significantly longer periods of time to switch between coordination patterns compared to healthy controls. As well, freezing was observed in 53.9% of the in-phase to anti-phase switch trials, yet in only 15.5% of the anti-phase to in-phase trials. The group with PD experienced more difficulty changing from the in-phase to anti-phase mode of coordination. We conclude that Parkinsonian freezing may occur during movement execution, especially when switching from more automatic to less automatic coordinated movements. These observations may be part of a deliberate strategy employed by individuals with PD when on-line modification of movement occurs during the execution of previously programmed movements.

Bimanual Coordination and Freezing in Parkinson's disease: The Influence of an Intentional Shift during Movement

Individuals with Parkinson's disease (PD) experience difficulty executing sequential and simultaneous movements. The clinical term akinesia has been used as an umbrella to characterize all bouts of movement impairment occurring at the initiation of movement. "Freezing" defined as the temporary inability to produce voluntary movement, has been labeled an important sub-category of akinesia (1) and is of particular interest because of the implications it has for independent living in individuals with PD. Interestingly, clinical evaluations by Giladi and colleagues (2) have revealed that 14% of impairments associated with freezing phenomena occur during the execution rather than initiation phase of movement. Each example presented in this retrospective study described an attentional shift, which resulted in marked delay or hesitation during the on-line challenge of switching to a new movement task. Examples included difficulty climbing the final step of a staircase before commencing gait on a flat surface; maintaining gait to enter an elevator when the door suddenly begins to close; continuing gait over a change in floor texture; and difficulty switching from forward to sideways locomotion. An early experimental study by Schwab and colleagues (3) observed that individuals with PD display amplitude, speed, and accuracy deficits when squeezing an ergogram bulb with one hand and simultaneously connecting points on a triangle with the other. In fact, some participants would completely cease one task, before completing the other.

A common explanation for this inability to maintain two voluntary and simultaneous tasks is that individuals with PD are unable to separate plans of action for each limb, which is presumably related to an attention-shifting deficit when transferring between two different motor tasks (3-6). Recent studies have documented this more severe interruption-to-movement impairment during the execution of complex movements. In tasks involving several movement segments, individuals with PD display a marked delay between the execution of each sequential movement segment, particularly when the segments involve different actions (7,8). Curra and colleagues made similar observations using a sequential line drawing task (9). Their results showed that individuals with PD encounter delays when required to complete a full sequence of movement to produce a drawing. In contrast, a step-wise cueing of each segment of the same drawing allows individuals with PD to perform with the accuracy and speed of healthy controls. They concluded that deficits in movement execution occur when individuals with PD are required to process a greater quantity of information per unit of time. The results of such studies support the notion that individuals with PD have difficulty with shifting attention when on-line modification of motor steps is required during the execution of a complex movement (4,10,11).

The present study of bimanual coordination provides a unique examination of on-line voluntary switching between relatively stable movement patterns. Bimanual movements that involve simultaneous limb actions toward and away from the midline of the body are termed in-phase, while movements involving both limbs moving synchronously to the left or right are termed anti-phase. Both patterns are considered

automatic because of the accuracy and consistency across a wide range of situations that they occur without practice (12,13). In fact the attraction to more automatic in-phase movements is so powerful that both young and older adults will spontaneously switch to in-phase movements when asked to perform other coordinated movements at a faster pace (14). Previous research findings indicate that deficits observed in sequential and simultaneous limb movements may be more apparent in anti-phase (defined as simultaneous contraction of opposite muscle groups) rather than in-phase (simultaneous symmetric contraction of homologous muscle groups) modes of coordination, and that this may be associated with their spatio-temporal coupling requirements (15-18). Our first experiment replicated these observations and also determined that impairment to anti-phase coordination was evident in the form of severe freezing and hypometric movement deficits. The objective of the current study was to determine whether the demands of a cued intentional shift from the execution of relatively stable in-phase movements to a less stable anti-phase mode of coordination (and vice-versa) would negatively influence movement performance in individuals with PD. To increase demands on the motor system, these voluntary switch trials were performed at three different movement frequencies (0.75, 1.25, 1.75 Hz), as paced by an external timing signal. Specifically, our aim was to establish if movement impairments, such as freezing, were more apparent in participants with PD when the task demanded a switch from a more automatic to less automatic movement.

Method

Participants. Thirteen participants with idiopathic PD recruited through the physiotherapy department of a regional health center for older adults in Hamilton, Ontario, Canada (M age = 68.1 years, range = 58-82 years), and 13 gender- and age-matched healthy control subjects recruited from the community (M age = 67.9 years, range = 52-81 years) participated in the experiment. All participants with PD were evaluated while they were maintaining their regular medication protocol. The assessment employed selected components from the motor examination section of the Unified Parkinson's Disease Rating Scale (UPDRS) (19) that were indicative of common upper limb PD symptoms, as well as the modified Hoehn and Yahr scale (20). Descriptive characteristics of participants with PD are shown in Table 1. Individuals were included if they scored between stages I and III of the Hoehn & Yahr scale. All participants participating in the study were assessed for working memory capacity using the Digit Span Test (21) and screened for dementia using the Mini-Mental State Examination (22) to verify that they were within their age-expected normal range. Participants were right-hand dominant, had normal-to-corrected vision in both eyes, and were free of shoulder injuries or other neurological deficits that might influence their ability to complete the required movement sequences.

Apparatus. Participants were seated comfortably so that their forearms were parallel to a table-mounted sliding mechanism. The sliding devices consisted of two 9 x 13cm metal blocks, with an 8cm plastic molded handgrip bolted vertically to the surface of each block. The blocks were attached with low-friction rollers to a metal track, which

restricted motion to a linear plane. Two clearly defined and symmetrical 16cm regions were marked on the base of the apparatus, one per hand, serving as visual cues for the boundaries of the required movements. Linear potentiometers (BEI Electronics Company, model 612R12KL.08) were attached in parallel to the sliding device to encode displacement (Figure 1).

An 80486 microprocessor was used to sample data at a frequency of 200HZ. The computer controlled the initiation and termination of each trial, as well as the external auditory timing device (Lafayette Instrument Co. 58025) for regulation of required speed, and the archiving of data. Switching between modes of coordination was signaled by a discriminatingly loud and higher-pitched tone produced by a separate external signal (Lafayette Instrument Co. 63250).

A computer monitor was centered just ahead of the sliding device and provided visual feedback during each trial in the form of a Lissajous figure. These figures were continuous, 2-dimensional plots of the relative motion of the two limbs. Right arm displacement followed the abscissa, while the left arm displacement followed the ordinate. An in-phase (0°) movement produced straight diagonal lines from the bottom left to top right of the computer screen, while an anti-phase (180°) movement produced the exact opposite diagonal (bottom right to top left). The result of an ideal switch trial would hence produce a perfect 'X' on the monitor (see Figure 2).

Procedure. Participants were instructed to continuously coordinate simultaneous displacements of the two linear sliding devices in a parallel plane toward and away from the midline of the body at a pace determined by the external auditory device. In each 20s

trial, a full cycle of movement was to be performed for each auditory tone emitted, using the 16 cm marked amplitude region on the sliding device as guides for the appropriate movement amplitude to be produced.

A total of 18 trials were administered. Nine of these trials started with the in-phase movements (symmetric movements toward and away from the midline), while the other nine trials started in the anti-phase mode (both limbs moving synchronously in the same direction). Each subsequent trial for a given phase was 20 s in length and progressed in order from slowest to fastest trial (0.75, 1.25 and 1.75 Hz) before a new block of three began. Participants were instructed that a louder and higher pitched tone would sound halfway (10 s) into the trial, at which time they were expected to switch from the coordination pattern from which they started into the other coordination mode. Participants were encouraged to make the appropriate phase shift as rapidly as possible after they heard the auditory stimulus, and to maintain the new phase pattern until the end of the trial. Participants were reminded which pattern they would start and switch into, after every block of three trials. Each block of trials for a specific phase was counter-balanced to avoid specific practice effects. Before the experiment started, participants practiced switching between phases without the external timing signal, to verify task comprehension. Participants were instructed that it was most important to move continuously (without stopping) during the entire 20 s trial.

Data Analysis. Data were calibrated to the real amplitude of movement in engineering units, and then processed through a Butterworth (low-pass filter) at 10 Hz using the DADiSP Software program. The final 10 s of each trial of limb movements was

extracted and saved in an interactive window for analysis. Within each extraction only the portion of the waveform in which a switch to the intended coordination pattern was accomplished, was further isolated into a second window for analysis of timing performance. A successful switch to a new phase was defined using more stringent criteria than those established by previous researchers (14,23). A switch was defined as achievement and maintenance of the intended coordination mode within 45° of relative phase for a minimum duration of two seconds. Relative phasing of the limbs was quantified by a continuous and instantaneous estimate of the position of the left limb with respect to the right limb, using the formula proposed by Kelso et al. (24) to compute phase relation:

$$\theta = \tan^{-1} [(dX_R/dt)/X_R]$$

where θ is the relative phase between limbs at each sample, X is the positions of the limb within a cycle rescaled to the magnitude [-1,1], (dX_R/dt) refers to the continuous, normalized instantaneous velocity. The mean of these relative phase angles over the number of point estimates provided a measure of average relative phase for each analyzed segment, where in-phase was quantified by a relative phase of 0° and anti-phase was represented by 180° relative phase. Accuracy of relative phasing performance was subsequently calculated as the absolute difference between the average relative phase and the relative phase of the intended pattern. Within-trial standard deviation provided a measure of stability for the segment of trial that met criterion. The dependent measure characterizing the time required to achieve a new mode of coordination was labeled 'voluntary switch time'. Voluntary switch time was defined as the latency between

presentation of the auditory switch cue and the start of the two-second bandwidth that successfully achieved the switch criterion (i.e., within 45° relative phase of the intended goal pattern for a minimum of 2 s).

In order to characterize impairments that occurred during the voluntary switch time interval, percentages of trials in which freezing and/or other "unusual" actions were calculated as the number of trials in which the particular situation occurred divided by the total number of trials (Table 2). In the present study freezing was defined as the 'temporary inability to execute voluntary movement' of Fahn and colleagues (2,26). Empirically, freezing was strictly defined as any period in which one or both of the limbs displayed no movement (as reflected by a zero change in amplitude) for a period of at least 1 s. Further, a 'delayed response' to the auditory switch cue was delineated by a voluntary switch time greater than two seconds.

Data were analyzed using a 3-factor mixed ANOVA, in which group was the only between-subject variable. The design was a Group (Parkinson's, control) x Phase (in-phase, anti-phase) x Speed (0.75, 1.25, 1.75 HZ). All significant effects and interactions were subjected to a Tukey's HSD post-hoc test.

Results

Examples of Coordination Performance. Figure 3 displays representative in-phase and anti-phase trials from a control subject, as well as sample freezing and delayed response trials experienced by PD participants. These movement impairments were not observed during any of the trials performed by healthy controls. Table 2 summarizes the frequency

and percentage of trials in which these deficits occurred in individuals with PD. Of all trials in which participants with PD were asked to switch from the in-phase to the anti-phase pattern, freezing was experienced in 11.1% of the right hand trials, 12.9% of the left hand trials, and 29.9% of the trials involving both hands. In contrast, when participants with PD were required to switch to the in-phase pattern, freezing was observed in only 3.4% of the right hand, 4.3% of the left hand, and 7.8% of trials involving both hands. Also, 3.4% of 'switch to anti-phase' trials were categorized as delayed response, while in 7.6% of trials a successful switch was never accomplished. Comparatively, there were no trials in which participants were unable to successfully switch to in-phase, and only 1.7% of trials resulted in delayed response. Overall, these results indicate that switching from the in-phase to the anti-phase coordination pattern was strongly associated with the much more severe execution impairments than switching from the anti-phase to the in-phase pattern.

Relative Phase. Performance accuracy, as represented by absolute mean error of relative phase, is illustrated in Figure 4 for the trials in which a successful switch was accomplished. The figure shows that the PD group performed as well as controls when transferring to the in-phase mode of coordination. However, participants with PD, unlike controls, exhibited detriments to accuracy after switching to the anti-phase mode. These findings were substantiated by significant main effects for group $F(1,24) = 9.73$, $p < .01$, and phase $F(1,24) = 18.70$, $p < .001$, as well as a group X phase interaction, $F(1,24) = 7.31$, $p < .01$. Post-hoc results indicate that the control group performed accurately regardless of the coordination mode to which they were required to switch. In addition, a

three-way interaction for group, phase, and speed, $F(2,48) = 3.71$, $p < .05$, was also significant, indicating that both groups were able to switch accurately to the in-phase pattern regardless of movement speed requirements. However, switches to the anti-phase pattern were performed with poorer accuracy across all speed conditions for the group with PD (Figure 5). Posthoc analyses confirmed that participants in the control group transferred to the anti-phase mode as accurately as they switched to the in-phase mode across all movement speeds except the fastest (1.75 Hz) condition, where switching to the anti-phase pattern was significantly less accurate. Interestingly, participants with PD displayed greater accuracy deficits when transferring from in-phase to anti-phase at the slowest and fastest movement speeds (0.75 and 1.75 Hz, respectively), when compared to the moderate speed (1.25 Hz) condition.

Figure 6 illustrates the finding that all participants were more variable (as reflected by standard deviation) when switching to the anti-phase, but not the in-phase coordination pattern. This variability was most evident in the PD group and was confirmed by main effects for group, $F(1,24) = 16.15$, $p < .001$, phase, $F(1,24) = 53.78$, $p < .00001$ and a significant two-way interaction between group and phase, $F(1,24) = 11.00$, $p < .01$. Post-hoc results further revealed that all participants were equally stable when switching to in-phase coordination, while participants with PD were significantly more variable than controls in switching to the anti-phase task. A main effect for speed, $F(2,48) = 4.06$, $p < .05$ was also found, indicating that there was an overall loss of stability associated with the slowest and fastest movement speeds. Post-hoc results indicate that a similar loss of stability was associated with both the slowest and fastest

movement speeds, while improvements were evident at the intermediate speed condition.

Voluntary Switch Time. The difficulty in switching from the in-phase to the anti-phase pattern was also confirmed by 'voluntary switch time' as a dependent measure (Figure 7). The group with PD required a substantially longer time to change to the anti-phase mode of coordination, when compared with switching to the in-phase task. In fact, post-hoc results indicate that participants with PD required no more time than controls when switching to the in-phase coordination mode. In contrast, voluntary switch time did not depend on the coordination pattern being switched to in the healthy control group. This was confirmed by a main effect for group, $F(1,24) = 11.38$, $p < .01$, and phase, $F(1,24) = 17.84$, $p < .001$ as well as a significant two-way interaction between group and phase, $F(1,24) = 6.44$, $p < .05$.

Discussion

Previous studies have provided evidence of movement execution impairments that individuals with PD experience when separating plans of action for different movement sequences (2-7). These difficulties are even more apparent when simultaneous bimanual tasks are performed (1,3,15). In the present study, a continuous bimanual coordination task was integrated with the intentional requirement of changing between coordination patterns midway through a trial. Our results reinforce the view that individuals with PD are less likely to be impaired when bimanual movements share common spatio-temporal elements, such as in-phase modes of coordination. Previous research predicts that

coordination of anti-phase movements should be more difficult for individuals with PD (15,16). Our first study confirmed this hypothesis and determined that difficulties in the execution of anti-phase movements became more apparent with severe freezing and hypometric deficits occurring in 8.1% and 5.1% of anti-phase trials, respectively. Although they share a common timing element (similar to in-phase movements), anti-phase movements are not mirrored and hence are not as spatio-temporally linked as in-phase movements. In our study, switching to an in-phase mode of coordination was achieved no differently than healthy controls. Difficulties in coordinating movements were reflected in the poor accuracy and stability achieved by individuals with PD after they switched to the anti-phase mode of coordination. Furthermore, similar to controls, accuracy and stability results showed that participants with PD were not influenced by speed requirements when transferring to the in-phase pattern only. Yet they were profoundly influenced by speed when required to switch to the anti-phase coordination task. Our results indicate that there may be an optimum speed at which individuals with PD can achieve coordination. It is suggested that individuals with PD may direct an inordinate amount of attention toward speed maintenance at extremely slow or fast speeds of movement.

Previous research examining intentional switches between in-phase and anti-phase movements suggests that general coordination tendencies act to constrain any intentional modifications to coordination mode (27). Healthy young and especially older adult populations demonstrate this finding in that they require more time when transferring from in-phase to anti-phase modes of coordination (compared to anti-phase

to in-phase shifts) due to a greater attraction for symmetrical in-phase movements (17,27). Our research indicates that these constraints are exacerbated in individuals with PD. Voluntary switches to the anti-phase task required more than double (2.65 s) the amount of time that healthy, older adults needed to make the same switch (1.11 s). Yet, participants with PD required no more time than controls when switching to the in-phase movement pattern. This it is suggests that the general coordination tendencies of individuals with PD are constrained by in-phase modes of coordination more so than in healthy older adults. Further, our results support the notion that more difficulty is associated with decoupling in-phase rather than anti-phase movements since the in-phase coordination mode is intrinsically more stable (14).

Difficulties in processing a voluntary switch within a movement task is perhaps most evident in the percentage of trials in which specific PD movement impairments occurred (Table 2). Remarkably, more than half of the trials (53.8%) requiring a switch from in-phase to the anti-phase pattern resulted in freezing for at least one full second. And, in 3.4% of the trials requiring a switch to the anti-phase pattern, participants with PD exhibited a delay greater than two-seconds in responding to the switch signal. Participants with PD were also completely unsuccessful at changing to the anti-phase mode in 7.6% of the trials. Although some of these impairments did occur when switching to the in-phase task, occurrences were less than a third of the observations made when switching to the anti-phase task.

Overall, the use of a continuous bimanual coordination task has enabled us to identify PD freezing associated with on-line changes in the execution of upper limb

movements. Our results suggest that freezing (and other movement impairments) are more likely to occur when switching to movements that involve anti-phase coordination. PD difficulties switching from in-phase to the anti-phase coordination mode were evident in all dependent measures (accuracy, stability, and voluntary switch time), although they were not present during intentional switches in the opposite direction. The results of this experiment suggest that freezing may occur during execution of coordinated simultaneous movements that involve on-line changes to relatively stable movement patterns, in addition to previously identified problems at the initiation of movement. Further experimentation is required to determine whether severe initiation and execution deficits, such as freezing are a result of the same underlying mechanisms.

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Table 1.
Parkinson's Disease Participant Characteristics Including Age, Gender, Clinical Evaluation and Medications

Case	Age (Yrs)	Sex	Hoehn & Yahr	UPDRS (III.21)	UPDRS (III.22)	UPDRS (III.31)	Side Affected	Medications
1	74	M	1	1	0	0	L	Sinemet, Selegiline, Bromocriptine
2	69	M	1.5	1	1	1	R>L	Sinemet
3	77	F	2	1	1	1	R	Sinemet
4	61	F	2.5	2	2	0	R=L	Sinemet CR, Sinemet, Requip
5	73	F	1	0	0	1	R	Sinemet, Selegiline
6	63	F	2	0	0	1	R	Sinemet, Requip
7	61	F	2	1	2	2	R	Requip, Trihexyphenidyl
8	82	M	2.5	2	2	2	L	Sinemet
9	58	M	2	3	2	1	L	Sinemet
10	59	M	2	1	0	1	L	Sinemet CR, Trihexyphenidyl
11	71	F	1.5	0	1	1	L>R	Mirapex, Sinemet CR
12	64	M	1.5	1	2	1	L	Sinemet
13	73	M	2.5	1	2	3	L	Sinemet, Selegiline, Permax

Note. UPDRS refers to the Unified Parkinson's Disease Rating Scale, section III reflects the motor examination scale where item 21 = tremor, item 22 = rigidity, and item 31 = overall bradykinesia and hypokinesia (on a scale of 0 to 4).

Table 2.
Movement Impairment Trials in Participants with Parkinson's disease

	Freezing - Right Hand	Freezing - Left Hand	Freezing – Both Hands	Delayed Response	No Switch Achieved	Total Freezing
Anti to In Switch	4 (3.4%)	5 (4.3%)	9 (7.8%)	2 (1.7%)	0 (0%)	18 (15.4%)
In to Anti Switch	13 (11.1%)	15 (12.9%)	35 (29.9%)	4 (3.4%)	9 (7.6%)	63 (53.8%)

Note. Percentage of trials is based on the total number of trials in a specific coordination mode performed by all PD patients (117 trials).

Figure Captions

Figure 1: Illustration of Apparatus.

Figure 2: Illustration of Visual Feedback Sequence:

a) In-phase performance before cue to switch.
b) Immediately after the cue (at 10 seconds), a switch to the anti-phase task.
c) Visual feedback at trial completion displays an "X".

Figure 3: Examples of Coordination Performance.

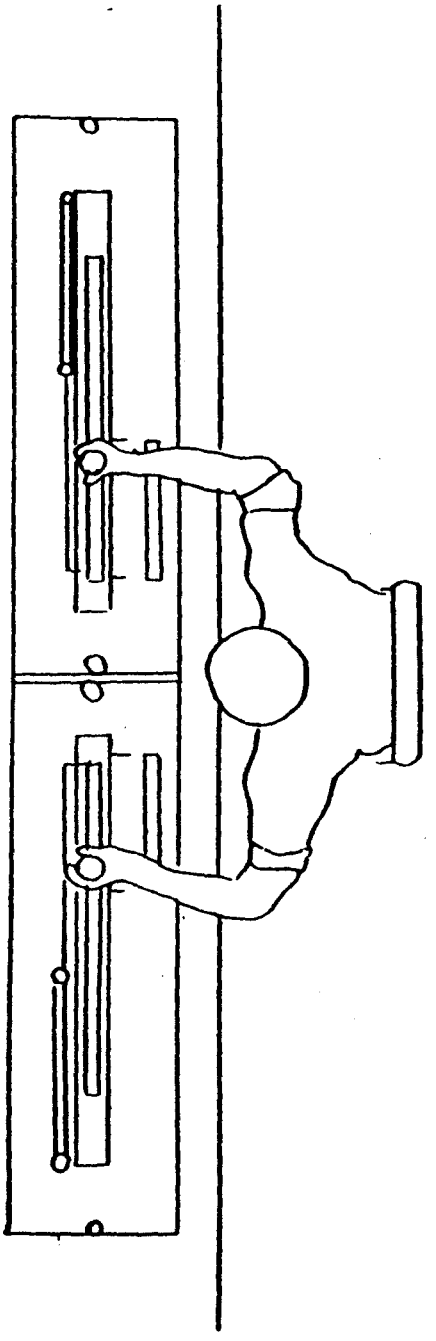
a) Healthy participant performs an in-phase to anti-phase switch.
b) Healthy participant performs an anti-phase to in-phase switch.
c) Participant with PD exhibits freezing upon switching to anti-phase.
d) Participant with PD exhibits a delayed response when switching to in-phase.

Figure 4: Absolute mean error performance in relative phase for the control and PD participants as a function of in-phase or anti-phase coordination pattern.

Figure 5: Absolute mean error performance in relative phase for the control and PD participants as a function of speed for the in-phase or anti-phase coordination patterns.

Figure 6: Standard deviation in relative phase for the control and PD participants as a function of in-phase or anti-phase coordination pattern.

Figure 7: Voluntary switch time for the control and PD participants as a function of in-phase or anti-phase coordination pattern.



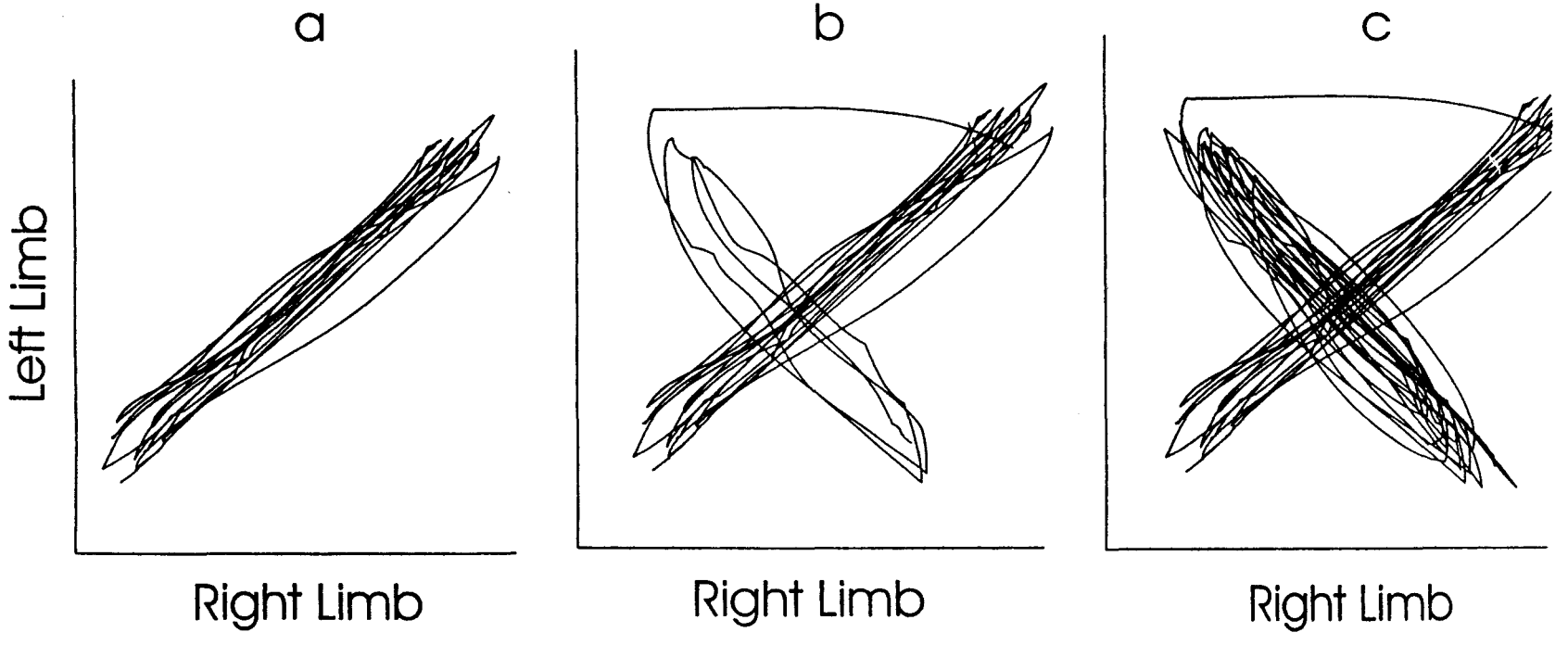
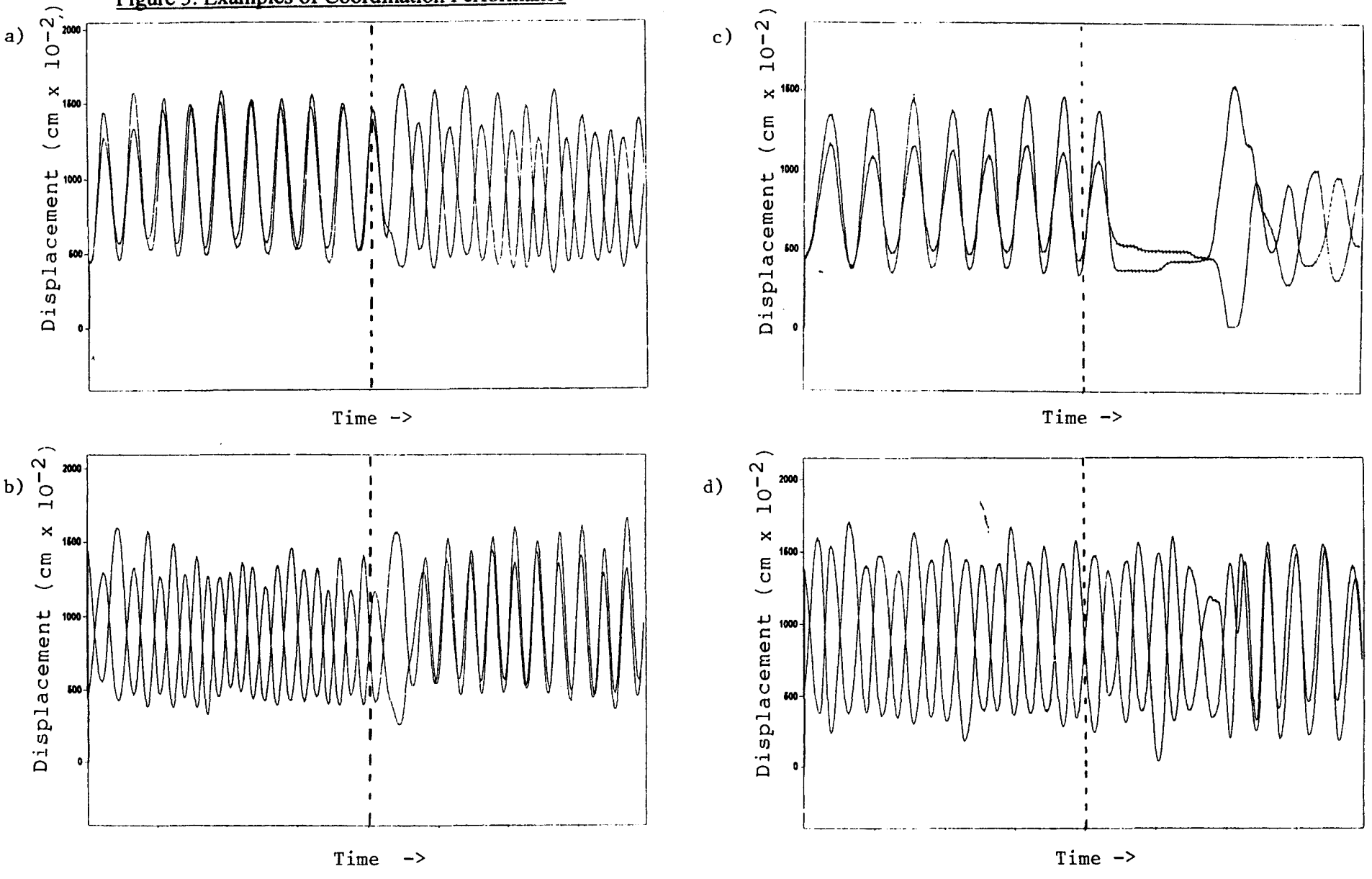
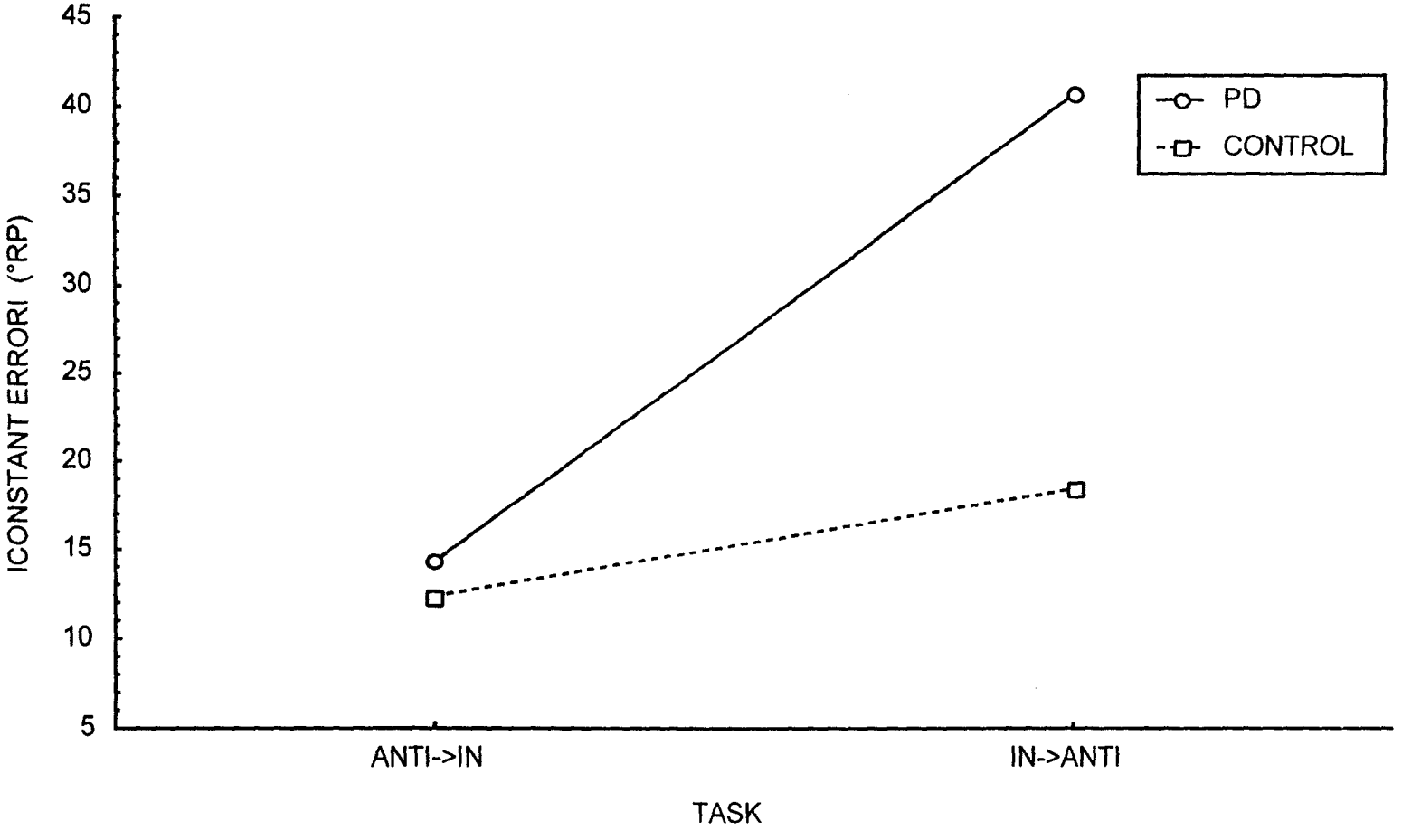
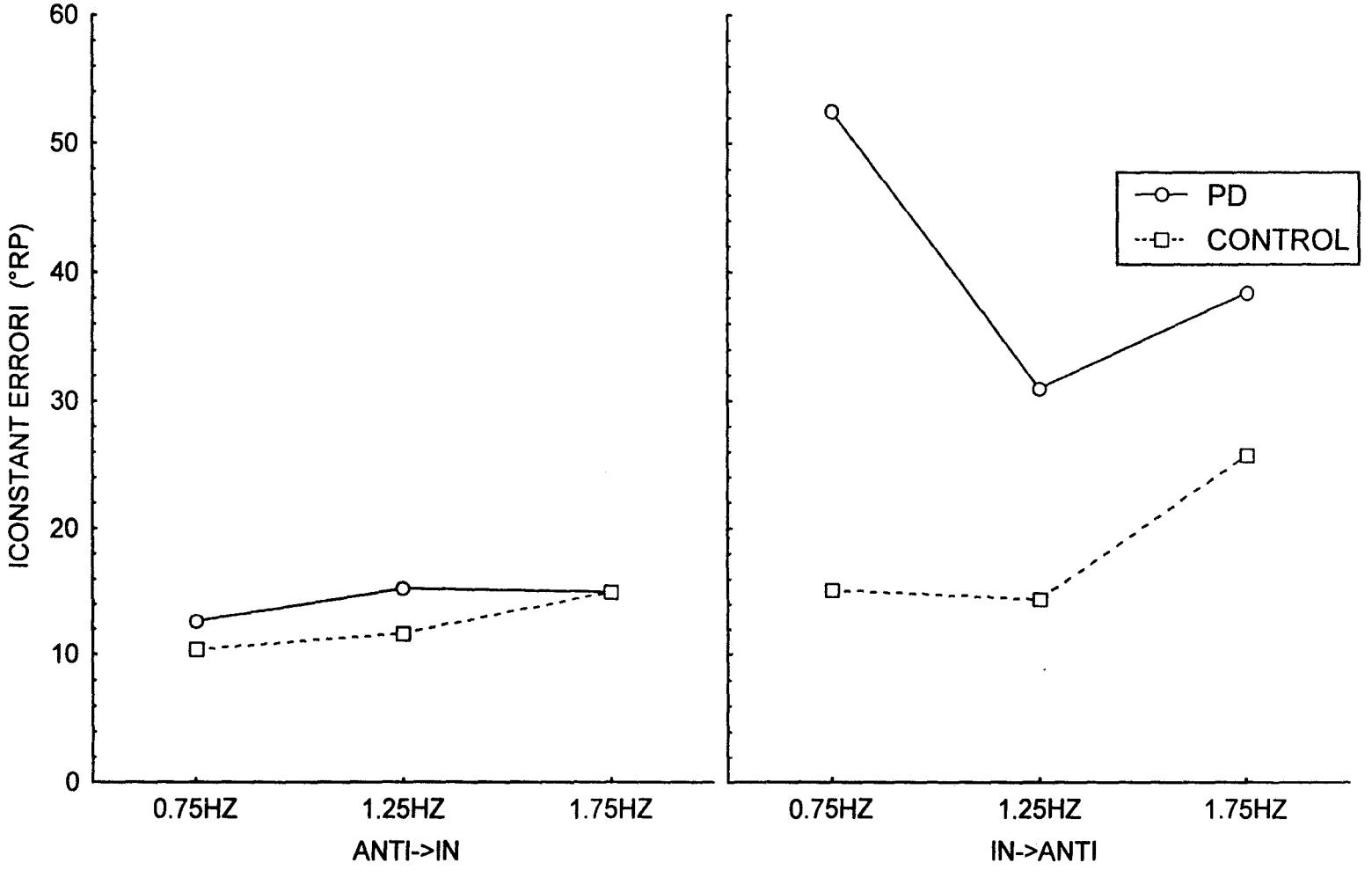
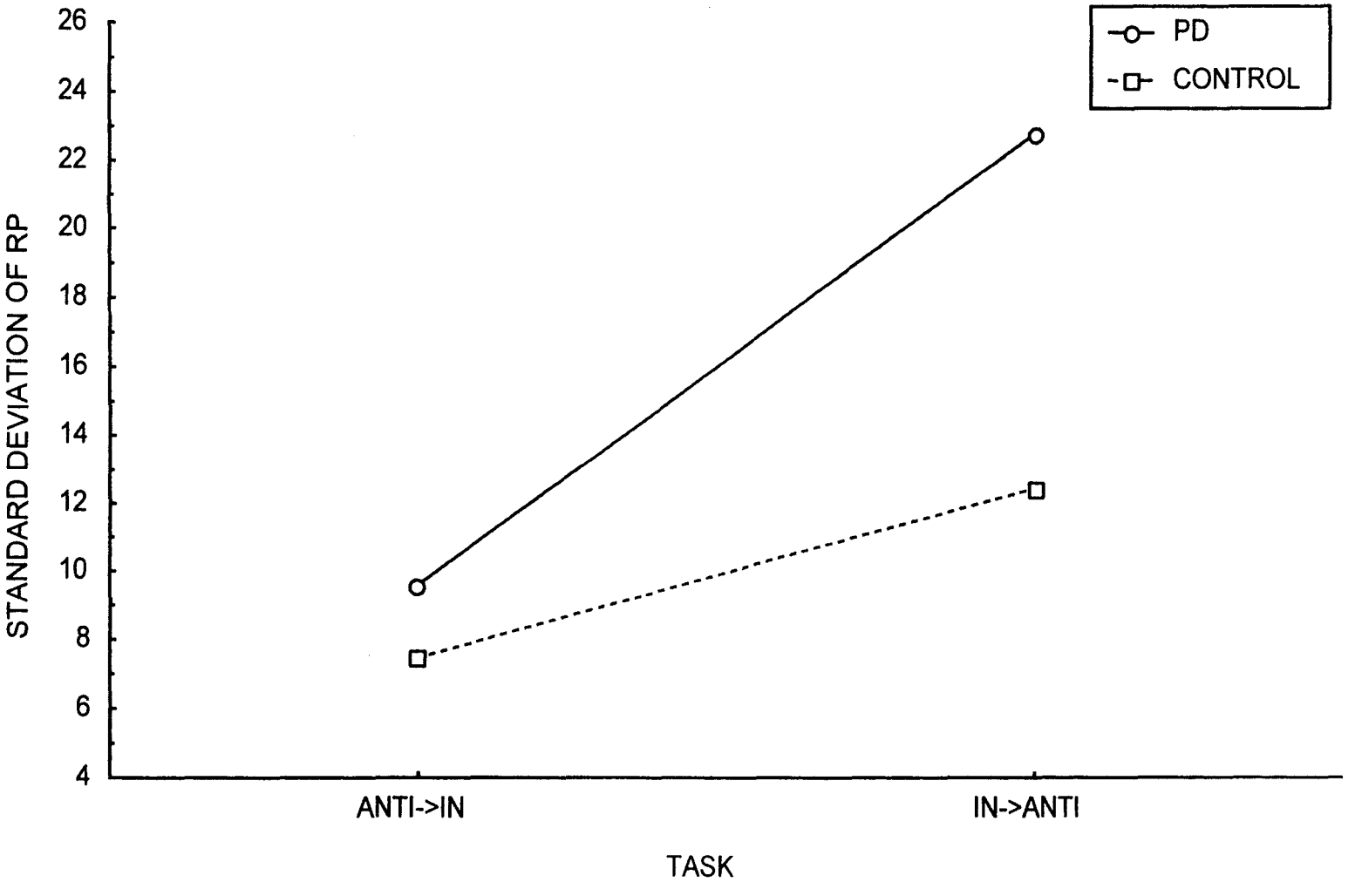

a
b
c
Left Limb
Right Limb
Right Limb
Right Limb

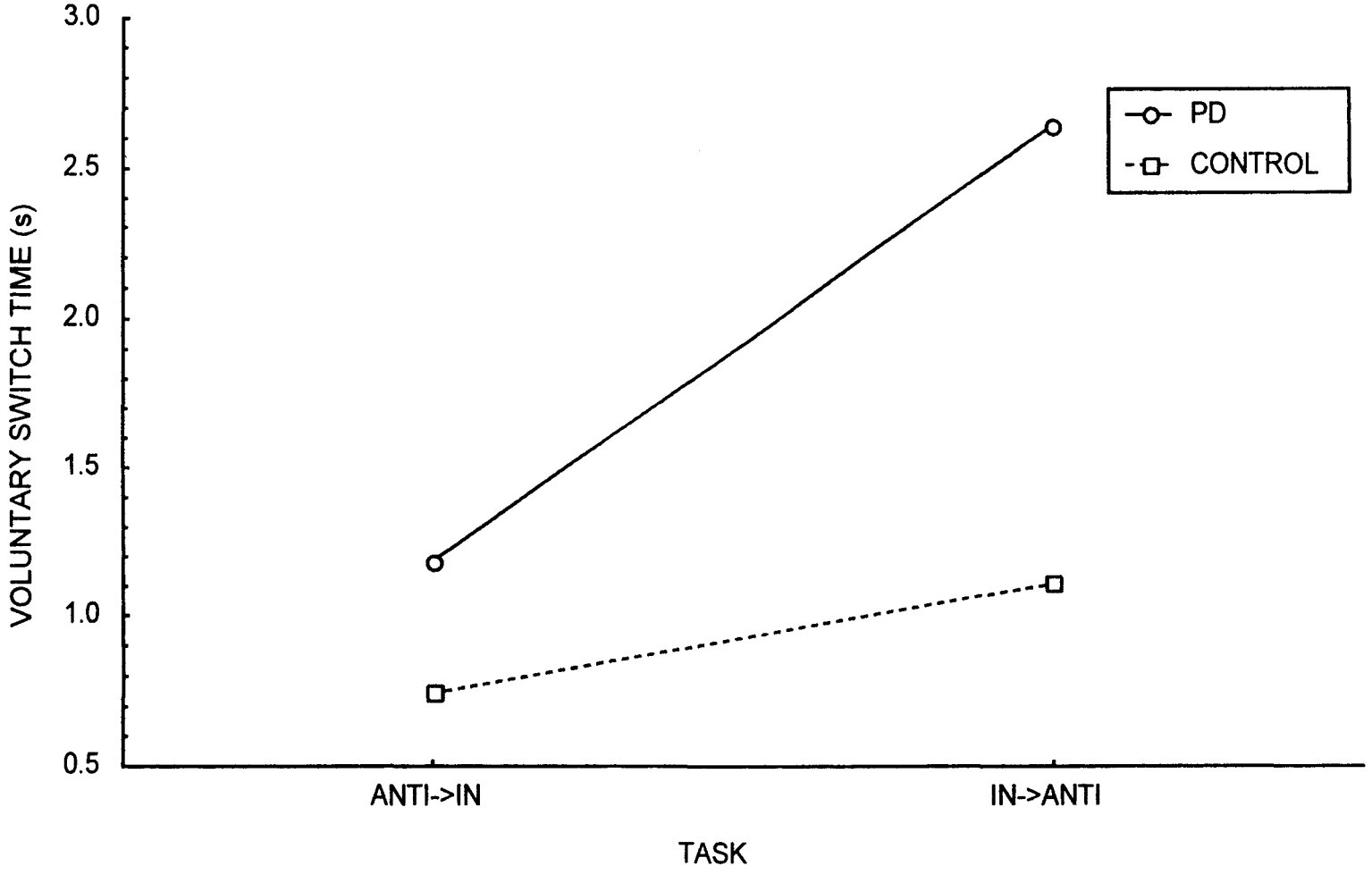
Figure 3. Examples of Coordination Performance




45
40
35
30
25
20
15
10
5
ICONSTANT ERRORI (°RP)
PD
CONTROL
ANTI->IN
IN->ANTI
TASK


60
50
40
30
20
10
0
ICONSTANT ERRORI (°RP)
PD
CONTROL
0.75HZ
1.25HZ
1.75HZ
ANTI->IN
0.75HZ
1.25HZ
1.75HZ
IN->ANTI


PD
CONTROL
STANDARD DEVIATION OF RP
26
24
22
20
18
16
14
12
10
8
6
4
ANTI->IN
IN->ANTI
TASK


3.0
2.5
2.0
1.5
1.0
0.5
VOLUNTARY SWITCH TIME (s)
PD
CONTROL
ANTI->IN
IN->ANTI
TASK

General Discussion

Individuals with Parkinson's disease (PD) experience many problems with movement execution. Some of these impairments may be severe and seriously limit independent functioning. Hence, it has become increasingly important to understand the underlying process of motor impairments and use this knowledge as a basis for therapeutic intervention. Previous research has generated many potential explanations for PD movement impairments including improper force generation, deficits in internal regulation of attention, and deficits in the ability to plan sequences of movement. The overall purpose of this research was to investigate PD impairments in the execution of continuous, simultaneous movements that involve repetitive sequences, and to determine which if any of these deficits were involved.

The first study (Section I) was designed to determine differences in executing in-phase and anti-phase coordination patterns. These movements have been well studied in healthy populations and are considered automatic because of the wide range of situations in which they occur without the need for practice (Baldissera, Cavallari, Marini, & Tassone, 1991) and also because they can be performed concurrently with other tasks without a decrement to performance. Previous research suggests that execution impairments associated with PD may be common to the less automatic anti-phase but not in-phase movements (Stelmach & Worringham, 1988; Samuel, Ceballos-Baumann, Blin, Uema, Boecker, Passingham, & Brooks, 1997; Swinnen, Van Langendonk, Vershueren, Peeters, Dom, & De Weerdt, 1997), although these observations have been made with little or no imposed challenge to the required speed of movement. In the present

investigations, participants performed a continuous bimanual coordination task at three different movement speeds (as paced by an auditory metronome) to further challenge the motor system. It was hypothesized that increased speed might reveal PD difficulties in the more automatic in-phase pattern, in addition to typical problems observed with anti-phase movements. However, this was not the case; an increase in movement speed impaired performance in only the anti-phase task. These observations were evident in measures of relative phase, movement amplitude as well as apparent freezing and hypometric deficits.

This first study was also designed to examine the influence of external auditory pacing on performance of these movements. Previous bimanual research in individuals with PD has focused on participants performing different tasks with each limb (Schwab, Chafetz & Walker, 1954; Talland & Schwab, 1964; Horstink, Berger, van Spaendonck, van den Bercken, & Cools, 1990; Lazarus & Stelmach, 1992). These findings have indicated that the need to internally regulate the amount of attention devoted to each limb may explain the difficulties experienced by individuals with PD in bimanual tasks. The provision of external cues as a useful attention strategy has since been supported as an effective way to improve movement performance in individuals with PD (McLennan, Nakano, Tyler, & Schwab, 1972; Freeman, Cody, & Schady, 1993; Georgiou, Iansek, Bradshaw, Phillips, Mattingley, & Bradshaw, 1993; Morris, Iansek, Matyas, & Summers, 1996; Oliveira, Gord, Nixon, Marshall, & Passingham, 1997). The first experiment (Section I) employed a protocol in which the availability of external timing cues was manipulated during the execution of coordinated movements. The objective was to

determine if internal time regulation as opposed to externally driven attention strategies would affect the ability to coordinate movements that were thought to be relatively automatic. Since participants with PD were having difficulty coordinating the anti-phase task when paced by the metronome, it was expected that the lack of external cues would further impact performance of this task. Unexpectedly, there were no main effects for tone, nor interactions between group, tone and/or phase suggesting that coordinated movements were not performed differently regardless of availability of external cues. Hence, provision of external cues does not appear to improve the regulation of attention during performance of the more difficult interlimb movements involved in the anti-phase task.

Although there was no indication that external cues improved timing and/or coordination performance of in-phase and anti-phase movements, the results of the first study still suggest that external cues play an important role in the focusing of attention. An interaction between group, hand and phase suggests that participants with PD focused on their dominant right hand when external cues were present (as seen with improved amplitudes for the right-hand but not the left during this condition). Attention was directed to the left hand when external cues were not present (i.e. improved amplitude for the left but not the right hand). In contrast, healthy controls displayed no bias toward either the right or left limb as a result of external cueing. It is therefore suggested that individuals with PD are able to use external cues to improve certain aspects of movement amplitude but not necessarily other measures reflective of timing performance (i.e. relative phase).

This experiment also permitted an indirect examination of force modulation as a potential factor that influences the execution of bimanual movements. Since both the in-phase and anti-phase tasks involved movements with continuous yet definite reversal and end-points, if force modulation affected this task, it could be predicted that participants with PD would display similar deficits in performance of both coordination patterns when compared to controls. As previously mentioned in-phase movements were performed as well by individuals with PD as healthy controls, whereas anti-phase movements were performed with significantly poorer accuracy and stability. It can be inferred from this observation that force production was not a factor since impairments were observed in only the anti-phase task.

Alternatively, researchers have speculated about the role of selective attention when individuals with PD attempt to coordinate limb movements. It has been suggested that selective attention may be related to deficits in the ability to separate plans of action (Horstink et al., 1990; Robertson & Flowers, 1990). According to this argument, in-phase movements are considered more automatic (and hence require less attention), and would not require separate plans of action for each limb given the spatio-temporal coupling that occurs when activating homologous muscle groups. In contrast, anti-phase movements that are considered relatively less automatic, involve a greater attention requirement because simultaneous activation of non-homologous muscle groups would involve a different action plan for the timing of each limb to be maintained. If individuals with PD had difficulty dividing attention between limb movements, they would likely reveal their coordination difficulties in anti-phase movement tasks. Hence,

the first study supported a Parkinsonian deficit in selective attention. The second study manipulated attention demands to further test this hypothesis.

In the second study, participants were required to intentionally switch to a secondary coordination task when signaled by an external cue. It was expected that individuals with PD would switch to the in-phase coordination task with no greater difficulty than healthy participants. In contrast, we expected that switching from the in-phase to anti-phase task would be accomplished with greater difficulty for the group with PD, if this movement required a greater attention capacity than the in-phase task. Our predictions were confirmed in both accuracy and stability of relative phase, as well as the time required to accomplish a successful switch. The group with PD switched from the in-phase to anti-phase pattern with more difficulty compared to healthy controls, and required more than double the amount of time to accomplish these switches. More importantly, freezing impairments were observed in 53.8% of the in-phase to anti-phase switch trials, whereas only 15.5% of the opposite switch resulted in such impairments. Although we expected no freezing in a switch to the more automatic in-phase task, the attention requirement of responding to the external stimulus is a probable explanation for the unexpected, but small percentage of freezing impairments observed in the anti-phase to in-phase switch task.

Overall, the two experiments have identified impairments in bimanual coordination associated with a selective attention deficit for individuals with PD. This deficit is one that does not appear to be influenced by the provision of external cues. In fact, freezing and other severe movement deficits noted in these experiments appear to be

related to the attention requirement of separating plans of action for each limb. This explanation could also apply to previous experiments (Schwab et al, 1954; Talland & Schwab, 1964; Horstink et al., 1990; Lazarus & Stelmach, 1992) in which different actions were required for each limb. Latash and Anson (1996) support the examination of underlying mechanisms that may lead to freezing. They argue that atypical movement outcomes may be the result of adaptation to a primary disorder rather than something pathologic. According to this view, individuals with PD may adapt to neural deficits by requiring more time to attend to certain components of movement. Hence, it is possible that the severe freezing impairments observed during our task may be evidence of an adaptive strategy employed by individuals with PD in attempt to give the motor system time to correct for poor selective attention mechanisms. It also becomes apparent that freezing difficulties associated with movement initiation may occur through a very different underlying mechanism than the selective attention processes examined during movement execution in this study. This may be the reason that external cueing is very effective in initiation tasks such as walking or rising from a chair, but ineffective when freezing occurs during movement execution (i.e., the present coordination task). The results of these experiments have implications for rehabilitation strategies in individuals with PD. It is important to understand selective attention mechanisms and the influence that they may have on certain atypical movements, when developing rehabilitation strategies to deal with Parkinsonian freezing.

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