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Movement deficits for Parkinson's disease patients in select functional behaviours : context opposes sequence and consequence

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MOVEMENT DEFICITS FOR PARKINSON'S DISEASE PATIENTS IN SELECT FUNCTIONAL BEHAVIOURS: CONTEXT OPPOSES SEQUENCE AND CONSEQUENCE

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DEDICATION

This thesis is dedicated to the greatest classroom I've ever sat in, 51 Lynhurst Park Drive. Much love and thanks to three fantastic classmates, Jan, Joyce, and Rob, and the two best teachers, my mother and father, Mary Jane and Warren Doan.

ABSTRACT

Contextual influence on movement was examined for a selection of everyday activities. Non-medicated and medicated Parkinson's disease (PD) patients and control subjects reached for a drinking glass target from both seated and standing postures, and stepped over a surface-level obstacle while walking on a constrained path. Contextual challenge was increased in the seated reach by filling the glass with water, in the standing reach by increasing the depth of the gap between target and stationary foot position, and in the obstacle negotiation trials by raising the gait path surface above floor level. In all cases, behaviour among PD patients was uniquely disrupted by contextual challenge. In addition, benefits of conventional medication therapy for PD patients were limited in challenging contexts. These results suggest an adapted movement control mechanism at work in PD patients, with the neural resources used in this adapted response prone for interference during contextual challenges.

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Finally, a special thanks to the many dedicated research participants in this project, especially our Parkinson's disease patients and their caregivers. It is an honour to work with a group who are motivated by their hopes for the future, while continuing to thrive in their present.

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1.0 INTRODUCTION

Despite greater than four centuries of anecdotal and clinical observation [Sacks, 1999] and two centuries of scientific investigation [Burch and Sheerin, 2005], Parkinson's disease (PD) insidiously persists. Scales that standardize assessment of cardinal symptoms and simple manifestation fail to penetrate the depression, decreased function, and diminished quality of life PD patients report, based on their progressive loss of independence and control in activities of daily living [Cahn et al.., 1998; Chapuis et al., 2005; Kuopio et al., 2000]. One suggestion for improved assessment of the parkinsonian deficit is a focus on real-world functional tasks [Morris, 2000], specifically the frequent disparity between willed intention and motor execution observed among PD patients on a variety of simple and complex tasks [Rubinstein et al., 2002]. The aim of this introduction is to provide a theory for the unique relationship between context and action observed in PD patients, and to provide supporting evidence for the premise from a selective review of experimental and observational studies, including Parkinson's original report. As a prelude to this theoretical development, a brief review of basal ganglia anatomy and function is provided. The paper then proceeds to the basic principles underlying context-dependent research in movement disorders, and a review of current experimental results on PD motor deficits, general deficits, and a brief discussion of current therapies.

1.1 THE BASAL GANGLIA

1.1.1 COMPONENT STRUCTURES

The basal ganglia (BG) is comprised of the caudate nucleus, the putamen (together defined as the striatum), the external globus pallidus (GPe), the internal globus pallidus (GPi) (these two plus putamen comprising the lenticular nucleus), the subthalamic nucleus (STN), and the substantia nigra (separately as pars compacta and pars reticulata), each structure existing bilaterally (Figure 1.1). These structures show a progressive convergence in volume, with the striatum outsizing the GPe, GPi, and STN by 12, 20, and 60 times, respectively [Yelnik, 2002]. The striatum is the BG's main site for input from the cerebral cortex, while the internal globus pallidus and substantia nigra pars reticulata (a combined structure) are the main source of output, projecting to the ventral lateral and ventral anterior thalamus. The basal ganglia has also been associated with ventral structures (specifically, nucleus accumbens and ventral tegmental area) that are involved in stress, reward, and fear responses [Schiffer, 1999].

1.1.2 INTRINSIC CONNECTIVITY

The current model of BG connectivity and function (Figure 1.2) was developed following comparative investigation of BG anatomy and movement disorders resulting from BG lesion or dysfunction [Albin, Young, & Penney, 1989; DeLong, 1990]. While the Albin-DeLong model has fallen into some suspect based on anatomical [Parent et al., 2001] and information processing [Bar-Gad & Bergman, 2001] analyses that suggest a more widely distributed network of BG inter-connections, the simplicity and explanatory power of the existing model continue to place it at the foundation of research into BG function and dysfunction. The appeal of this simplicity is not to be under-estimated - Marsden's classic

paper '*The mysterious motor function of the basal ganglia*' has been cited in peer-reviewed manuscripts over 525 times since its publication in 1982, possibly indicative of just how mysterious the function of the basal ganglia is [Marsden, 1982]. For the purposes of this review, a dual path (Albin-DeLong) model of BG structure will be adopted.

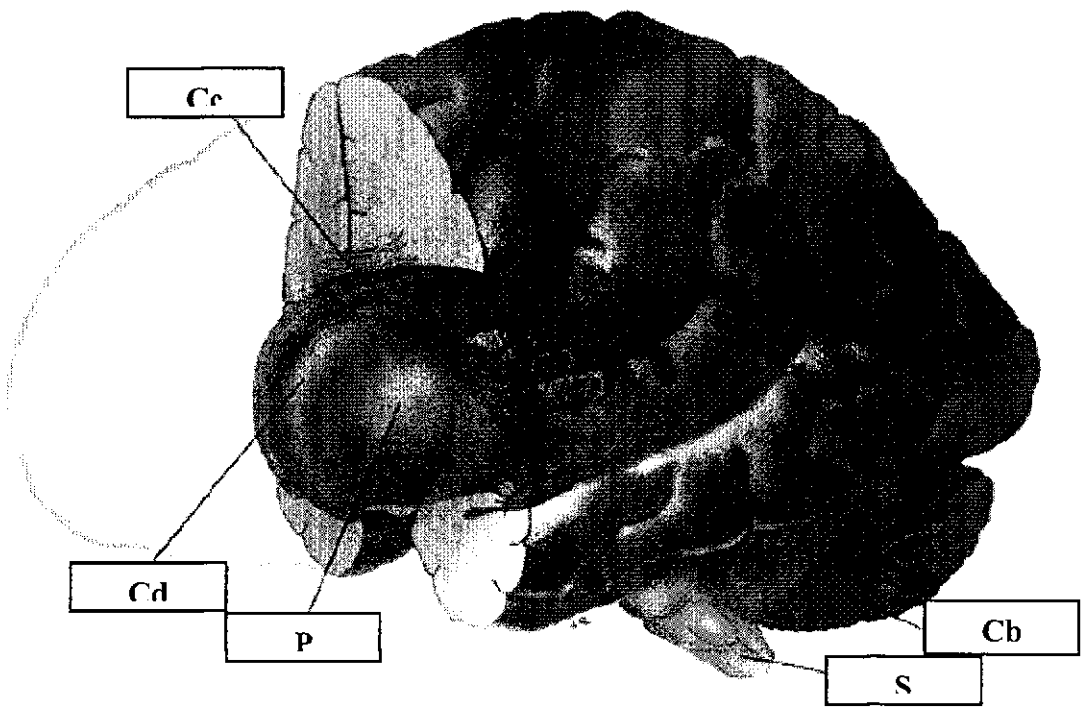


FIGURE 1.1 Anatomical model of basal ganglia. (adapted from Hendelman, 2000) A fronto-sagittal view of the human brain, with frontal cortex and anterior temporal lobes cut away to expose the basal ganglia. The caudate (Cd) and putamen (P) are labeled, along with other cortical [corpus callosum (Cc)] and subcortical [(brain stem (S), cerebellum (Cb)].

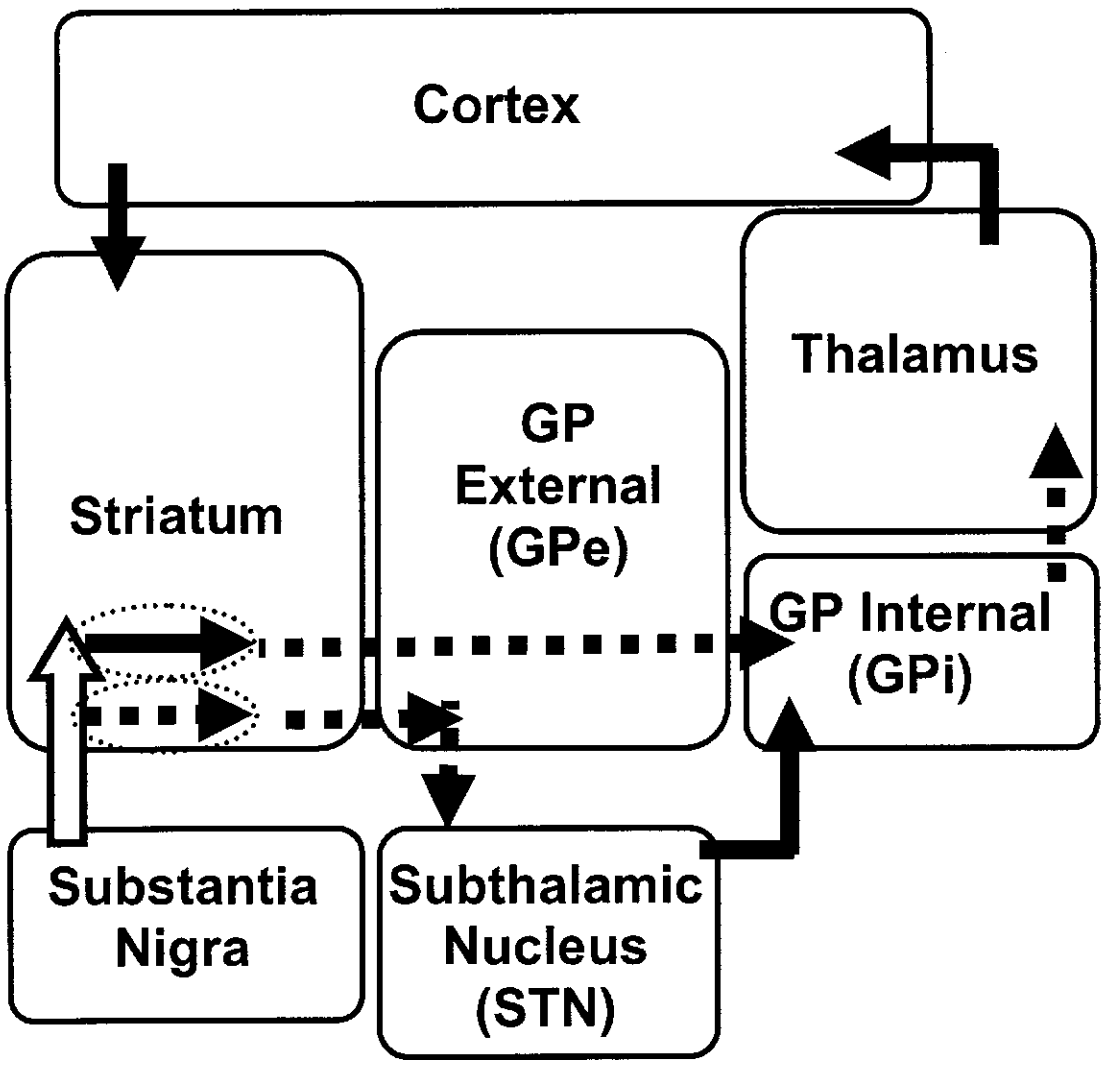

Cortex
Striatum
GP
External
(GPe)
Thalamus
GP Internal
(GPi)
Substantia
Nigra
Subthalamic
Nucleus
(STN)

FIGURE 1.2 Connectivity model of normal basal ganglia function

(adapted from Burch and Sheerin, 2005)

Dual path connectivity model for normal BG function, as initially proposed by Albin, Young & Penney (1989) and DeLong (1990). Solid arrows indicate excitatory projections (Glutamatergic) and broken arrows indicate inhibitory projections (GABAergic). Dopamine influx is indicated with the open arrow. The direct pathway travels from striatum to internal globus pallidus (GPi) to thalamus, and is net excitatory: excitation from cortical input increases direct inhibition of GPi, which decreases inhibition of thalamus, which increases excitation of specific cerebral cortex areas. The indirect pathway travels from striatum to external globus pallidus (GPe) to subthalamic nucleus (STN) to GPi to thalamus, and is net inhibitory: cortical input excites the striatum, which inhibits GPe and subsequently increase activity of STN, increasing activity in GPi and inhibiting thalamus. Dopamine produces an amplified excitatory effect though excitation of D1 receptors in the direct loop and inhibition of D2 receptors at the start of the indirect loop (receptors in broken ovals).

As shown in Figure 1.1, the Albin-DeLong model of BG function features dual pathways from input to output. Specifically, the direct pathway consists of an inhibitory (GABAergic) efferent from striatum to external globus pallidus/substantia nigra pars reticulata. A subsequent GABAergic projection has an inhibitory influence over the thalamus. The indirect pathway features GABAergic projections from striatum to internal globus pallidus, and from internal globus pallidus to subthalamic nucleus. A subsequent excitatory glutamatergic projection leads to the thalamic output nuclei. Current research suggests that these pathways remain somatotopically segregated throughout the basal ganglia [Romanelli et al., 2005].

1.1.3 EXTRINSIC CONNECTIVITY

In complement to the intrinsic dual path model of BG function is the extrinsic segregated circuit model proposed by Alexander, DeLong, and Strick [1986]. Their extensive review of anatomical and physiological findings led to the suggestion that five anatomically and functionally distinct neural circuits were incorporated in and modified by the basal ganglia. While topographically distinct with respect to BG nuclei input and output sites, these circuits are proposed to each be structured and controlled on the dual path model of Albin-DeLong [Crutcher & Alexander, 1990]. The circuits, with basic paths outlined in Table 1.1, are: Motor (originating in supplementary motor area); Oculomotor (originating in frontal eye fields); Prefrontal I or Complex (originating in dorsolateral prefrontal cortex); Prefrontal II (tentatively identified as related to set switching) (originating in lateral orbitofrontal cortex); and Anterior Cingulate (originating in anterior cingulate) [Alexander, DeLong & Strick, 1986]. The significance of multiple segregated functional loops in the basal ganglia, in the scope of this thesis, lies in the potential for idiosyncratic BG-related

deficits of motor, oculomotor, cognitive, and/or limbic function due to circuit-localised lesion or loss. This complex symptom manifestation is frequently observed among the PD population [Jahanshahi & Frith, 1998].

TABLE 1.1 Frontostriatal circuits (adapted from Alexander, DeLong, & Strick, 1986)

	CIRCUIT				
NODE	Motor	Oculomotor	Prefrontal I (Complex)	Prefrontal II (Set?)	Anterior Cingulate
Cortex Output	Supplementary Motor Area	Frontal Eye Fields	Dorsolateral Prefrontal	Lateral Orbitofrontal	Anterior Cingulate Area
BG Input	Putamen	Caudate	Caudate	Caudate	Ventral Striatum
BG Output	GPi / SNpr	GPi / SNpr	GPi / SNpr	GPi / SNpr	GPi / SNpr
Thalamic Input	Ventral Lateral	Ventral Anterior	Ventral Anterior	Ventral Anterior	Medial Dorsal

1.1.4 INTRINSIC FUNCTION - MODEL

As previously stated, Albin-DeLong's dual path model of the basal ganglia provides the currently accepted explanation for BG function [Yelnik, 2002]. In this model (Figure 1.1), the direct pathway facilitates BG output when stimulated by the cerebral cortex. Specifically, excitatory glutamatergic inputs from cortex would increase inhibitory output from the direct path neurons of the striatum, leading to subsequently increased inhibition of the internal globus pallidus. This inhibition decreases the GPi's subsequent inhibitory effect on the thalamus, allowing for increased thalamic excitation of the cerebral cortex. In contrast, the indirect pathway inhibits BG output when the system is activated by cortical input. In this pathway, cortical excitation inhibits the external globus pallidus, leading to disinhibition of the subthalamic nucleus, increased excitation of the internal globus pallidus, and increased inhibition of the thalamus as a net result. In the dual path model, the direct and indirect loops can be characterized as a reciprocal balance [Graybiel, 2000]. The transient release of dopamine into the system during glutamatergic stimulation from the cortex produces an amplified excitatory effect, through excitation of D1 receptors at the striatal junction of the direct path and inhibition of D2 receptors at the striatal junction of the indirect path [Sian et al., 1999].

1.1.5 INTRINISIC DYSFUNCTION - MODEL [PARKINSON'S DISEASE]

In the parkinsonian model of basal ganglia function, decreased dopamine levels limit any net excitatory effect in the basal ganglia, allowing the negative feedback control of the indirect loop to dominate BG operation. As indicated in Figure 1.3, limited excitation from the direct loop combined with reduced inhibition in the indirect loop causes severely

diminished output from the thalamus, and submaximal returned excitation to the cortex. The pathological loss of dopamine in PD patients has been reported as critical at levels exceeding 80%, with a clinical diagnosis of marked parkinsonism associated with dopamine losses of 99% in the putamen and 92% in the caudate [Hornykiewicz, 2001]. The high level of dopamine loss necessary for diagnosis of PD provides some indication of the robust nature of BG operation – function appears normal even with only ¼ of neurologically normal dopamine levels [Hornykiewicz, 2001]. This observation does not overlook the involvement of other neuropathologies in the progression of Parkinson's disease, specifically the early appearance of extra-nigral Lewy bodies [Braak et al., 2003; del Tredici et al., 2002].

1.1.6 EXTRINSIC FUNCTION AND DYSFUNCTION

It is important to establish that extrinsic function of the BG is typically inferred from extrinsic dysfunction, often through application of the classical neuropsychological model of double dissociation [Kolb & Whishaw, 1995]. Specifically, behavioural comparisons between a BG-lesion group and neurologically normal group provide evidence of function(s) lost following lesion, as well as behaviours that are novel (though typically neither functional nor preferential) to the BG-lesioned group. While other movement disorders related to basal ganglia dysfunction exist (e.g. hyperkinetic disorders, dystonic disorders), this work will concentrate on hypokinetic movement disorders of the basal ganglia, specifically Parkinson's disease.

This dissociative approach has led to the development of various hypotheses for the extrinsic function of the basal ganglia in organizing and executing behaviour. Specifically, activity in the basal ganglia has been associated with the interpretation of set [Hocherman et al., 2004b], the assembly of movement elements into an appropriate chunked motor

response [Agostino et al., 1992], the initiation of the appropriate chunked motor response [Jog et al., 1999], the sequencing of movement elements [Benecke et al., 1987; Marsden, 1982], the switching between motor responses [Fama & Sullivan, 2002; Harrington & Haaland, 1991; Pollux, 2004] and/or sets [Chong et al., 2000; Woodward et al., 2002], and procedural learning of set/response relationships [Krebs et al., 2001; Zalla et al., 2000]. Contrary results exist as well, specifically identifying undisturbed movement execution [Majsak et al., 1998] and learning [Helmuth et al., 2000] among PD patients under specific experimental conditions. Given this breadth of findings and hypotheses, an alternative approach to experimentation and classification may be required to help illuminate the darkened basement that is BG function and dysfunction [Kinnier Wilson, 1920 (referenced in Graybiel 2000; Marsden 1982]. The following section of this introduction will outline such an alternative explanation, supported by studies that adhere to the paradigm.

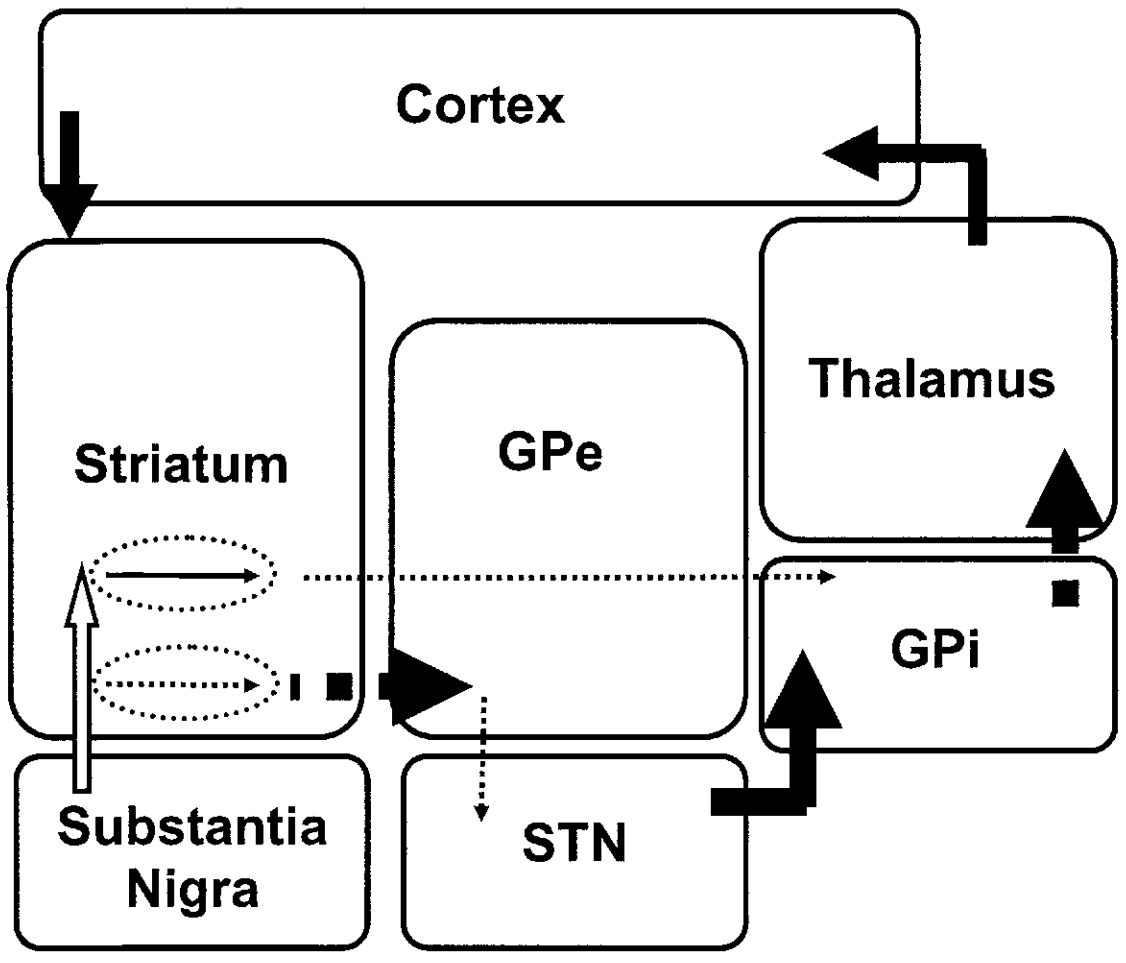

Cortex
Striatum
GPe
Thalamus
GPi
Substantia
Nigra
STN

FIGURE 1.3 Connectivity model of parkinsonian basal ganglia function (adapted from Burch & Sheerin, 2005)

The solid arrows indicate excitatory projections (Glutamatergic) and broken arrows indicate inhibitory projections (GABAergic). Dopamine influx is indicated with open arrow. In the parkinsonian model, degeneration of the dopaminergic production and projection from substantia nigra to striatum leads to reduced net excitation. The direct pathway has limited inhibition of the GPi, which in turn increases inhibition of thalamus, and subsequently decreases excitation of cortex. The indirect pathway fails to inhibit the subthalamic nucleus, subsequently increasing activity in GPi and inhibiting thalamus.

1.2 ENVIRONMENTAL CONTEXT AND INFORMATION PROCESSING CAPACITY

For neurologically normal animals, behaviour is influenced by context. Indeed, normal behaviour can be defined as actions that are in concordance with the physical and social constraints of their external context [Dunn et al., 1994]. This interrelationship presents an unique but imperative prospect for experimentation into behaviour and movement disorders, specifically the opportunity to manipulate context as an independent variable in behavioural analyses [Teasdale & Stelmach, 1988]. For PD research, such an approach may dissociate movement impairments that are a direct result of BG deficit, and impairments that are an adaptive response to the general PD effect of diminished precision of movement [Phillips et al., 1994]. This dissociation could have important implication in the design and delivery of more effective rehabilitation therapies [Montgomery, 2004]. Equally important is the need to establish these experimental contexts as relevant to real-world tasks, to increase research validity while allowing for transferability of the observed human performance principles to everyday tasks and situations [Czaja & Sharit, 2003]. This is critical in the study of Parkinson's disease, where spatiotemporally-constrained real-world situations can lead to disruption in the execution of action [Fahn, 1995; gray & Hildebrand, 2000; Stolze et al., 2004].

Prior to the execution of an action, several steps of information processing are required [Jahanshahi & Frith, 1998]. Reviewing the neuroanatomical basis of all information processing steps is beyond the scope of this paper, but the basic processing path includes sensory integration, goal setting, response selection, scheme programming, inhibition of contentious schemes, and response initiation [Le Bras et al., 1999]. For non-reflexive movements, a higher-order supervisory processing system is theorized to control this

processing [Kropotov & Etlinger, 1999]. Norman and Shallice's model of the Supervisory Attentional System outlines the function of such a system, and links its operation with the frontal lobes and prefrontal cortex [Shallice & Burgess, 1993]. Paramount in the model is the demand on attention for information processing. Therefore, information processing capacity can be defined as task-available attention [Heuer & Wing, 1984]. While the remainder of this review will discuss experimental and everyday examples of information processing deficits among PD patients with specific focus on context-based manipulations of information processing, it is relevant at this point to outline current models of information processing capacity experimentation used in the observation of motor behaviour disturbances.

1.2.1 INFORMATION PROCESSING CAPACITY EXPERIMENTATION

In a recent review, Wollacott and Shumway-Cook [2002] have provided an excellent exposition of current experimental studies that explore the relationship between information processing capacity and critical everyday activities, specifically posture and gait, that rely on the availability of information processing capacity. They conclude, in part, that 'applications of attention and postural control research are improving our understanding of motor control problems in patients with specific types of pathology, such as PD'. This justification, combined with the previously identified imperative for ecologically-based investigation of movement disorder [Teasdale & Stelmach, 1988], lends support for a brief inspection of experimental methods for manipulation of information processing capacity pertinent to the study of the parkinsonian movement disorder in activities of daily living.

1.2.1.1 CONCURRENT DEMANDS ON INFORMATION PROCESSING CAPACITY: DUAL-TASK INTERFERENCE

The dual task paradigm involves the simultaneous presentation of two separate task stimuli to participants [Abernethy, 1988]. This model is predicated on Kahneman's theory of finite attentional capacity, which suggests that attention is available as a common resource pool with a finite capacity [Kahneman, 1973]. Given this instantaneous limit on information processing, the dual task methodology follows the hypothesis that task performance will decrease when the combined attention required in multiple concurrent tasks exceeds the finite information processing capacity [Abernethy, 1988]. As an example, Ho and colleagues [2002] measured the initiation and ongoing volume control of PD patients' speech while the patients were either conversing freely or reciting number sequences as a primary task. In the secondary task, patients and control participants used a joystick and a computer monitor to perform a target-needle tracking task. The results showed that PD patients used lower mean speech volume, as well as greater ongoing volume decay and increased duration of pauses between words, with the introduction of the secondary task. It is interesting to note that patients and controls had equal levels of performance on the secondary task, possibly indicative of the benefit of visual feedback in potentiating motor behaviour among PD patients [Rubinstein, Gliadi, & Hausdorff, 2002]. Dual tasks models can involve any combination of motor and cognitive tasks, and measurements can be made (and inferences drawn) about the demands of tasks and the associated integrity of processing and activation systems in either psychomotor modality [Wollacott & Shumway-Cook, 2002].

1.2.1.2 COMPOUND DEMANDS ON INFORMATION PROCESSING CAPACITY: SINGLE-TASK CONTEXT

Manipulations of task difficulty have a longer history in behavioural experimentation. In a classic example, Fitts [1954] showed that decreasing the size of a target for a repetitive pointing task led to the need for a log-linear decrease in speed among neurologically normal adults to maintain acceptable task accuracy. Extensions of this work have shown a similar relationship in experimental reaching tasks [Bootsma et al., 1994] and reaches to functional targets [Latash & Jaric, 2002]. Furthermore, the same Fitts'-type relationship has been found to exist among PD patients, but at a steeper decrement – that is, PD patients had greater decreases in velocity and acceleration magnitudes as target size decreased [Sanes, 1985; Weiss et al., 1996]. This decrement may be normalized with PD medication [Montgomery & Nuessen, 1990]. A possible analogous condition exists in the 'pop-out' paradigm, where time required to visually search and locate a target in a field of stimuli increases as either target decreases in size or target increases in feature similarity to field stimuli [tresilian, 1998]. Moderate to severe PD patients have been shown to exhibit increased search times for 'pop out' tasks [Berry et al., 1999]. Marteniuk and colleagues [1987] used a series of functional tasks with implicit task demand constraints (e.g. reaching for both robust (tennis ball) and fragile (light bulb) targets of equal object size) to establish that movement planning and execution are unique to task constraint, or difficulty. This finding emphasizes the importance of attention to context in preparing and executing an movement. Shallice and Burgess [1993] suggest that the Supervisory Attentional System would be active in controlling behaviour in tasks that are technically difficult, among other situations. It follows that increased attentional resources are required for planning and executing

movements as task difficulty increases [Wu et al., 2005], even within a single-task paradigm. In summary, the nature of single-task demand manipulations in behavioural analysis are to increase the difficulty of a motor task, ideally in an ecologically-valid manner, without explicitly loading the system with additional tasks, or changing the skeletomuscular contributors to task completion.

1.2.1.3 COMBINING INFORMATION PROCESSING CAPACITY DEMANDS

Differentiating these two experimental models for attentional manipulation and behavioural outcome also leads to the suggestion for a possible combined model, which capitalizes on the interrelationship of context and movement. As an example, a participant population could be asked to ascend a staircase with closed risers, and could be measured on ascent initiation latency, mean velocity of ascent, and average time spent with both feet on separate treads (double support time). Given the same staircase with risers removed, we could hypothesize that the 'open' appearance of the staircase structure would lead to increased latency of ascent initiation, decreased mean velocity of ascent, and increased time spent in double support. In this example, no explicit secondary task has been added to the movement. In addition, no change has been made to the goals of the task, the set and sequence of action patterns that would most directly lead to those goals, or the end result of successful completion of the task. However, a change to the single-task context (removal of risers) has made an implicit intrusion on attention (attention diverted to some aspect or potential outcome of the open spaces between the stairs), leading to a form of attentional interference, specifically split attention between task and environment [Dunn, Brown, &

McGuigan, 1994]. In this example, information processing capacity has been diverted to a stimulus that is completely or near-completely extraneous to successful completion of the task (similar to dual-task model) but which is entirely within the environmental context of the action (similar to single-task model). As a final note, it has been shown that attentional interference appears to have an anxiety-driven bias, where, for example, individuals who fear pain experience greater attentional interference when presented with pain-related images as the environment for a reaction time task, in comparison to either neutral or general negative images [Asmundson et al., 2005]. Following on this foundation, it can be suggested that PD patients may be particularly sensitive to attentional interference from contexts that impose spatiotemporal constraints on action, given evidence of parallel deficits in motor performance and attentional function [Fama and Sullivan, 2002]. This hypothesis is supported by qualitative [Gray & Hildebrand, 2000] and quantitative [Bennett et al., 1995] experimental results, and provides an evolving framework for the assessment [Chapuis et al., 2005] and management [Morris, 2000] of PD.

1.2.1.4 INFORMATION PROCESSING – SUMMARY

Two conclusions may be suggested from this brief methodological inspection of experimentation into context, information processing capacity, and behaviour. First, context and behaviour are inherently entwined, and movements are uniquely prepared and executed in accordance with intention and context [Marteniuk et al., 1987]. Secondly, experimental tasks that incorporate real-world contexts and quantifiable measures of behaviour can provide strong inference for the function and dysfunction of neural mechanisms that

prepare and execute movement [Czaja & Sharit, 2003]. An overriding aim of the research in this dissertation was to incorporate the spirit of the second conclusion, within a framework that is cognizant of the first. In the long-term, this approach will hopefully bear results that support the development of PD rehabilitation therapies that can target specific, troublesome contexts [Morris, 2000].

1.2.2 REVIEW OF LITERATURE

Saint-Cyr [2003] makes a novel distinction in the classification of evidence for frontostriatal function and dysfunction, dividing his review of the current literature into operational domains based in information processing. These domains are *CONTEXT*, *SEQUENCE*, and *CONSEQUENCE*, and it is Saint-Cyr's assertion that these categories could make 'fundamental basal ganglia processes ... more clearly inferred ... by isolating the various phases of information processing in time'. Based on this endorsement (and the logic behind it), a similar division will be adopted here. However, where Saint-Cyr's work primarily focused on reviewing neurophysiological experimental data, this review will focus on motor and cognitive studies among human PD patients, a widely-observed example of intrinsic dysfunction in the BG. Where possible, explicit discussion will be made of the environmental context and/or information processing demands that are incorporated in the experimental protocol.

1.2.2.1 CONTEXT

It has been suggested that directed attention is an adaptive strategy PD patients use to plan and execute movements [Morris et al., 2000]. While the system level of incorporation of this strategy is undetermined [Bezard et al., 2003], the general hypothesis is supported by the PD-specific motor deficits observed in experimental applications of attentional interference, where primary or secondary task context is enhanced, to subdivide attentional resources. As previously established, context encompasses the external factors that influence the preparation and execution of behaviour [Dunn, Brown, & McGuigan, 1994]. Inherent in this definition of context are the inclusion of reciprocal internal constructs, such as behavioural set, goal identification, understanding of situational guidelines, and expected reward [Sait-Cyr, 2003]. It is the selection, maintenance, and refinement of these internal constructs that is attentionally demanding.

Bond and Morris [2000], Canning [2005], and Rochester et al. [2004] all used gait as the foundation motor task for investigations into contextual and explicit attentional interference among PD patients. In free gait (single task, self-selected speed), medicated PD patients exhibited disturbed performance parameters (decreased mean velocity, decreased step size) in comparison to neurologically normal adults in both laboratory- [Bond & Morris, 2000] and home-based comparisons [Rochester et al., 2004]. The addition of a secondary motor task, specifically carrying a tray with glasses on it, led to a further decrease in performance, uniquely among the PD group. Bond and Morris [2000] report a significant reduction of speed and stride length for PD patients with the addition of the secondary task, while Rochester et al. [2004] report similar decreases, at a non-significant level. The addition of a secondary cognitive task (recall of autobiographical information) led to significant

performance decreases among the home-based study group, either as a unique secondary task or in combination with the secondary motor task of tray carrying [Rochester et al., 2004]. The work of Canning [2005] indicates that this attentional interference can be subverted. When patients were asked to direct attention toward 'maintaining big steps while walking', the secondary motor task of tray-carrying provoked no evidence of attentional interference in the primary task – that is, gait performance was at similar levels as walking in the no-tray (single task) condition. This result suggests a contextual (using disproportionately large but largely non-specific cortical resources) rather than a structural (using proportionately appropriate but same specific cortical resources) interference resulting from tray carrying, a finding which is supported by the absence of gait parameter disturbances in 'empty tray' (no glasses) carrying [Bond & Morris, 2000]. Taken together, these studies show that secondary task can interfere with motor performance uniquely among PD patients, and that the interference can be created by a secondary task with high attentional demands (tray with glasses, autobiographical recall). Furthermore, the work of Canning [2005] indicates that suitably directed attention can 'normalize' PD movements and reduce attentional interference. This finding is supported by the study of Landers et al. [2005], who found that PD patients improved postural stability when they directed their attention to reducing the rotation of a balance platform. Stallibrass and colleagues [2004] and Macht and Ellgring [1999] report improvements in gait mobility for PD patients using directed attention as a situational strategy. The improvements facilitated by therapy and training in directed attention strategies were also found to be long-lasting (6+ months) [Stallibrass et al., 2004] and multi-modal, extending beyond improvements in motor performance to increases in the affective domain and cognitive responsiveness [Macht & Ellgring, 1999].

Studies of attentional interference during PD gait have a strong foundation in functional PD deficits, specifically the transient appearance of motor blocks and freezing. Contextually-challenging situations, including narrow spaces and crowded areas, along with concurrent motor tasks, such as turning while walking, have been found to elicit disruptions in the initiation or continuation of gait among PD patients [Fahn, 1995; Giladi et al., 1992; macht & Ellgring, 1999], possibly due to the diversion of attention from motor performance to context. Morris and colleagues [2000] have also shown that a cognitive secondary task can lead to increased postural instability and risk of falling, a result that is supported by an epidemiologic investigation of freezing and falls in PD [Bloem et al., 2004].

The previous studies suggest that the threat imposed when the consequences of an incorrect action are increased (e.g. possibility of dropping glasses in tray-carrying task, compared to carrying empty tray) may be, in part, the basis of high attentional demand in either a primary or secondary task context involving whole body motor tasks. Bertram and colleagues [2005] explored PD movement deficit as a function of primary task context threat in a reaching task. In their example, non-medicated PD patients and neurologically normal older adults reached for full drinking glasses that were either covered or uncovered. The results indicate that PD patients and controls used similar reach times in low threat conditions, but patients alone were slowed by the threat associated with reaching and grasping the uncovered glass. Bennett and colleagues [1995] also found slowed onset of reaching among PD patients when reaching for a half-full plastic glass, though comparisons are not provided to either empty or completely full glass targets. Again, these results support a threatening context-driven interference in movement preparation and execution unique among a BG-damaged group. One hypothesis alternative strengthened by these findings is

that attention is diverted to accessing neural mechanisms for movement among PD patients, and that attention to threat may be disrupting this adaptation.

Analogous non-naturalistic assessments of context effects on PD movement are numerous. An unexpected restriction of whole body displacement led to decreased movement velocity and increased need for corrective submovements among non-medicated PD patients in a standing targeted reach task, indicating that rapid changing of movement context is more disruptive to patients than controls [Tunik et al., 2004]. Rand and colleagues [2000] showed that PD patients used slower whole arm movements, with more iterative corrections to movement trajectory, to move a pointer to a small target (0.03 m x 0.03 m) compared to a similar amplitude movement with no target restriction, while Weiss and colleagues [1996] demonstrated a similar restriction on movement initiation and peak movement velocity among PD patients when elbow flexion movements were accuracy-constrained. In a comparison of medicated and non-medicated PD patients, Montgomery and Nuessen [1990] found that non-medicated patients did not increase whole arm movement speed at the same rate as medicated patients or controls, given reduced task context (increased size of targets). Fine control of grasping has also shown increased kinematic and spatial deficits among PD, indicating that tasks such as pronation, supination, grasping, and releasing may involve a contextual-challenge that exceeds or subverts that attentional control and motor output available among PD patients [Gordon, 1998; Negrotti et al., 2004; Whishaw et al., 2002].

1.2.2.2 SEQUENCE

Complimentary to accurate representation of external and internal context is the process of appropriately sequencing a response to that context [Saint-Cyr, 2003]. Sequencing is not an exclusively discrete operation – for many functional tasks, co-ordination and co-activation of multiple segments is required for completion [Marteniuk et al., 1987]. The focus of this section will be on the wealth of studies investigating cognitive and motor sequencing deficits among the PD population.

Benecke et al. [1987] identified a progressive slowing for PD patients performing unilateral or bilateral sequential movements (i.e. movement two slower than movement one), combined with an extended pause between movements. This prolonged pause has also been observed for PD patients between movements in target-constrained experimental tasks [Rand et al., 2002; Weiss et al., 1997] and more functional movement components, such as reaching for a glass then bringing that glass towards the mouth [Bennett et al., 1995] and walking then turning [Vaugoyeau et al., 2003]. It is possible that this pause reflects separate planning of movement segments, compared to a more integrated planning strategy used by non-parkinsonian participants [Rand et al., 2002]. This loss of smooth integration can also be inferred from the more uniaxial movement patterns observed for segment end-points (e.g. wrist) during PD reaching [Alberts et al., 2000; Isenberg & Conrad, 1994] and from the more frequent corrective movements ('jerk') in action patterns observed among PD patients [Alberts et al., 2000; Teulings et al., 1997]..

Progressive slowing of sequential actions has also been observed in more functional movements, specifically targeted reaching [Castiello et al., 2000; Gentilucci & Negrotti, 1999; Rand et al., 2002], handwriting [Van Gemmert et al., 2001], standing rise-to-toes [Frank et

al., 2000], seated sit-to-stand [Bishop et al., 2005], and gait [Morris et al., 2001]. These deficits have been associated with the combined and serial processing demands of the actions, and a corresponding inability among PD patients to sequence muscle activation and inhibition appropriately [Frank, Horak, & Nutt, 2000]. For example, Agostino and colleagues [1992] showed that the time taken to trace each side of a geometric figure progressively increased for PD patients as the number of figure sides increased from two to five, while controls used equivalent movement durations to trace each side, regardless of side number. Fama and Sullivan [2002] used a series of motor sequences with increasing complexity (e.g. SIMPLE – bilaterally alternating fist/fingers spread with both elbows continuously extended; COMPLEX – alternating unilaterally between fist on tabletop, hand edge on tabletop, hand flat on tabletop fingers spread) to establish that executive processing deficits, specifically picture sequencing, were most strongly correlated with motor sequencing deficits among PD participants. Van Spaendonck et al. [1996] also report that motor symptoms of PD, most notably rigidity, were associated with executive dysfunction, as assessed in the Wisconsin Card Sorting Task, which involves reiterative acquisition of non-verbal sorting rules, and tests a participant's ability to switch sorting rules based on feedback and internal cueing [Kolb & Whishaw, 1995].

Cognitive sequencing and set-switching deficits have been previously identified in patients with BG dysfunction, adding support to Alexander et al.'s [1986] multi-modal segregated circuit hypothesis. Zalla and associates [2000] showed that PD patients took more time than neurologically normal or prefrontal damaged participants to generate and describe an appropriate sequence of events for either a routine (i.e. 'getting ready to leave the house in the morning') or novel (i.e. 'opening a new business') activity. Further cognitive disorders in task switching, specifically in making internal changes in stimulus-identification

rules such as in various forms of the Stroop task, have been repeatedly identified among PD patients [Brown & Marsden, 1988; Brown & Marsden, 1991; Richards et al., 1993; Woodward, Bub, & Hunter, 2002]. Both Brown and Marsden [1991] and Woodward and colleagues [2002] relate this resource limitation to attentional interference – in the Brown and Marsden study, resource-demanding secondary tasks (i.e. random number generation, repetitive foot tapping) resulted in an increase in response time for the primary Stroop response task, while switching stimulus rules led to greater response delay than maintaining rules or inhibiting incongruent stimuli in the work of Woodward and associates [2002]. Similar attentional resource limitations among PD patients have been revealed by measuring concurrent deficits in tasks of mental rotation [Lee et al., 1998], visual search [Rowe et al., 2002], visuomotor tracking [Hocherman et al., 2004a], speech production [Ho et al., 2002], and grammatical interpretation [Grossman et al., 2002]. Attentional interference models may provide an improved experimental methodology for dissociating the cognitive effects of PD from general dementia, a frequent concomitant disorder among the PD population [Pezzoli et al., 2004; Schrag et al., 2002].

1.2.2.3 CONSEQUENCE

Comparison between the presented context and the performed sequence creates consequence. Repeated positive consequences lead to the learning and incorporation of the sequence (response) as a match for the context (stimulus), while negative consequences should result in correction. A full description of learning and memory as a BG function is

outside the scope of this review (but see [Packard and Knowlton, 2002]), but a brief expansion is warranted.

Jog et al. [1999] provided neurophysiological evidence of this iterative refinement in a simple maze-learning paradigm with rats. In their study, striatal neurons were active during action-selection aspects of tasks during learning trials. Following behavioural asymptote, striatal activity was greatest during activation of the entire sequence, rather than during the stimulus-specific behavioural response. This transition of neural activity, from attention-demanding BG co-activation during a task to BG-activated initiation and automatic execution of a task, is supported by the work of Agostino and colleagues [2004]. They found that prolonged practice (2+ weeks) on a targeted motor task of upper extremity reaching did not lead to continued improvements in timing for PD patients, unlike controls. They suggest that the movement failed to reach an 'automatic' execution status, a function that may require the BG. Krebs and colleagues [2001] also found deficits in procedural learning among PD patients in a targeted reach task, specifically in novel movement phases, such as following an implicit change in task demands, which further support a failure to automate task response without intact BG function. Graybiel [1998] supports this habit learning and forming function for the BG, suggesting that neural encoding of a sequence of responses for a given stimulus may provide the foundation for a system of 'action chunking' that permits simplified motor processing while creating combined movement patterns that are impervious to any interference except volitional control. Subsequent selection and execution of these action chunks (and inhibition of inappropriate chunks) may be initiated by activity in the BG [Kropotov & Etlinger, 1999]. Any consequence function of the basal ganglia may operate on multiple time scales, allowing for iterative learning or modulating of behaviours that last milliseconds to multiple seconds [Ruskin et al., 1999]. In addition,

learning deficits may bear an associative relationship with other measures of dysfunction, including executive deficits [Sarazin et al., 2002] and disease duration and progression [Graham & Sagar, 1999].

1.3 PARKINSON'S DISEASE

As the experimental investigation of PD rapidly expands, it is important to regularly emphasize that Parkinson's disease is a human disorder, with serious daily challenges for patients and their caregivers [Jacopini, 2000]. While these disruptions and potential implications provide further justification for an ecologically-focused approach to PD movement deficit experimentation, they also provide evidence of the true consequences of the dysfunctional information processing that exists in Parkinson's disease. The following sections will provide a discussion of the novel insight and continued relevance of Parkinson's original observations, followed by an exploration of current knowledge in both the individual impact and therapy of PD.

1.3.1 PARKINSON'S ORIGINAL ESSAY

Parkinson's publication of *An essay on the shaking palsy* in 1817 was not the first use of the term [Burch and Sheerin, 2005]. However, his work provided a detailed behavioural analysis of Parkinson's disease such as had not been previously documented. The categorical and symptomological content of the essay reflects his parallel passions for medicine, paleontology, chemistry, and geology, while the colourful style of his writing seems influenced by his early literary efforts in political and topical areas [Parkinson, 1817]. While a full critical review of Parkinson's work, in perspective with his life and times, would take us too far in this thesis, a brief review should provide interesting insight for the reader.

In the *Shaking palsy's* preface alone, Parkinson identifies some of the features of parkinsonism that continue to confound diagnosis and treatment, including the "stages of its progress", the "long duration" of the disorder which "requires a continuance of observation", the misinterpretation of "its characteristic symptoms as distinct and different disease", and the critical constraint of "analogy (as) the substitute for anatomical investigation".

Parkinson's case definition is no less accurate or current:

> "Involuntary tremulous motion, with lessened muscular power, in parts not in action and even when supported; with a propensity to bend the trunk forwards, and to pass from a walking to a running pace: the senses and intellects being uninjured."

Burch and Sheerin [2005] identify two classic PD symptoms not identified by Parkinson in his 1817 essay, namely rigidity and loss of affect. However, Parkinson's full essay is established through six cases (and possible undisclosed additional observation), two of whom (Cases IV and V) were observed briefly, and/or distantly [Parkinson, 1817]. It is possible that this small sample did not present loss of affect, or that it was unrecognized due to limited information on the patient's pre-parkinsonian expression. Given current clinical assessments for PD, rigidity seems less likely to go unobserved, but Parkinson's clinical observations appear to stem from observation and questioning more than direct manipulation. Yet these seem like minor limitations, given the overall quality and contribution of Parkinson's essay.

Parkinson's essay also highlights elements of the parkinsonian condition that are associated with the main themes of this introduction. Parkinson [1817] broaches the topic of *context*, and action/environment interaction, stating that '(t)he submission of the limbs to the directions of the will can hardly ever be obtained in the performance of the most ordinary offices of life.' Parkinson [1817] also makes several notes of the influence of attention on overcoming PD symptoms, indicating that '(w)alking becomes a task which cannot be performed without considerable attention', but reporting positively that 'the care and exertion required to ensure (walking's) safe performance' can provide PD patients with a distraction from other symptoms. Parkinson's observations of deficits of *sequence* are restricted to walking, but he notes in several places the seemingly anomalous condition of festination, wherein:

> "The propensity to lean forward becomes invincible, and patient is thereby forced to step on the toes and fore part of the feet, whilst the upper part of the body is thrown so far forward as to render it difficult to avoid falling on the face. In some cases, when this state of the malady is attained, the patient can no longer exercise himself by walking in his usual manner, but is thrown on the toes and forepart of the feet; being, at the same time, irresistibly impelled to take much quicker and shorter steps, and thereby to adopt unwillingly a running pace. In some cases it is found necessary entirely to substitute running for walking; since otherwise the patient, on proceeding only a very few paces, would inevitably fall."

Finally, Parkinson [1817] details a progressive history of PD deficit *consequence*. One striking example is his description of PD eating, which he observes as migrating from an 'unstreadiness of the hand' where 'the hand fails to answer with exactness to the dictates of the will' to a situation where 'the fork not being duly directed frequently fails to raise the morsel from the plate; which, when seized is with much difficulty conveyed to the mouth' to a point where '(t)he power of conveying the food to the mouth is at length so much impeded that he is obliged to be fed by others', and finally, 'he is not only no longer able to feed himself, but when the food is conveyed to the mouth ... the food is with difficulty retained in the mouth'.

Parkinson's work provides fascinating insight into the clinical approach and concept of movement disorders that existed in his day. It also provides a foundation for understanding the human impact of this 'tedious and most distressing malady', a topic which will be discussed in a more current research framework in the next section.

1.3.2 QUALITY OF LIFE

Given the scope of deficit associated with BG dysfunction previously outlined, it is important to characterize the associated impact on quality of life among PD patients. This information can help frame the importance of context and sequence processing in human existence, while providing a more comprehensive assessment of PD patients and the psychosocial conditions that could be influencing their behaviour. Before proceeding, however, it is critical to highlight that the signs and symptoms of PD are not exclusively a result of BG dysfunction, just as BG lesions in animal experimentation provide a parallel but

incomplete model of parkinsonism. Various confounding physical and psychological conditions may exist among the human PD population, including premorbid depression, dementia, anxiety, shyness, decreased novelty seeking, and advanced age [Bodis-Wollner, 2003; Mahant & Stacy, 2001]. Given this caveat, there is still much merit in establishing an account of perceived quality of life and daily activity independence among PD patients.

Schrag and colleagues [2000] established that PD patients have a diminished self-impression of quality of life, across sexes and at all ages. This impression centered around functional aspects of subsistence (mobility, physical functioning, social functioning) but extended to psychosocial elements (independence, well-being, cognition) as well. Quantitative functional measures, such as postural instability and occurrence of falls, were strongly associated with increased depression, as was perceived disability [Schrag et al., 2001]. Kuopio and colleagues [2000] also identified depression as the strongest influence on most subjective measures of quality of life among PD patients, with clinical stage (measured on Hoehn and Yahr scale) exerting more influence than depression only on patients' impressions of physical functioning. These results highlight the impact of depression on PD existence and dysfunction, and suggest that treatment of PD should include some form or forms of management for depression. This management may include directed alteration or amendment of the consequence processing previously ascribed to BG function. For example, Stallibrass and colleagues [2004] used a re-educative balance and movement protocol, called the Alexander technique, to superimpose a conscious movement strategy over habitual responses in 28 PD patients. This approach resulted in decreased depression and anxiety among the participants during activities of daily living, along with improved patient function in sitting, transferring from sitting to standing, standing, and walking.

Dysfunctions in these activities of daily living among PD patients are also associated with decreased perception of quality of life. Movements with significant axial components (e.g., turning in bed, sit-to-stand, gait, posture without falls) were found to be prone to complication among PD patients, with the number of patients experiencing complications increasing with increased disease duration, increased depression, and decreased self-assessment of quality of life [Schrag, Ben-Shlomo, & Quinn, 2002]. More clinical classifications of PD complications (e.g. dyskinesia, akinesia, motor fluctuation) have also been associated with decreased perception of quality of life, most frequently in mobility and activities of daily living [Chapuis et al., 2005]. Motor complications among PD patients have been previously connected with context processing, specifically in threatening conditions. For example, Stolze and colleagues [2004] identified obstruction or environmental context as a major contributor to gait disturbance and falls among PD patients. These complications may arise from physical contact with the threatening context, or from a context-associated cognitive complication among patients [Strubel et al., 2001]. For example, PD patients have reported an increased fear of falling in fall-threatening contexts (e.g reaching while standing on a chair, entering or exiting a car, walking on an icy surface) [Adkin et al., 2003]. These cognitive complications can result in greater dysfunction for PD patients in multi-modal activities of daily living, such as driving, telephone dialing, and shopping [Cahn et al., 1998].

As previously suggested in this review, structuring the assessment and interpretation of PD-related dysfunction in an information processing model provides an opportunity to connect the motor deficits observed among PD patients with the abnormal context and sequence processing that may be leading to those deficits. Including this review of the perceived quality of life among PD patients provides further evidence of dysfunctional

context and sequence processing as a functional impairment, while suggesting a possible macro-level for dysfunctional consequence processing. Specifically, decreased perceptions for quality of life among PD patients may be a result of disturbances in processing emotional information [Dujardin et al., 2004] in possible combination with diminished feedback through limbic circuits [Wolters, 2000].

1.3.3 PD THERAPY

An extensive review of pharmacotherapies and surgical treatments for PD is beyond the scope of this study (but see [Goetz et al., 2005] for a recent review). As pharmacological dopamine replacement continues to be the most frequent method of treatment [Ahlskog, 2001], despite the prevalence of long-term complications [Marsden, 1990], a brief inspection of movement studies employing a pre- and post-dopa medication methodology is warranted.

Rocchi and colleagues [2002] have shown that postural control, already deficit among PD patients, was not improved by the administration of dopaminergic medication. This continued deficit may reflect a nondopaminergic basis for PD deficits in sequenced response timing, a finding that is supported by continued parkinsonian deficits in rise-to-toes [Frank, Horak, & Nutt, 2000] and gait [Blin et al., 1991] following the administration of dopamine. Upper limb movement sequencing deficits have also been observed following the administration of dopamine [Melvin et al., 2005], though general improvements in rate of movement are typically observed for both targeted single movements [Castiello et al., 2000] and non-targeted repetitive movements [Johnson et al., 1994]. Fattaposta and colleagues [2002] suggested that dopamine replacement allowed a partial re-automatization of behaviours among PD patients, through the restoration of more normal neurophysiological activity. This suggestion has received subsequent support from electrophysiological studies,

which have shown a decreased activation of inappropriate attentional circuits among medicated PD patients, along with improved performance on psychological tests of executive function, as compared to unmedicated patients [Kobayashi et al., 2004].

1.4 SUMMARY

In summary:

1.4.1 The basal ganglia are a network of neural structures that have a modulatory control over motor, oculomotor, attentional, and emotional circuits through the human cortex.

1.4.2 Basal ganglia dysfunction, specifically the over-inhibition that results from dopaminergic depletion of parkinson's disease, leads to variant deficits in behaviour generated in any or all of the aforementioned circuits.

1.4.3 Parkinson's disease patients appear to have an unique response to environmental context, commonly exhibited as an increased susceptibility to attentional interference. This contextual-bias may be a reflection of an adapted reliance among PD patients on directed attention as a means to select and initiate action, combined with diminished function in executive attention and information processing.

1.4.4 The ecological genesis and manifestation of this contextual-bias can lead to severe reductions in quality of life and daily activity independence among Parkinson's disease patients, even with pharamcotherapeutic intervention.

1.5 OUTLINE OF RESEARCH AND DISSERTATION

1.5.1 A BRIEF DEFINITION OF TASK AND TASK STABILITY

The development of skilled task performance as a process is beyond the experimental or explanatory scope of this thesis. The concept of task performance stability, however, is an important consideration in justifying the ecological validity of experimental tasks. Smith and Thelen [2003] define the current dynamic systems model of motor skill development, suggesting that an experience combining action and environment drives a functional self-organization of the numerous and complex critical elements in the neuromuscular system. In a simple model, this self-organization may involve combining sensory stimulation and existent motor primitives into a functional (and shared) neural network, following Hebbian networking principles [Thoroughman & Shadmehr, 2000]. The outcome of this organization is a motor behaviour with some level of stability, where increased stability is defined as reduced variability in behavioural outcome on multiple trials in identical context [Smith and Thelen, 2003]. Based on this interpretation of motor skill development, and the previously established components of context, we can suggest that motor tasks that share context with common activities of daily living should be in a 'stable' dynamic condition; that is, non-pathological adults should possess a stable behavioural response in these tasks. Previous authors have described these tasks as 'learned', 'over-learned' [Hausdorff et al., 2005], or 'non-novel' [Krebs et al., 2001]. As a contrast, non-

familiar tasks and contexts can be associated with behavioural instability, and the tasks themselves could be characterized as 'unstable' (comparable with 'unlearned' or 'novel').

1.5.2 THEORY AND HYPOTHESES OF BG FUNCTION AND DYSFUNCTION

Based on the information presented in this introduction, a theory of basal ganglia function can be proffered.

The basal ganglia are responsible for the automatization of information processing, notably the selection and execution of appropriate motor responses. Dysfunction in the basal ganglia leads to a loss of automatization, and the need for an adapted information processing mechanism. Among Parkinson's disease patients, this adaptation involves attention-driven information processing in cortical regions, rather than in the deficit structures of the subcortex.

This theory leads to three testable hypotheses, specifically:

1.5.1.1 PD patients are able to perform stable tasks that do not require major attentional resources (tasks of daily living with low task- intrinsic or task-extrinsic context).

1.5.1.2 PD patients exhibit deficits when challenged with stable tasks that require major attentional resources (tasks of daily living with high task-intrinsic and/or high task-extrinsic context).

1.5.1.3 PD medication increases motor response rates (gross motor performance) but does not reduce functional (e.g. movement sequencing and structuring) motor response deficits (fine motor skill) that are induced by stable tasks that require major attentional resources.

The remainder of this document is divided into three experimental sections, followed by a general discussion that serves to associate task context parameters with motor performance of Parkinson's disease patients. Each experimental section is the investigation of a separate functional behaviour, meaning that each of the previously-identified hypotheses are addressed in each experimental section. In addition, the experimental sections are each structured as a stand-alone manuscript, concentrated as follows:

SECTION 2.0

MOTOR DEFICITS IN PARKINSONIAN REACHING: DOPA-SENSITIVITY INFLUENCED BY REAL-WORLD TASK CONSTRAINT

A quantitative comparison of the biomechanical sequence in the seated reaching movement, as performed by three groups (non-medicated PD patients, medicated PD patients, age-matched control participants) in an everyday task (seated reaching to grasp a glass, lift to lips, and drink) with two levels of task-intrinsic context (empty glass, full glass) and one level of task-extrinsic context (seated).

SECTION 3.0

ENVIRONMENTAL CONTEXT DISTURBS THE CO-ORDINATION OF POSTURAL CONTROL AND REACH KINEMATICS AMONG PARKINSON'S DISEASE PATIENTS

Quantitative analysis of reach and postural sequences of three groups (non-medicated PD patients, medicated PD patients, age-matched control participants) in a naturalistic task (standing reach to grasp a glass, lift to lips, and drink) with one level of task-intrinsic context (full glass) and two levels of task-extrinsic context (non-threatening fall potential, threatening fall potential).

SECTION 4.0

OBSTACLE AVOIDANCE IN PARKINSON'S DISEASE IS LIMITED BY THREATENING CONTEXT

Qualitative and quantitative analysis of obstacle negotiation sequence adopted by three groups (non-medicated PD patients, medicated PD patients, age-matched control participants) in an activity with two levels of task-intrinsic context (no obstacle, ground-level obstacle) and two levels of task-extrinsic context (non-threatening fall potential, threatening fall potential).

2.0 MOTOR DEFICITS IN PARKINSONIAN REACHING: DOPA-RESPONSIVENESS INFLUENCED BY REAL-WORLD TASK CONSTRAINT[1]

2.1 ABSTRACT

Parkinson's disease (PD) patients can perform many daily activities, but movement deficits are evident. These deficits may be increased when the required movement is constrained in accuracy. Research has shown variable improvements with PD medication, with sensitivity to task constraint evident in some studies. The purpose of this study was to quantify both specific movement deficits and improvements for PD patients in a reaching task. PD patients on and off medication both showed a need for greater ongoing control in movements with higher task accuracy constraints. Increased task accuracy constraints further compromised movement timing and structure among PD off medication, suggesting non-medicated PD patients may typically compensate with more conscious control of movement, resulting in increased slowing and segmentation of components when higher task accuracy is required.

[1]Section 2.0 is published in a modified form; Doan, J, Whishaw, IQ, Pellis, SM, Suchowersky, O, & Brown, LA. (2006). Motor deficits in parkinsonian reaching: Dopa-sensitivity influenced by real-world task constraint. *Journal of Motor Behavior, 38(1):* 45 – 59.

2.2 INTRODUCTION

The motor deficits associated with Parkinson's disease (PD) negatively impact the performance of many daily activities in those who suffer from this disease. These motor performance deficits can be further exacerbated by increased task or movement constraints [ALberts et al., 2000; maeshima et al., 1997; Montogmery, 2004]. Early work has related PD movement deficit to task demands, showing that challenging task constraints significantly affected the timing and accuracy of PD motor output [Agostino et al., 1996]. More recent research has demonstrated that an endpoint accuracy constraint on an upper limb aiming movement causes prolonged movement duration among PD patients, especially in the deceleration phase, as well as increased corrective movement control during task execution [Rand et al., 2000]. Likewise, endpoint accuracy constraints in an arm flexion task lead to prolonged movement times and decreased arm velocities in these patients [Weiss et al., 1996]. Similar results have been frequently reported in a variety of experimental contexts and across a range of novel movement tasks, such as movement of a stylus to a physical target [Montgomery & Nuessen, 1990], movement of a lever with on-screen accuracy feedback [Sheridan et al., 1987], and movement of hand switches to match a cued sequence [Harrington & Haaland, 1991].

PD movement studies have typically used novel experimental tasks that standardize target conditions and constrain motor output to explore how movement kinematics are influenced by PD. Although novel experimental tasks offer the opportunity for clear comparative designs with strong internal validity, novel tasks also suffer from several inherent confounds. For example, novel tasks may inaccurately assess the nature and scale of motor deficits among participants by imposing an artificial motor and/or cognitive challenge during task execution [Connor & Abbs, 1991; Czaja & Sharit, 2003; Marteniuk et

al., 1987; Teasdale & Stelmach, 1988]. In addition, performance on novel experimental tasks may be confounded by an implicit motor learning effect, which has been shown to be differentially expressed between patients with moderate to severe parkinsonism and controls [Agostino, Sanes, & Hallett, 1996; Krebs et al., 2001]. One solution to overcome the limitations of novel tasks involves the use of more functional tasks, which permit valuable understanding of motor performance within a realistic context. In addition, functional tasks provide ethologically-relevant opportunities for the representation of movement planning and expression as a function of practical task constraints.

In this study, our goal was to combine the benefits of experimental research with the validity of a real world task, and to investigate deficits and compensation in PD throughout the entirety of a functional movement sequence. To this end, we used the drinking action as an ethologically-valid task performed within the controlled environment of a laboratory setting. Upper limb kinematics involved in drinking have previously been analyzed in healthy adult [Buckley et al., 1996; Latash & Jaric, 2002; Safaee-Rad et al., 1990] and medicated PD [Bennett et al., 1995] populations. Latash and Jaric's work [2002] identified a Fitts' Law-type relationship between glass fill level and transport-to-mouth movement kinematics for healthy adult participants, indicating a strong task-specific constraint on movement expression in this activity of daily living. In the PD testing, Bennett et al. [1995] highlighted PD deficits in the integration of the reach and grasp movements in the drinking task, and also illustrated an increased temporal pause between the movement components of reaching and transport for PD patients. Of equal interest, but previously unexplored, are motor output improvements enabled by current PD drug therapy, specific to thorough investigation in an ethologically-valid task.

The purpose of this experiment was to investigate reach kinematics of PD patients in

a functional task with variable task accuracy constraint, and to identify how these deficits were improved with conventional PD drug treatment. We examined upper limb kinematics for all pertinent preparation and movement components of a drinking task while we altered target glass fill level between high task accuracy (glass full to within 1 cm of lip) and lower task accuracy (glass full to less than 15% volume) levels. Specifically, we were interested in examining kinematic deficits evident among PD (PD patients off medication compared to healthy older adults), the motor effects of conventional PD treatment within a patient group (PD patients tested both off and on their regular pharmacological treatment), and the effectiveness of current PD drug treatment in restoring motor performance to levels that approximate non-pathological populations (medicated PD patients compared with an adult control group) for this reaching task. It was hypothesized that greater task accuracy constraint (high liquid fill level in target glass) would cause more dysfunction of motor expression among PD patients than among a healthy elderly group. Additionally, it was hypothesized that PD medication would allow for improvements in the kinematics and control of the reach, at either level of task accuracy constraint.

2.3 METHODS

2.3.1 PARTICIPANTS

Eight participants with idiopathic PD (mean age: 66.6 ± 9.7 years; clinical characteristics in Table 2.1) and seven age-matched controls (mean age: 69.7 ± 8.3 years) served as subjects. One PD patient (Subject 8 in Table 2.1) was tested only in the OFF medication condition, due to difficulties reaching a good quality ON in the laboratory. One subject (Subject 7) was not tested in the OFF condition due to apprehension associated with

forgoing her PD medication. Thus, participant samples include seven subjects in each group. All participants were informed on the nature of the study and provided written consent. Approval to conduct this study was provided by the Human Research Ethics committee of the University of Lethbridge. Reaching movements in the PD participants were examined for the limb predominant in parkinsonian symptoms, as determined by a neurologist (OS) during patient screening with the Unified Parkinson's Disease Rating Scale - motor subsection (UPDRS III - questions 18 through 31). PD predominant limb coincided with self-reported hand dominant limb in 4 of 8 PD patients, while 2 patients were clinically rated as PD symmetrical. Control subjects were matched with PD patients with respect to use of dominant or non-dominant limb.

PD patients were all receiving dopaminergic medication as PD treatment, and each PD subject was tested in both OFF (>12 h removed from last oral drug dose) and ON (between 1h and 2 h following regular medication administration) medical treatment conditions in the same laboratory visit (same day) in this experiment. All patients were tested in the OFF then ON order for practicality and patient comfort. Quality of ON condition was confirmed both by patient self-report and clinical assessment, using the same questions from the UPDRS.

Table 2.1 Clinical information of Parkinson's disease patient group.

Patient	Age (yr)	Disease Duration	Sex	UPDRS – III*		Symptoms				Medication
				ON	OFF	Bradykinesia	Action Tremor	Resting Tremor	Dyskinesia#	
1	64	9	f	23	46	Y	N	N	N	sustained release levodopa/carbidopa pramipexole
2	66	10	f	16	35	Y	Y	N	Y	levodopa/carbidopa pramipexole entacapone amantadine
3	74	1	m	7	20	Y	Y	Y	N	levodopa/carbidopa
4	63	7	m	12	43	Y	Y	N	Y	sustained release levodopa/carbidopa levodopa/carbidopa pramipexole entacapone amantadine
5	53	29	f	18	46	Y	Y	Y	N	levodopa/carbidopa pramipexole
6	79	5	m	26	42	Y	Y	Y	N	sustained release levodopa/carbidopa pramipexole
7	56	8	f	5†		N	N	Y	N	levodopa/carbidopa amantadine
8	77	12	f		44‡	Y	Y	Y	N	sustained release levodopa/carbidopa
Mean (SD)	66.6 (9.7)	10.1 (8.3)		15.3 (7.8)	39.4 (9.3)					

* Unified Parkinson's Disease Rating Scale – III (motor component – questions 18-31), with higher scores indicative of greater motor deficit.
\# Dyskinesias were observed in laboratory during testing.
† Mild parkinsonian (verified by OS) – included only in ON group.
‡ Only tested in OFF condition.

2.3.2 REACHING TASK

Subjects performed a seated drinking task, comprised of a targeted reach, grasp, transport to mouth, sip, and return to lap. Task accuracy constraint manipulation consisted of a plastic glass (target diameter = 0.06 m, maximum fill volume = 150 ml) filled with water to a level less than 0.01 m below the top edge (high task demand condition (HIGH), fill volume ≥ 110 ml), or the same glass with a minimal fill level (low task demand condition (LOW), fill volume ≤ 20 ml). Pilot testing was used to establish the experimental parameters of glass size and fill. The HIGH glass level was chosen as the maximum volume that was practicable for transport and set-up by experimental research assistants. The LOW glass level was established as a trace volume that would still force participants to make a true sip. In both FILL conditions, the glass was placed on a self-standing pedestal (pedestal height = 0.77 m, maximum target height = pedestal height + 0.08 m) at a horizontal reach amplitude (subject's seated, hip marker to target centre) normalized to subject's reach arm length (100% of length from shoulder to base of index finger). All participants in each group (PD ON, PD OFF, OAC) completed 2 randomly presented trials with each target condition, as well as other seated target reaching trials, as part of a larger study.

Participants wore vision-occluding goggles (PLATO, Translucent Technologies, Toronto, ON) that served to initially conceal target condition and prevent any performance confounds due to movement pre-planning, a common compensatory response among PD patients [Brown & Marsden, 1988; Johnson et al., 2003; Stemach et al., 1986]. Specifically, the goggles allowed the investigators to standardize participant exposure to the visuomotor stimuli (for another experimental example, see [Kritikos, Beresford & Castiello, 2002]), thus controlling information processing time [Johnson et al., 2004]. During pre-test instructions, subjects were informed that there would be two preparatory events: the opening of the

goggles, followed by an audio GO signal. Instructions to subjects emphasized using the GO signal latency period (time between goggles opening and audio go signal) to 'think about how to reach for the glass' (investigator script). Goggles were initially set to closed so participant vision was occluded. Once the reach target was in place, the investigator informed subjects that a new trial was ready to commence. At a random interval following this warning, the goggles were opened. The audio GO signal sounded 800 ms following goggles opening.

Participants were seated on the edge of a height adjustable seat platform. Seat depth, seat height, and target reach distance were normalized for each subject to ensure equal endpoint accuracy constraints between subjects. Seat depth (horizontal distance from seat platform edge to subject hip marker in seated position) was marked at 50% of the subject's upper leg length (upper leg length = distance between greater trochanter and mid-line of knee joint) while seat height (vertical distance from floor to surface of seat platform) was adjusted such that each subject's thigh segments were approximately horizontal. Seat depth alignment was checked regularly between trials.

Once seated, each participant was reminded of the procedures and equipment at use in the experiment. Subjects were given an opportunity to reach from the start position (START; palm of reach hand resting on reach-side mid-thigh) to the target pedestal with no target in place. After further instructions, participants performed 2 practice trials with the HIGH target in place. Following the practice trials and final instructions, subjects were directed through the experimental trials. Priority in subject instruction was placed on successful completion of the task, and all subjects were reminded of the purpose of the testing following alternate trials, to reduce the possibility of any mistrials due to inattention.

2.3.3 DATA COLLECTION AND ANALYSIS

Participants were fitted unilaterally (reach side) with passive infrared-reflective markers at: the head of the fifth metatarsal, the lateral malleolus, the lateral epicondyle of the femur, the greater trochanter, the ulnar styloid process, the radial styloid process, the head of the second metacarpal, the base of the index fingernail, the base of the thumb fingernail, the lateral epicondyle of the humerus, mid-humerus, the acromion process, and the zygomatic bone. Additional midline markers were placed on the forehead and at the sternal notch, and a modified marker was also placed at the target support surface. Positional data were collected at 120 Hz using a Peak MOTUS motion analysis system (Peak Products, Englewood, CO). Three-dimensional marker position reconstruction was performed with Peak MOTUS software. Reach wrist ulnar styloid marker displacement data were filtered using a dual pass, 4^{th}-order digital Butterworth filter with a cut-off frequency of 3 Hz, and subsequent interpolation was performed using a custom-written visual inspection/linear correction computer routine (MatLab; The MathWorks, Natick, Mass.). Unidimensional marker velocities were calculated using the finite differences method. These velocities were resolved into a single resultant measure, for further differentiation to acceleration, and for calculation of kinematic parameters. Electromyographic signals (EMG) were collected at a frequency of 600 Hz from both the anterior deltoid and the bicep of the reach arm with pre-paired single differential surface electrodes (Delsys Incorporated, Boston, Mass.) in standard anatomical placement. For this study, only results of anterior deltoid recordings were analyzed.

Movement onset and conclusion times were determined from the reach wrist velocity derivative using the velocity threshold algorithm developed by Teasdale, Bard, Fleury, Young , & Proteau [1993]. In the current study, maximal velocity values used for

calculating movement onset and conclusion thresholds were uniquely determined for each dynamic movement phase. An example of movement traces with overlaid onset marks is shown in Figure 2.1. The reach-to-target phase (REACH; interval c-d on Figure 2.1) was defined as the time between initial wrist velocity onset and the subsequent wrist velocity conclusion. The transfer-to-mouth phase (TRANS; interval e-f on Figure 2.1) was defined as the time between the second wrist velocity onset and the subsequent wrist velocity conclusion on the approach to the mouth. HANDLE (interval d-e on Figure 2.1) was the time between the REACH and TRANS phases. MOUTH was the time from movement conclusion in the movement to the mouth (end of TRANS) to the next positive movement onset, again determined using the velocity threshold algorithm (Teasdale et al., 1993). Two further phases were extracted from the time series data. These were premotor time (PMT; interval a-b on Figure 2.1), which was the time between audio go signal and onset of deltoid activity, and response time (RT; interval a-c on Figure 2.1), which was the time between audio go signal and onset of movement. While RT provided a standard stimulus-motor response latency measure [Evarts, Teräväinen, and Calne, 1981; Hick, 1952], PMT gave indication of the stimulus-motor recruitment latency period, a measure which has previously provided equivocal results in PD movement studies [Evarts, Teräväinen, and Calne, 1981; Dick et al., 1986; Frank, Horak, and Nutt, 2000; Horak et al., 1996; Salenius et al., 2002; Sheridan, Flowers, and Hurrell, 1987]. Time of EMG onset was equal to the first sample in a 50 ms bin where all samples were greater than the mean value of the EMG signal during quiet sitting (prior to goggles opening) plus 2 standard deviations of the same signal sub-sample. Two phase sub-groupings were also used in the data analysis: the 'static' phase group included phases with negligible resultant displacement (PMT, RT, HANDLE,

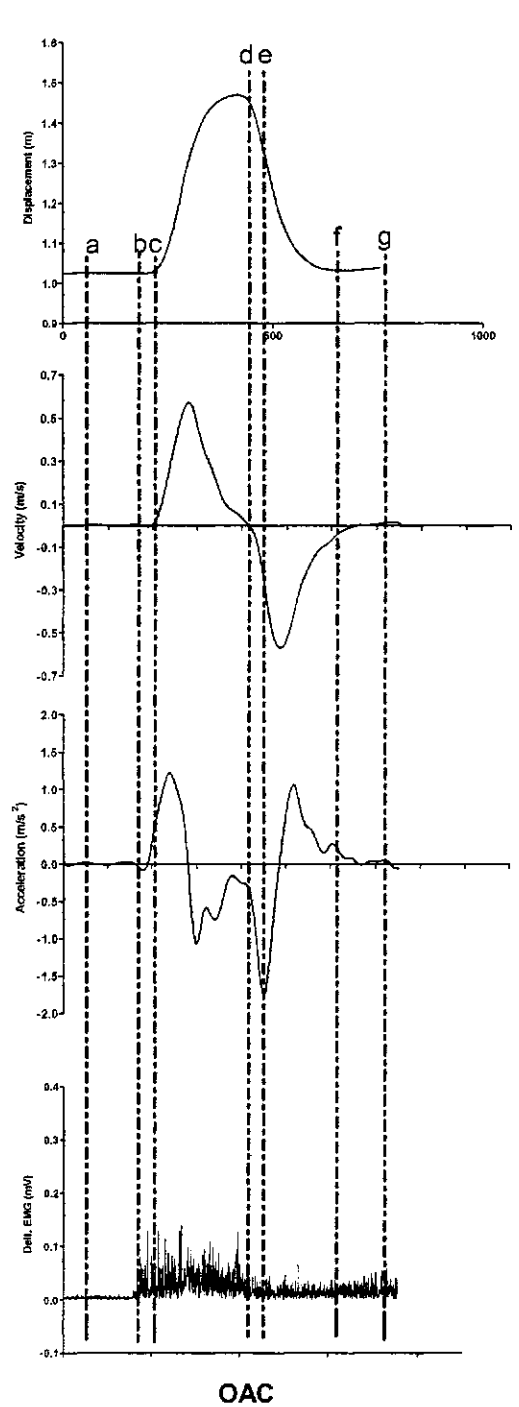
MOUTH), while the 'dynamic' phase group incorporated phases with large meaningful displacement (REACH, TRANS).

A measure of movement quality and structure was also extracted from the kinematic data to provide indication of the number and duration of reach and transport trajectory corrections made by subjects. This measure isolated discrete movement units, previously established as a meaningful measure of movement substructure [Abend et al., 1982; Jagacinski et al., 1980]. These movement units were derived from the acceleration signal, with the start of the first movement unit corresponding to movement onset, and subsequent movement units terminating at deceleration-acceleration transition points. Common measures, all indicative of the 'quality' of the movement, include the number of movement units required for the action (a higher number of movement units indicates more need for ongoing correction to the movement), the mean duration of movement units (shorter movement units also indicate more need for ongoing correction), and duration of the first movement unit, which is suggested to indicate the robustness of the initial feedforward signal in the motor plan [Fallang et al., 2000; Jagacinksi et al., 1980]. In the current study, REACH phase movement units of duration less than 50 ms were excluded as possible tremor or system noise [Jagacinksi et al., 1980]. This threshold was removed in the TRANS phase, as preliminary analysis showed most OAC trials exhibited some movement units with duration less than 50 ms, typically at the beginning of the action.

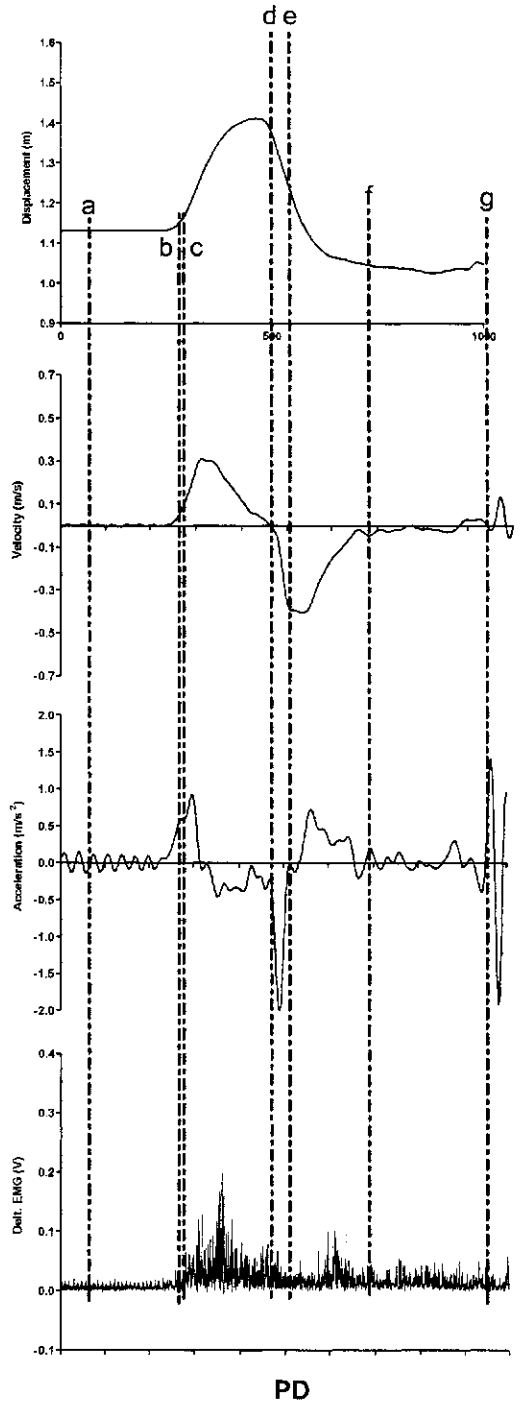
Dependent variables quantified for each of the dynamic movement phases (REACH, TRANS) were group means of: a) event time, the duration of the event, both as an absolute value and as a percentage of total movement time; b) peak resultant velocity (PV), acceleration (PA), and deceleration (PD); c) time to peak resultant velocity (TPV), peak acceleration (TPA), and peak deceleration (TPD), all as a percentage of phase time, and d)

number of movement units (MU), mean movement unit duration (MUD), and duration of first movement unit (FMUD). For the static phases, only event times were calculated.

Three separate comparisons were conducted on the data, using GROUP (PD OFF vs OAC; PD OFF vs. PD ON; PD ON vs. OAC) x FILL (LOW vs. HIGH) analyses of variance with level of significance set at $\alpha = .05$. A descriptive analysis of the movement paths, as well as the coordinate system used in qualitative representations is provided as a starting point for comparisons, similar to recent studies in human stroke [Roby_brami et al., 1997] and PD [Whishaw et al., 2002] reaching. Comparisons between PD OFF and PD ON were restricted to the 6 subjects (subjects 1 through 6 in Table 2.1) who completed trials in both conditions. Follow-up comparisons within any single group were conducted with the respective full sample (n=7 in each case).


a
b
c
d
e
f
g
Displacement (m)
Velocity (m/s)
Acceleration (m/s²)
Delt. EMG (mV)

OAC


a
b
c
d
e
f
g
Displacement (m)
Velocity (m/s)
Acceleration (m/s²)
Delt. EMG (V)

PD

Figure 2.1. **Sample reach wrist kinematic traces, with event onset marks**

Resultant reach wrist displacement, velocity, and acceleration, plus EMG activity from reach side anterior deltoid muscle (figures top to bottom) for a sample control (left) and nonmedicated Parkinson's disease patient (right) in the LOW FILL condition. Task phases are as follow: a to b - Premotor response time (PMT); a to c – response time (RT); c to d – reach to glass (REACH); d to e – grasp glass (HANDLE); e to f – glass to mouth (TRANS); f to g – glass at mouth (MOUTH).

2.4 RESULTS

Much previous research has demonstrated various general deficits of upper limb movement among parkinsonians [Alberts et al., 2000; Castiello et al., 2000; Gordon, 1998; Harrington & Haaland, 1991; Montgomery & Nuessen, 1990; Seidler et al., 2001; Stelmach, Worringham, & Strand, 1986; Teulings et al., 1997; Weiss, Stelmach, & Hefter, 1997]. The purpose of this study was to determine any increase in this movement deficit, related to task accuracy constraints.

2.4.1 MOVEMENT PATH

2.4.1.1 PD OFF VERSUS OAC

Figures 2.2 through 2.4 compare reach movement paths of a control subject with the matched PD patient OFF and ON, respectively, in two orthogonal planes. The shape of the movement path, along with the resultant velocity profile, allow for visual comparison of the spatial aspects of the movement [Roby-Brami et al., 1997]. Inspection shows that the control subject used relatively direct movement paths for the REACH and TRANS phases, in both the transverse and sagittal planes, for each reach. Additionally, both the LOW and HIGH velocity profiles show a single peak in the REACH and TRANS phases, with smooth acceleration and deceleration (positive and negative slopes of velocity curves, respectively) in all movements. PD OFF medication used less direct movements, with a uniaxially segmented movement observed in both phases. This segmented movement strategy, previously reported for PD patients [Isenberg & Conrad, 1994; Alberts et al., 2000] is exacerbated in the HIGH condition, where PD OFF used nearly horizontal sagittal movement paths to complete the REACH and start the TRANS phases. Unlike the PD

OFF LOW condition, or OAC in either FILL condition, PD OFF in the HIGH condition used a combination of a less upright trunk posture and a lower, forward head position to bring the full glass to the MOUTH phase, despite similar initial postures for all three groups. This was evidenced by the inferior position of the wrist marker, compared to the sternal marker, at the end of PD OFF TRANS (Figure 2.3), as well as a lower and more anterior final position of the head marker, and a roughly horizontal A-P translation of the sternal marker. The velocity profile for the HIGH condition shows increased irregularity in movement control approaching the REACH and TRANS endpoints, as well as reduced peak velocities, in comparison with PD OFF LOW, and OAC in either FILL condition.

2.4.1.2 PD OFF VERSUS PD ON

Medication served to remove some of the uniaxial movement segmentation, most notably in the TRANS phase of the HIGH glass condition for PD ON (Figure 2.4). PD ON did continue to use an inferior and anterior head position in bringing the HIGH glass to the MOUTH phase. Medication also helped smooth the control of the movement, with less irregularity in the LOW and HIGH velocity profiles. Velocity magnitudes were mostly unchanged by medication, even showing a slightly decreased peak resultant velocity when compared to the PD OFF LOW condition.

2.4.1.3 PD ON VERSUS OAC

Like PD OFF, PD ON continued to show an axially segmented movement pattern, in both glass fill conditions, when compared to OAC. As previously highlighted, the HIGH condition required inferior and anterior positioning of the head to complete the MOUTH task, a strategy not observed in OAC.

While velocity irregularities are not present in either PD ON reach, an extended HANDLE plateau can be observed in both reaches. This extended duration, increased in the HIGH condition for PD ON, is absent from either OAC reach.

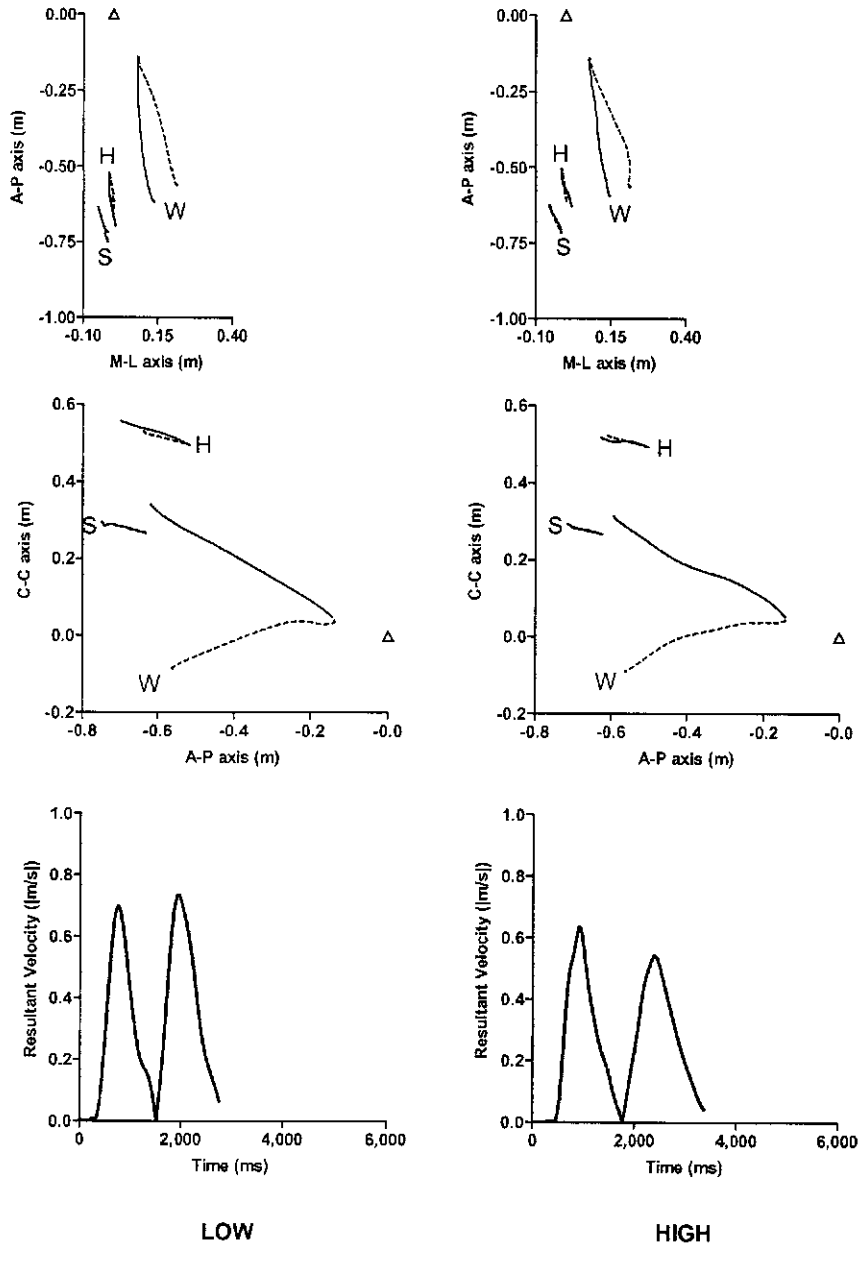

0.00
-0.25
-0.50
-0.75
-1.00
A-P axis (m)
-0.10
0.15
0.40
M-L axis (m)
H
S
W
Δ
0.6
0.4
0.2
0.0
-0.2
C-C axis (m)
-0.8
-0.6
-0.4
-0.2
-0.0
A-P axis (m)
1.0
0.8
0.6
0.4
0.2
0.0
Resultant Velocity (|m/s|)
0
2,000
4,000
6,000
Time (ms)
LOW
HIGH

Figure 2.2. Displacement patterns for seated reach by adult control participant. Movement path of sternal (S), head (H), and reach wrist (W) markers for a representative adult control participant for a single reach in both the LOW and HIGH conditions. Movements towards the target glass (RT, REACH, HANDLE) are in broken lines, while movements with the glass in hand (TRANS, MOUTH) are in solid lines. The target location is represented by the open triangle. The stick figures on the left of the displacement plots indicate mediolateral (M-L), craniocaudal (C-C), and anteroposterior (A-P) axes, as oriented from the origin (target starting position), used for qualitative analysis (Figures 2.2 through 2.4). A conventional coordinate system was used for quantitative kinematic analysis.

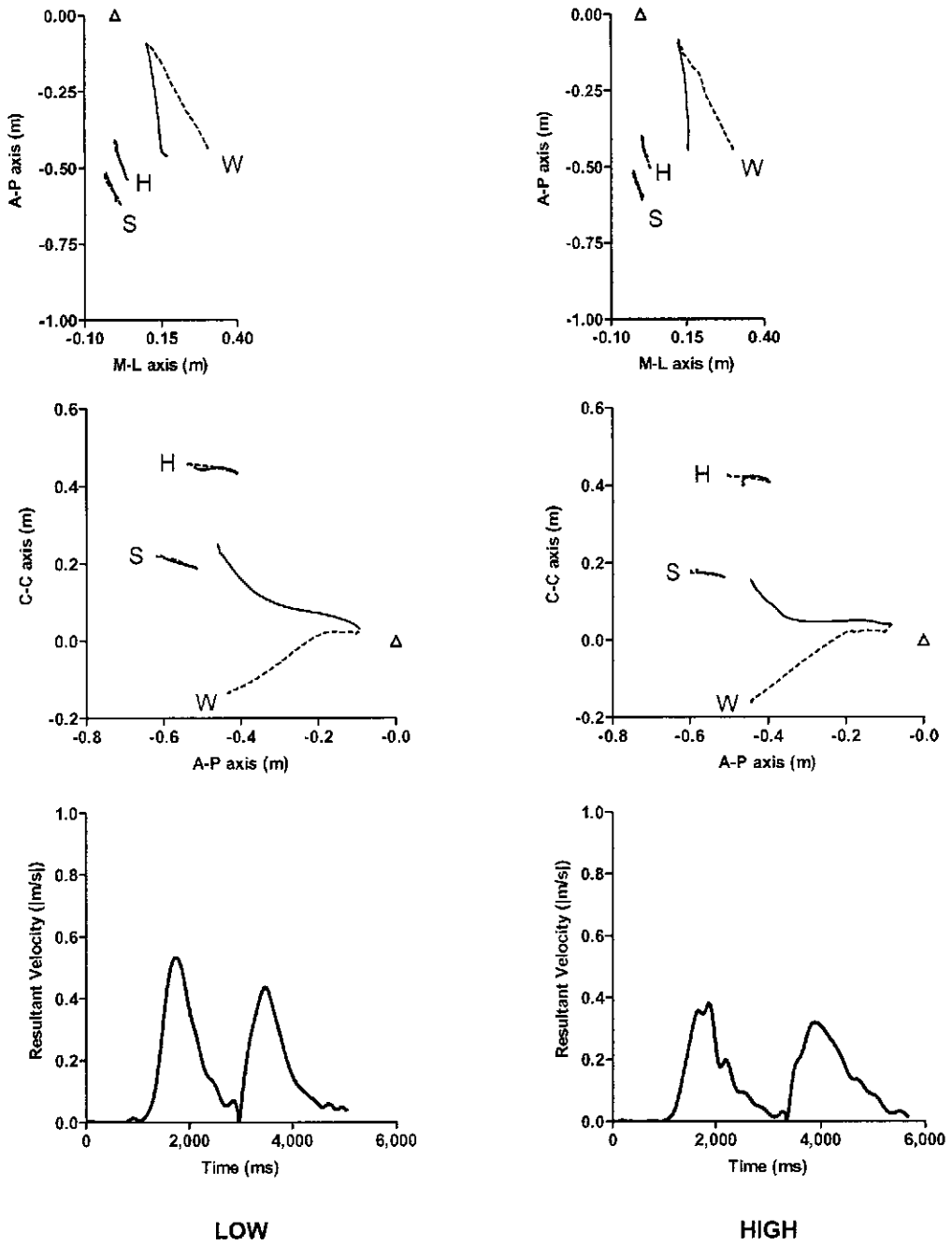
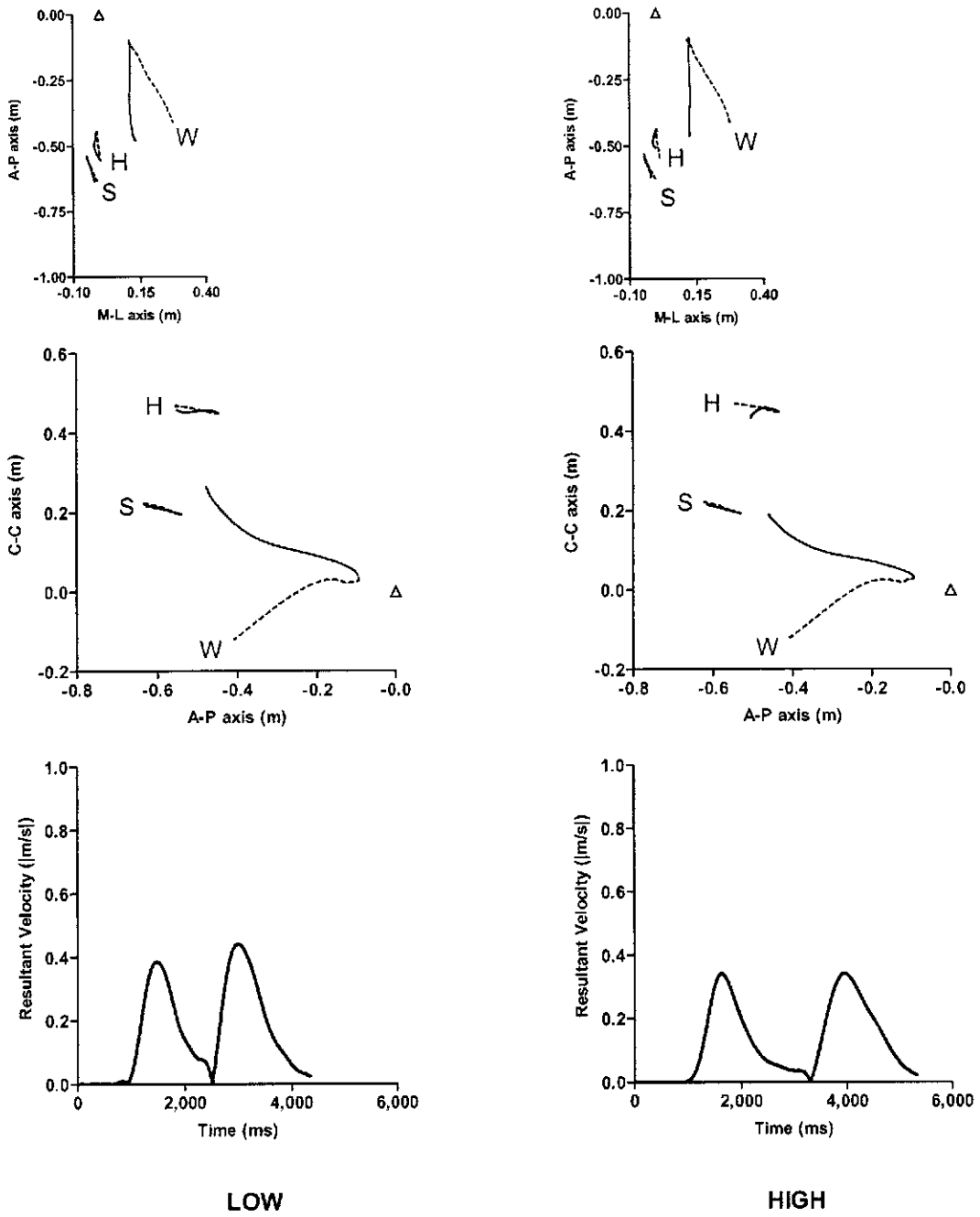

0.00
-0.25
-0.50
-0.75
-1.00
A-P axis (m)
Δ
H
S
W
-0.10
0.15
0.40
M-L axis (m)
0.6
0.4
0.2
0.0
-0.2
C-C axis (m)
-0.8
-0.6
-0.4
-0.2
-0.0
A-P axis (m)
1.0
0.8
Resultant Velocity (|m/s|)
0
2,000
4,000
6,000
Time (ms)
LOW
HIGH

Figure 2.3. Displacement patterns for seated reach by non-medicated PD patient. Movement path of sternal (S), head (H), and reach wrist (W) markers for a non-medicated PD patient (PD OFF 3 from Table 2.1) for a single reach in both the LOW and HIGH conditions. Movements towards the target glass (RT, REACH, HANDLE) are in broken lines, while movements with the glass in hand (TRANS, MOUTH) are in solid lines. The target location is represented by the open triangle.


A-P axis (m)
0.00
-0.25
-0.50
-0.75
-1.00
-0.10
0.15
0.40
M-L axis (m)
H
S
W
Δ
C-C axis (m)
0.6
0.4
0.2
0.0
-0.2
-0.8
-0.6
-0.4
-0.2
-0.0
A-P axis (m)
Resultant Velocity (|m/s|)
1.0
0.8
0.6
0.4
0.2
0.0
0
2,000
4,000
6,000
Time (ms)

LOW HIGH

Figure 2.4. Displacement patterns for seated reach by medicated PD patient. Movement path of sternal (S), head (H), and reach wrist (W) markers for a medicated PD patient (PD ON 3 from Table 2.1) for a single reach in both the LOW and HIGH conditions. Movements towards the target glass (RT, REACH, HANDLE) are in broken lines, while movements with the glass in hand (TRANS, MOUTH) are in solid lines. The target location is represented by the open triangle.

2.4.2 MOVEMENT PHASE TIMES

2.4.2.1 PD OFF VERSUS OAC

The slowness of movement associated with PD was observed in both recruitment and movement phases. PD OFF were significantly slower than the OAC group in the PMT ($F(1,12)=6.099$, $p=.030$), REACH ($F(1,12)=13.962$, $p=.003$), HANDLE ($F(1,12)=5.078$, $p=.044$), TRANS ($F(1,12)=14.933$, $p=.002$), and MOUTH ($F(1,12)=5.657$, $p=.035$) phases. Mean phase values for each group are presented in Table 2.2.

A FILL effect was observed within the PD OFF and OAC groups, both for the RT phase ($F(1,12)=5.013$, $p=.045$) and for the movement phases where the participant was in direct contact with the target, with significantly longer movement times observed in HANDLE ($F(1,12)=5.461$, $p=.038$) and TRANS ($F(1,12)=4.825$, $p=.048$) for both groups. A strong counter-effect was observed for MOUTH ($F(1,12)=7.961$, $p=.015$), where sipping from the HIGH glass took less time than sipping from the LOW glass.

2.4.2.2 PD OFF VERSUS PD ON

Medication significantly reduced the extended phase times exclusively in PMT, where trials with PD ON were significantly shorter in duration than PD OFF ($F(1,10)=6.738$, $p=.048$). Other movement phases showed non-significant decreases in phase time with medication (Table 2.2).

In the pre-movement 'static' phases, medicated and non-medicated PD patients took significantly longer for PMT ($F(1,10)=6.709$, $p=.049$) and RT ($F(1,10)=22.35$, $p=.005$) in the HIGH glass condition. The trend toward a decreased duration for the HIGH MOUTH phase continued in comparisons with trials for non-medicated and medicated PD patients ($F(1,10)=6.106$, $p=.056$). This relationship approached a FILL * GROUP interaction ($F(1,10)=5.809$, $p=.061$) for the MOUTH phase.

2.4.2.3 PD ON VERSUS OAC

No significant GROUP differences were observed between PD ON and OAC in movement phase times. For PD ON, the delayed RT to the HIGH target was shared with the OAC group ($F(1,12)=5.120$, $p=.043$). No FILL effects were observed for the REACH phase duration. Both PD ON and OAC showed a FILL effect for 'static' movement phases where target and subject were in direct contact, specifically HANDLE ($F(1,12)=5.538$, $p=.036$) and MOUTH ($F(1,12)=13.377$, $p=.003$). In MOUTH, this was a counter-effect, as sipping from the LOW glass took more time than sipping from the HIGH.

Table 2.2. **Phase times for complete reach task.**

		OAC		PD OFF		PD ON		GROUP	FILL
		LOW	HIGH	LOW	HIGH	LOW	HIGH	EFFECTS	EFFECTS
PMT	(ms)	392 ± 43	406 ± 69	560 ± 68	716 ± 48	396 ± 44	440 ± 55	A, B	B
RT	(ms)	408 ± 49	437 ± 84	608 ± 88	732 ± 93	432 ± 74	564 ± 91		A, B, C
REACH	(ms)	968 ± 58	954 ± 70	1461 ± 109	1723 ± 193	1237 ± 82	1238 ± 78	A	
HANDLE	(ms)	222 ± 14	426 ± 84	650 ± 130	865 ± 208	391 ± 48	500 ± 50	A	A, C
TRANS	(ms)	1288 ± 35	1460 ± 51	1859 ± 171	2112 ± 115	1645 ± 114	1700 ± 102	A	A
MOUTH	(ms)	1137 ± 118	725 ± 58	1393 ± 161	1240 ± 109	1577 ± 223	987 ± 161	A	A, C

All values are mean ± SE.
[A] OFF/OAC, $p < 0.05$; [B]OFF/ON, $p < 0.05$; [C]ON/OAC, $p < 0.05$

2.4.3 MOVEMENT KINEMATICS – REACH PHASE

2.4.3.1 PD OFF VERSUS OAC

PD OFF exhibited decreased magnitude of movement kinematics, when compared to OAC, for mean velocity ($F(1,12)=18.015$, $p=.001$), peak velocity ($F(1,12)=13.541$, $p=.003$), and peak acceleration ($F(1,12)=10.423$, $p=.007$) in the REACH phase (Table 2.3). PD OFF were also significantly delayed in relative time to peak acceleration ($F(1,12)=6.572$, $p=.025$), as shown in Table 2.3. A significant FILL * GROUP interaction for peak acceleration existed ($F(1,12)=7.453$, $p=.018$), where OAC tended to increase peak acceleration in the HIGH condition ($t(6)=1.825$, $p=.118$) while PD OFF tended to decrease peak acceleration magnitude to meet task demands ($t(6)=-2.030$, $p=.089$).

2.4.3.2 PD OFF VERSUS PD ON

For the REACH phase, a significant FILL * GROUP effect ($F(1,10)=7.021$, $p=.045$) existed between PD OFF and PD ON for mean velocity (Table 2.3). PD ON exhibited increased mean velocity for the HIGH REACH, similar to OAC, while PD OFF showed a decrease in mean velocity. Neither FILL effect was significant in post-hoc tests ($t(6)=.524$, $p=.619$ and $t(6)=-1.995$, $p=.093$, respectively).

2.4.3.3 PD ON VERSUS OAC

Despite the addition of medication, parameters of REACH movement kinematics (Table 2.3) were still significantly lower for PD ON, compared to OAC, for mean velocity ($F(1,12)=7.290$, $p=.019$), peak velocity ($F(1,12)=9.096$, $p=.011$), peak acceleration ($F(1,12)=10.019$, $p=.008$), and peak deceleration ($F(1,12)=5.623$, $p=.035$) across both tasks. Both PD ON and OAC used a decreased relative time to peak acceleration to reach for the HIGH glass, an opposite control strategy to that employed by PD OFF. This behaviour provided a significant FILL effect for relative time to peak acceleration in REACH ($F(1,12)=5.162$, $p=.042$).

2.4.4 MOVEMENT UNIT ANALYSIS – REACH PHASE

2.4.4.1 PD OFF VERSUS OAC

PD OFF required significantly more sequenced movement units to complete both their LOW and HIGH REACH, when compared with OAC ($F(1,12)=9.824$, $p=.009$). Increased glass fill level also increased the number of movement units ($F(1,12)=6.474$, $p=.026$) for both groups, as shown in Table 2.4. Significant GROUP ($F(1,12)=11.721$, $p=.005$) and FILL ($F(1,12)=13.082$, $p=.004$) effects were also observed for mean REACH movement unit duration, while the mean duration for the first movement unit was also significantly shorter for the HIGH glass condition ($F(1,12)=8.019$, $p=.015$).

2.4.4.2 PD OFF VERSUS PD ON

PD medication did not completely eradicate the task accuracy constraint effect, as both PD ON and PD OFF used more movement units ($F(1,10)=14.976$, $p=.012$) of shorter mean duration ($F(1,10)=36.084$, $p=.002$) to complete the HIGH REACH, as indicated in Table 2.4. However, a FILL * GROUP interaction ($F(1,10)=22.907$. $p=.005$) existed for duration of the first movement unit, with PD ON making a longer duration first movement unit to the HIGH target, compared to patients in the non-medicated state.

2.4.4.3 PD ON VERSUS OAC

Despite these medicated improvements, PD ON used significantly more movement units ($F(1,12)=7.388$, $p=.019$) of significantly shorter duration ($F(1,12)=6.106$, $p=.028$) than OAC in both REACH conditions. Both groups used more movement units ($F(1,12)=6.464$, $p=.026$) of shorter duration ($F(1,12)= 9.473$, $p=.010$) to complete the HIGH REACH. All results are available in Table 2.4.

Table 2.3. **Movement kinematic parameters for reach-to-target (REACH) phase.**

		OAC		PD OFF		PD ON		GROUP	FILL
		LOW	HIGH	LOW	HIGH	LOW	HIGH	EFFECTS	EFFECTS
REACH									
TPV	(%)	37.1 ± 2.6	37.5 ± 2.3	45.8 ± 6.1	46.8 ± 8.7	37.8 ± 3.9	36.8 ± 3.3		
TPA	(%)	16.7 ± 1.4	12.6 ± 0.7	33.7 ± 9.1	43.2 ± 12.9	24.3 ± 5.0	12.7 ± 1.9	A	C
TPD	(%)	56.7 ± 4.1	59.9 ± 2.9	63.5 ± 7.0	71.3 ± 10.2	68.5 ± 5.6	70.8 ± 5.6		
MV	(cm/s)	34.2 ± 2.6	33.5 ± 3.6	16.3 ± 2.4	16.0 ± 2.6	20.4 ± 3.0	22.4 ± 3.1	A, C	BxB
PV	(cm/s)	63.8 ± 5.0	61.5 ± 6.3	37.5 ± 3.6	34.4 ± 2.9	37.2 ± 5.4	38.4 ± 4.4	A, C	
PA	(cm/s^2)	271 ± 36	287 ± 34	148 ± 29	118 ± 17	142 ± 27	139 ± 17	A, C	AxA
PD	(cm/s^2)	199 ± 31	190 ± 23	191 ± 47	181 ± 44	114 ± 21	116 ± 19	C	

All values are mean ± SE.
[A]OFF/OAC, $p<0.05$; [B]OFF/ON, $p<0.05$; [C]ON/OAC, $p<0.05$; NxN indicates interaction effect, $p<0.05$

Table 2.4. Movement unit parameters for REACH and TRANS phases.

	OAC		PD OFF		PD ON		GROUP	FILL
	LOW	HIGH	LOW	HIGH	LOW	HIGH	EFFECTS	EFFECTS
REACH								
MU (#)	4.0 ± 0.7	5.1 ± 1.1	10.9 ± 1.8	20.5 ± 5.4	7.4 ± 1.2	10.2 ± 1.6	A,C	A,B,C
FMUD(ms)	408 ± 57	378 ± 62	373 ± 68	207 ± 69	329 ± 61	341 ± 69		A,BxB
MUD (ms)	364 ± 28	315 ± 39	248 ± 30	165 ± 23	285 ± 31	210 ± 20	A,C	A,B,C
TRANS								
MU (#)	3.2 ± 0.4	4.5 ± 0.8	10.1 ± 2.3	16.2 ± 4.7	14.1 ± 2.8	10.0 ± 2.2	A,C	
FMUD(ms)	83 ± 15	65 ± 21	82 ± 15	80 ± 34	60 ± 7	67 ±18		
MUD (ms)	308 ± 22	193 ± 25	184 ± 25	229 ± 51	169 ±11	176 ±14	C	AxA,C,CxC

All values are mean ± SE.
[A]OFF/OAC, $p<0.05$; [B]OFF/ON, $p<0.05$; [C]ON/OAC, $p<0.05$; NxN indicates interaction effect, $p<0.05$

2.4.5 MOVEMENT KINEMATICS - TRANS PHASE

2.4.5.1 PD OFF VERSUS OAC

In the TRANS phase, PD OFF achieved significantly lower mean and peak movement velocities than OAC ($F(1,12)=14.130$, $p=.003$; $F(1,12)=11.430$, $p=.005$ respectively), with mean values indicated in Table 2.5. These lower magnitude velocities for the PD OFF group were accomplished in conjunction with significantly longer relative time to peak acceleration ($F(1,12)=7.636$, $p=.017$) (Table 2.5). A significant FILL effect was also observed for the TRANS phase, with both groups using decreased magnitudes of mean velocity ($F(1,12)=15.473$, $p=.002$) and peak velocity ($F(1,12)=23.205$, $p=.000$) to transport the HIGH glass.

2.4.5.2 PD OFF VERSUS PD ON

The FILL effect persisted in the TRANS phase for PD ON medication, with both PD OFF and PD ON using significantly decreased mean velocities ($F(1,10)=9.026$, $p=.030$) and peak velocities ($F(1,10)=33.394$, $p=.002$) to transport the HIGH glass (Table 2.5).

2.4.5.3 PD ON VERSUS OAC

Similar to non-medicated Parkinson's disease patients, PD ON used significantly decreased magnitudes of peak velocity ($F(1,12)=8.033$, $p=.015$) and peak deceleration ($F(1,12)=5.404$, $p=.038$) in the TRANS phase of the movement, as compared to OAC (Table 2.5). Unlike PD OFF, however, PD ON were not significantly different from OAC in initial sequencing of the TRANS phase, specifically relative times to peak velocity and acceleration. Indeed, PD ON seemed to show a similar kinematic control strategy as OAC in response to transport of the HIGH glass. A FILL effect existed for the relative ($F(1,12)=40.325$, $p=.000$) time to peak velocity measures, a control strategy possibly dictated by the lower magnitude mean and peak velocities ($F(1,12)=6.48$, $p=.026$ and $F(1,12)=16.562$, $p=.002$ respectively) used by OAC and PD ON for HIGH TRANS movements. All TRANS group mean kinematic parameter values are shown in Table 2.5.

2.4.6 MOVEMENT UNIT ANALYSIS - TRANS PHASE

2.4.6.1 PD OFF VERSUS OAC

PD OFF used significantly more movement units than OAC to complete the TRANS phase (Table 2.4), regardless of task accuracy constraint ($F(1,12)=10.861$, $p=.006$). There was also a FILL * GROUP interaction ($F(1,12)=6.818$, $p=.023$), with OAC significantly decreasing movement duration for the HIGH TRANS ($t(6)=3.388$, $p=.015$) while PD OFF showed a non-significant increase of movement duration for the HIGH TRANS trials.

2.4.6.2 PD OFF VERSUS PD ON

No significant differences in movement unit measures were observed in comparisons between non-medicated and medicated PD patients.

2.4.6.3 PD ON VERSUS OAC

Medication failed to improve TRANS movement unit deficits, as PD ON still used significantly more TRANS movement units than OAC ($F(1,12)=27.318$, $p=.000$; Table 2.4). In addition, a significant FILL * GROUP effect for TRANS mean movement unit duration was observed ($F(1,12)=9.051$, $p=.011$), with OAC making significantly shorter average movement units in the HIGH task ($t(6)=3.388$, $p=.015$).

Table 2.5. Movement kinematic parameters for target-to-mouth (TRANS) phase.

		OAC		PD OFF		PD ON		GROUP	FILL
		LOW	HIGH	LOW	HIGH	LOW	HIGH	EFFECTS	EFFECTS
TRANS									
TPV	(%)	35.6 ± 0.9	39.0 ± 1.8	37.9 ± 3.2	42.6 ± 6.9	29.5 ± 1.9	39.5 ± 3.0		C, CxC
TPA	(%)	11.6 ± 1.8	10.2 ± 1.8	18.9 ± 5.1	27.8 ± 8.0	10.6 ± 2.1	15.4 ± 3.4	A	
TPD	(%)	56.0 ± 1.9	61.0 ± 2.8	61.4 ± 6.2	48.9 ± 10.4	51.4 ± 2.8	56.4 ± 4.3		
MV	(cm/s)	31.4 ± 1.4	27.0 ± 1.7	22.6 ± 1.8	17.4 ± 2.6	24.6 ± 2.9	23.3 ± 2.8	A	A,B,C
PV	(cm/s)	58.0 ± 2.5	48.4 ± 2.1	42.5 ± 3.3	36.8 ± 3.9	45.4 ± 2.7	42.0 ± 3.1	A,C	A,B,C
PA	(cm/s^2)	176 ± 8	152 ± 19	140 ± 10	146 ± 28	142 ± 5	128 ± 16		
PD	(cm/s^2)	121 ± 7	105 ±15	107 ± 8	148 ± 34	89 ± 11	82 ± 7	C	

All values are mean ± SE.
[A]OFF/OAC, $p<0.05$; [B]OFF/ON, $p<0.05$; [C]ON/OAC, $p<0.05$; NxN indicates interaction effect, $p<0.05$

2.5 DISCUSSION

The purpose of this study was to explore the effect of task accuracy demands on movement expression for PD patients. To overcome current difficulties with novel tasks we used an ethologically-valid task paradigm within the controlled environment of a laboratory. High task accuracy constraint was imposed by maximizing target glass fill level. Kinematic analyses were made of all sequential phases of the seated drinking action for PD subjects on and off medication, as well as an age-matched group. The analysis revealed movement deficits typical of PD, along with some motor improvement for medicated PD patients. In addition, our results showed that all participant groups were sensitive to task demands and accommodations were made in movement expression to avoid upset conditions. For example, all groups spent more time in the HANDLE and TRANSPORT phases, and less time in the MOUTH phase, with the FULL target, as would be expected based on previous investigations of prehension and drinking [Latash & Jaric, 2002; Marteniuk et al., 1987]. The novel finding we present is that task accuracy constraint had an unique effect on nonmedicated PD patients. Specifically, additional movement impairments were exhibited by PD patients OFF medication when reaching for, and drinking from, the full glass.

2.5.1 MOVEMENT DEFICITS IN PARKINSON'S DISEASE

PD patients off medication exhibited prolonged slowness on all phases of the task, including premotor time (PMT) and total response time (RT). This general slowness agrees with previous studies of discrete movements and parkinsonism [Evarts, Teräväinen, and Calne, 1981; Harrington & Haaland, 1991; Sanes, 1985; Sheridan, Flowers, & Hurrell, 1987] and confirms that PD affects movement planning, motor recruitment, and movement execution. Interestingly, while medication decreased phase times in all movement phases, significant improvements were observed only in the static pre-motor phase (PMT), with the next largest medicated improvement occurring in the quasi-static fine movement (HANDLE) phase. A similar phase-specific improvement in kinematics has been previously observed for PD gait [Blin et al., 1991], where stride and swing duration (dynamic gait phases) were not improved with l-dopa, while duration of double support (quasi-static gait phase) was improved with drug treatment. Our findings of improved movement phase times for static and quasi-static movement phases agree with those of Blin et al. [1991] and extends the finding of phase-specific improvements into the domain of reaching. The results of the current study also provide support for the suggestion of Bennett et al. [1995] that the basal ganglia play a role in controlling and sequencing specific motor activations in the drinking task. A role for the basal ganglia in coding and recalling movement initiation and interval times has been the focus of much recent research [Harrington et al., 1998; Nenadic et al., 2003; O'Boyle et al., 1996; Rao et al., 2001; Rao et al., 1997; Ruskin et al., 1999]. Our finding of reduced PRT observed among medicated PD participants in this study supports this proposed role of the basal ganglia, as this phase involves the voluntary initiation of a motor response.

Patients ON and OFF medication both showed a decreased magnitude of peak velocity and peak acceleration for the REACH phase compared to healthy adult controls. Consequently, these slower movements led to longer movement durations for both the REACH and TRANS phases. These persistent deficits may be indicative of dysfunctional motor activity, and infer that some movement components could be unresponsive to dopaminergic medication. Inability to adequately recruit, sustain, and scale motor unit activation is a well-established deficit associated with PD [Marsden, 1982]. In the current study, the reduced velocity for the REACH and TRANS phases, in addition to the prolonged response and movement times, support some impairment in motor recruitment. Previous research has also shown that PD patients on l-dopa exhibited decreased latency to initiate voluntary movement [Frank et al., 2000], a proposed result of the improved synchrony of motor unit recruitment observed with medicated PD patients [Salenius et al., 2002]. Dopamine may also provide improvement for any movement interval timing function in the basal ganglia, allowing pre-existing programs for the duration of acceleration and deceleration phases to be matched [O'Boyle et al., 1996]. This improved relative timing also has the effect of making arm movements appear more 'smooth', a result previously demonstrated through a reduced frequency of acceleration/deceleration alternations [Castiello et al., 2000; Rand et al., 2000]. In the current study, the decreased duration for the PMT phase and the decreased number of REACH movement units observed among PD ON agrees with these previous findings. However, despite these medicated improvements, both PD groups showed some increased motor deficit in situations with higher task accuracy constraint.

2.5.2 TASK ACCURACY CONSTRAINT EFFECTS

Increasing task accuracy constraint led to the appearance of three strikingly different reaching control strategies, specific to subject group. Control subjects increased peak acceleration and peak deceleration in the HIGH REACH. These increases, combined with a decrease in time to peak acceleration and increase in time to peak deceleration for the high task accuracy condition, allowed the control group to accomplish the REACH phase in near identical timing for both LOW and HIGH task demands, both in absolute time and phase time relative to entire task. In essence, small refinements to the motor plan for a well-learned task enabled the expression of a reach movement that was consistent across both accuracy conditions. These refinements could be provided through sequencing modulation at intact basal ganglia, a result previously observed for a discrete experimental upper extremity task [Johnson et al., 2003].

Conversely, PD patients OFF medication decreased peak velocity, peak acceleration, and peak deceleration to reach for the target in the high accuracy constraint condition. PD patients OFF medication also decreased the duration of their first REACH movement unit. However, these decreases were accompanied by increased duration of the planning (PMT) and REACH phases, with increased number of REACH phase movement units and variability of REACH phase duration for the high task accuracy condition. This combination of decreased peak kinematic parameters, increased number of corrective movement units, and delayed timing suggests an over-riding task accuracy constraint on movement expression. PD OFF did not adjust aspects of their motor response to maintain overall REACH phase duration consistency, but instead were deficit on all measures in the high task accuracy constraint condition. In addition, PD further increased the number of

reach movement units, while decreasing the duration of the first movement unit, to satisfy HIGH task accuracy demands. These deficits may be evidence that the cognitive resources required to encode and respond to the high task accuracy constraint limit the remaining resources available to cortically mediate the reach movement. Subsequently, initiation and expression of the reach movement is delayed. This concept of task planning/task mediating interference is further supported by the increased duration required for the premotor time (PMT) in the HIGH task, primarily exhibited by PD OFF. The static PMT phase relies solely on cortical resources, and the increased duration observed for this phase in this study provides strong evidence that the high task accuracy constraint is imposing greater cognitive interference among the OFF medication PD subjects. This inference of attentional interference lends support to the current theory that PD patients make use of conscious control to help produce movement [Hausdorff et al., 2002; Henderson & Goodrich, 1993; Morris et al., 2000]. Canning [2005] has recently shown that directed attention can improve rate and amplitude of focal movement among PD, while attention directed to a secondary task accuracy constraint can interfere with the production of the focal movement. Our current work is aimed at identifying the influence of pre-planning time on the effectiveness of directed attention, and the appearance of attentional interference, in reaching and other activities of daily living.

PD patients ON medication demonstrated a tertiary task accuracy response strategy, one of minimal change between target conditions. PD ON showed only small modifications to kinematic parameters within the REACH phase, and were significantly deficit on kinematic parameters in either condition, compared to OAC. However, the magnitude of the relative time to peak acceleration was not significantly different between PD ON and OAC. These results suggest that replacement of dopamine in the deficient nigrostriatum can

partially restore movement timing, possibly by re-enabling processing in automatic motor loops in the basal ganglia [Fattapposta et al., 2002]. No task accuracy effect was observed among PD ON for number of reach movement units or duration of first movement unit, indicating a medicated improvement in the selection and execution of the initial (feedforward) motor plan, regardless of implicit task accuracy constraint. This result is also supported by the findings of Fattapposta et al. [2002], who analyzed movement related potentials among medicated and non-medicated PD patients, and suggested that dopamine treatment re-automated motor learning and performance for PD patients, probably through altered elctrophysiology.

2.5.3 FUNCTIONAL IMPLICATIONS

At a functional level, this experiment illustrated that PD patients were able to perform ethologically-valid tasks requiring high accuracy. No errors (spills; failure to grasp glass or to bring glass to lips) were observed for any group. This result implies the continued existence of learned movement patterns in PD patients, a result previously illustrated for a variety of complex tasks involving the upper extremity [Agostino et al., 1992; Alberts et al., 2000; Bennett et al., 1995; Bonfiglioli et al., 1998; Gordon, 1998; Weiss et al., 1996; Whishaw et al., 2002]. However, despite their successful performance, Parkinson's disease patients did show changes in the relative timing of movements, using prolonged duration of movement in both acceleration and deceleration segments to satisfy the task demands. Examples of this re-organized event structuring have been previously observed for walking [Blin et al., 1991], pointing, and reaching [Bennett et al., 1995] among PD participants. From the present study, it appears that a primary benefit of dopamine may be to make temporal alterations to

achieve reach and transport phases that have acceleration and deceleration periods sequenced more similarly to controls. Yet despite this improved kinematic sequencing, PD participants ON medication continued to exhibit reduced peak movement velocities and accelerations, closer in magnitude to those of dopamine-depleted patients than to controls. Previous research has linked these kinematic deficits with force production errors, specifically rigidity-related coactivation and low-level motor unit recruitment [Evarts, Teräväinen, and Calne, 1981]. Further research examining the influence of movement planning on motor preparation and recruitment is warranted to more clearly illustrate the relationship between task difficulty, advance information, and motor output.

2.6 CONCLUSION

In conclusion, the present study shows that the reaching movement of non-medicated PD patients is adversely affected by an increase in glass fill level for an ethologically-valid reaching task. We have interpreted these findings to indicate that probable increases in cognitive demands, imposed by the higher task accuracy condition, may be interfering with the processing of motor response, leading to subsequent changes in timing and expression of the reach. These changes do not appear to be part of a planned strategic response, but rather the influence of an over-riding task constraint. Understanding the interaction between task accuracy demand and motor output may help to improve the mobility and safety of PD patients in daily activities, while providing a more specific baseline for evaluating both progression and treatment of Parkinson's disease.

3.0 ENVIRONMENTAL CONTEXT DISTURBS THE CO-ORDINATION OF POSTURAL CONTROL AND REACH KINEMATICS AMONG PARKINSON'S DISEASE PATIENTS

3.1 ABSTRACT

The standing reach movement requires coordinated activation of postural and focal motor responses. For PD patients, both components of this reaching task exhibit evidence of motor deficit. In the present experiment, we examined these motor responses during a standing reaching task in a challenging environmental context. PD patients (n = 8) and control participants (n = 8) were asked to reach and drink from a plastic stemmed glass while standing on a raised platform (0.6m) with and without an additional anterior platform. Removal of the anterior platform placed participants in a higher postural threat context, as there was no opportunity for a compensatory forward step to control any postural instability. Displacement data were captured from markers on relevant body landmarks to provide reach limb and whole body movement kinematics, which were interpreted in conjunction with postural kinetics. Our results showed that non-medicated PD patients made uncoordinated behavioral changes in the elevated environmental context, specifically delaying both peak anterior centre of mass velocity and reach limb acceleration phase during the forward reach. These contextual deficits may contribute to the frequent falls observed among the PD population during voluntary movements in challenging environmental contexts.

3.2 INTRODUCTION

Reaching and grasping are major components of many activities of daily living, from basic functional tasks to complex volitional movements [Buckley et al., 1996; Safaee-Rad et al., 1990]. For standing reaching, any targeted focal movement must be coupled with the appropriate anticipatory and on-going postural adjustments to maintain equilibrium [Massion, 1992; Thomas, Corcos, Hasan, 2003]. These concurrent actions pose an unique challenge to Parkinson's disease (PD) patients, a group who exhibit bradykinesia and postural instability among their clinical symptoms [Uitti et al., 2005]. Current medical treatments and rehabilitation strategies can moderate bradykinetic and postural deficits in many simple clinical and functional tasks [Bejjani et al., 2000; Montgomery, 2004; Rocchi et al., 2002]. More complex tasks, such as standing reaching, may present a greater challenge to both the parkinsonian motor control system and to conventional PD treatment. Previous research has shown that PD patients produce decreased postural muscle activity and smaller preparatory (posterior) CoP displacement amplitudes during standing reaches to touch or grasp targets, despite the influence of pharmacotherapy [Aruin et al., 1996; Bazalgette et al., 1986; Latash et al., 1995; Lee et al., 1995].

Challenging context has also been shown to exacerbate deficits in the regulation of posture, locomotion, and upper extremity movements among PD patients [Bertram et al., 2005; Bond and Morris, 2000; Canning, 2004; Fahn, 1995; Giladi et al., 1992; Macht and Ellgring, 1999; Rochester et al., 2004; Tunik et al., 2004]. These contextual challenges can be either task-related (e.g. reaching for a water glass that is full) or environmental task-specific (e.g. standing on a raised platform to reach into a top shelf) [Steenbergen et al., 1995]. Contextual challenges in everyday life are common and debilitating, and recent studies indicate that both the threat and the event of falls in challenging situational contexts are fear-

inducing [Adkin et al., 2003] and frequent among the PD population [Stolze et al., 2004; Strubel et al., 2001]. Given this ecological evidence, it is possible that challenging contexts may exacerbate PD motor deficits in the coordinated activation of preparatory postural adjustment, focal movement, and focal postural adjustment.

The purpose of this study was to compare how the control and execution of a functional motor task among PD patients and neurologically normal older adults are influenced by an environmental context that challenges postural control. Specifically, we examined upper limb kinematics and postural control for all movement components of a standing reach-to-grasp task performed at the edge of a raised platform. This context has previously been demonstrated to influence postural control among non-neurological subjects [Carpenter et al., 2001]. Furthermore, standing reach in this context suggests an experimental analogue of reaching while standing on a chair, an activity of daily living associated with severely reduced balance confidence among PD patients [Adkin et al., 2003]. For this study, we suggest that standing targeted reach from a raised platform incorporates both postural and focal movement demands, while addressing the documented need for movement disorder studies to use ethologically-valid tasks conducted in realistic environmental contexts [Czaja and Sharit, 2003; Morris et al., 1999; Teasdale and Stelmach, 1988]. We hypothesized that PD patients would exhibit postural and focal movement deficits, due to a combination of general postural instability [Bronte-Stewart et al., 2002] and kinematic deficits in upper limb [Doan et al., 2006] and whole body movements [Kurek et al., 2005] resulting from a challenging task context.

3.3 METHODS

3.3.1 PARTICIPANTS

Eight participants with idiopathic PD (mean age: 66.8 ± 8.6 years; clinical characteristics in Table 3.1) and eight age-matched controls (CTRL; mean age: 69.5 ± 7.7 years) served as subjects. All participants were informed on the nature of the study and provided written consent. The Human Research Ethics committee of the University of Lethbridge had previously approved all procedures in the study. PD participants were tested only on reaches with the limb predominant in parkinsonian symptoms, as determined by a neurologist (OS) during UPDRS screening. PD predominant limb coincided with self-reported hand dominant limb in 6 of 8 PD patients. Control subjects were matched with PD patients with respect to use of dominant or non-dominant limb, and tested only on reaches with that limb.

All PD patients were receiving dopaminergic medication as PD treatment (Table 3.1), and each PD subject was tested OFF (>12 h removed from last oral drug dose) and ON (between 1h and 2 h following regular medication administration) pharmacological treatment in the same laboratory visit (same day). All patients were tested in the OFF then ON order for patient practicality and comfort. Quality of ON condition was confirmed both by patient self-report and qualified clinical assessment.

3.3.2 STANDING PLATFORM AND POSTURAL THREAT

Participants stood on the edge of a portable force plate (Bertec Corporation, Columbus, OH), embedded in a wooden deck (1.8 m long by 1.2 m wide) topping a height adjustable hydraulic lift (Figure 3.1). The deck was cut away at the front edge such that the forceplate was centred on the A-P midline of the deck, flush with the top and front edges of the deck. Each subject performed trials in two context conditions: LOW context (Figure 3.1A), where a stable secondary surface (0.45 m depth by 1.2 m length top surface area) was added to the front of the standing reach deck, enabling a compensatory step if required (McIlroy and Maki, 1993) and HIGH context, where the secondary platform was removed (Figure 3.1B). In both conditions, the height of the forceplate surface was 0.6 m. Pilot testing for this study indicated that some PD OFF participants would be unwilling and/or unable to approach the limits of their base of support (reach forward to target) when standing at a height exceeding 0.6 m. For all trials, a removable, height-adjustable safety railing was firmly attached in a parasagittal plane on the non-reaching side, 25 cm lateral to the edge of the force plate.

Table 3.1. Clinical information of Parkinson's disease patient group.

Patient	Age (yr)	Disease Duration	Sex	UPDRS – III* ON**	UPDRS – III* OFF***	Symptoms (OFF) Bradykinesia	Action Tremor	Resting Tremor	Dyskinesia (ON)#	Medication
1	64	9	f	23	46	Y	N	N	N	levodopa/carbidopa; pramipexole
2	66	10	f	16	35	Y	Y	N	Y	levodopa/carbidopa; pramipexole entacapone; amantadine
3	70	1	m	7	20	Y	Y	Y	N	levodopa/carbidopa
4	53	29	f	18	46	Y	Y	Y	N	levodopa/carbidopa; pramipexole
5	79	5	m	26	42	Y	Y	Y	N	levodopa/carbidopa; pramipexole
6	56	8	f	5	11	N	N	Y	N	levodopa/carbidopa; amantadine
7	80	5	f	29	55	Y	Y	Y	N	levodopa/carbidopa
8	66	2	m	15	42	Y	Y	Y	Y	levodopa/carbidopa; pramipexole
Mean (SD)	66.8 (9.6)	8.6 (8.8)		17.4 (8.5)	37.1 (14.7)					

* Unified Parkinson's Disease Rating Scale – III (motor component – questions 18-31), with higher scores indicative of greater motor deficit.
\# Dyskinesias were observed in laboratory during testing.
** ON – testing commenced between 1 and 2 hours following administration of regular medication dose.
*** OFF – testing commenced after 12+ hours (overnight) withdrawal from regular medication dose

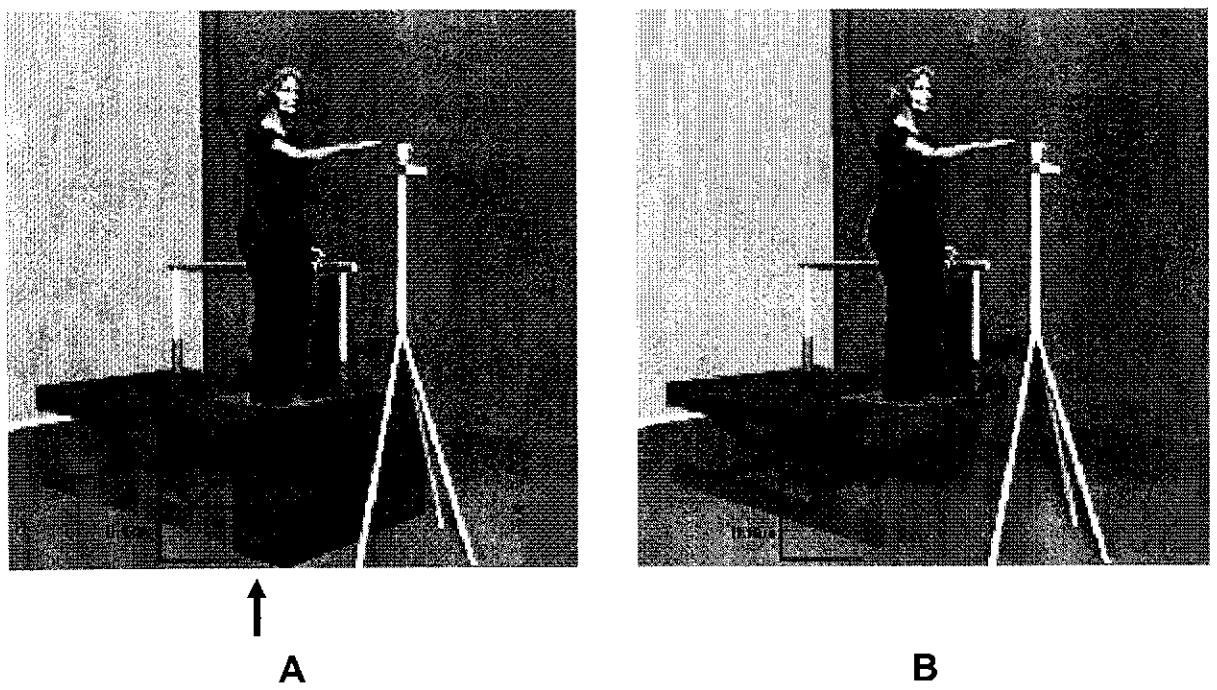


Figure 3.1. Standing reach environmental context.

Sagittal view of A) LOW and B) HIGH context reaching conditions. A removable platform, equal in height to the surface of the forceplate (0.6 m), was available in the LOW context condition (step indicated by arrow).

3.3.3 STANDING REACH TASK

Subjects performed a standing reaching and drinking task, consisting of a reach targeted at a drinking glass, with subsequent grasp of the target, transport to mouth, sip, and stop at waist-level. The glass was clear plastic, with a drinking rim diameter of 6.0 cm, and a height of 8.0 cm from base to drinking rim. In all trials, the glass was filled with water to a level less than 1 cm below the top edge, providing a fill volume ≥ 110 ml (>75% maximum possible volume). This fill volume was chosen for practicality – it was the greatest fluid volume that experimental research assistants could reliably transport and position without spilling. The glass was placed on a vertically-extended tripod with a custom platform top (height to top of glass on pedestal = 1.90 m) at a horizontal reach amplitude (subject's standing heel marker to target centre) normalized to subject's reach arm length (100% of length from shoulder to base of index finger). All participants in each group (PD ON, PD OFF, OAC) completed 2 standing reach trials in each context condition (4 standing reach trials total), as well as other seated target reaching trials and quiet standing trials (34 trials total), as part of a larger study. Order of context condition presentation (LOW then HIGH or HIGH then LOW) was blocked for each subject, and counter-balanced between subjects. Each reaching trial was initiated with two separate commands to the subjects: the investigator informed the subject that a new trial was ready to commence, and then a subsequent auditory stimulus was computer-delivered (GO signal; random latency 1 to 3 seconds after investigator instructions) to start the trial. Any trials where reaching proceeded the auditory stimulus were deleted, and subjects were reminded to wait for the GO signal. In all cases, subjects were directed to reach 'as accurately as possible' (investigator script).

3.3.4 DATA COLLECTION AND ANALYSIS

Participants were first outfitted with a whole-body safety harness, with a posterior mid-shoulder hook for tethering to the overhead safety restraint system. Participants were then fitted unilaterally (reach side) with passive infrared-reflective markers at: the head of the first metatarsal, the lateral malleolus, the lateral epicondyle of the femur, the greater trochanter, the ulnar styloid process, the radial styloid process, the head of the second metacarpal, the base of the index fingernail, the base of the thumb fingernail, the lateral epicondyle of the humerus, mid-humerus, the acromion process, and the zygomatic bone. Additional midline markers were placed on the forehead and at the sternal notch, and a modified marker was also placed at the target support surface. This unilateral simplification was made based on previous work by Schenkman et al. [2001], which showed that forward trunk flexion exhibited the largest segmental excursion during standing arm flexion among PD patients, while thoracic rotation provided small contribution to the maximum forward reach.

Positional data were collected at 120 Hz using a Peak MOTUS motion analysis system (Peak Products, Englewood, CO). Three-dimensional marker position reconstruction was performed with Peak MOTUS software, and any necessary interpolation was performed using a custom-written visual inspection/linear correction computer routine (MatLab; The MathWorks, Natick, MA.). Unidimensional displacement data were filtered using a dual pass, 4^{th}-order digital Butterworth filter with a cut-off frequency of 5 Hz, and unidimensional marker velocities were calculated using the finite differences method. These velocities were resolved into a single resultant measure, for further differentiation to acceleration, and for calculation of kinematic parameters. Force plate output signals were

collected at a frequency of 600 Hz, and were also Butterworth filtered (dual pass, 4th order, 5 Hz cutoff).

Centre of mass (CoM) estimates were created from the displacement data using symmetrical transformation of static quiet standing joint coordinates from the reaching (marker) to the non-reaching (non-marker) side, as defined in Table 3.2. Transformation to a bilateral model was made using a symmetrical estimation for lower extremity segments, and by deducting a unilateral static arm CoM value (non-reaching arm segment endpoints at initial shoulder and wrist values for reaching arm) from the HAT segment (Head, 2 Arms, Trunk) while including dynamic CoM values for the unilateral reach upper arm and forearm-hand segments.

Movement onset and event onset times were derived from the resultant reach wrist velocity, using positive and negative versions of the velocity threshold algorithm developed and validated by Teasdale et al. [1993]. An example of reach wrist resultant displacement and CoP displacement, with overlying phase onset marks, is shown in Figure 3.2. The time between audio GO signal and onset of movement was categorized as response time (RT; interval a on Figure 3.2), a standard stimulus-motor response latency measure. This measure has consistently revealed bradykinesia among PD in previous studies [Evarts, Teräväinen, & Calne, 1981; Salenius et al., 2002; Sanes, 1985]. The reach-to-target event (REACH; interval b on Figure 3.2) was defined as the time between first movement onset and minimal velocity prior to arrival at the target. The transfer-to-mouth event (TRANS; interval d on Figure 3.2) was defined as the time between movement onset at the target and minimal velocity on the approach to the mouth. HANDLE (interval c on Figure 3.2) was the time between the REACH and TRANS phases, when the reach arm segment endpoint is at the target. MOUTH (interval e on Figure 3.2) was the time from minimal velocity in the movement to

the mouth (end of TRANS) to the next movement onset, again determined using a velocity threshold algorithm [Teasdale et al., 1993]. Within each active phase (RT and HANDLE excluded), mean and peak resultant velocity, along with absolute and relative phase time to peak resultant velocity, were calculated. The range of angular displacement at the shoulder, hip, and knee joint in the sagittal plane were also calculated.

Reach wrist resultant velocity trial data were normalized for trial length and then averaged within group and threat condition to provide representative velocity profiles. Characteristics of these profile types have previously been used to examine pathological targeted reach movements [McRea and Eng, 2005; Rand et al., 2000]. Specifically, velocity profile skew provides indication of perception and preparation for task demand. Positive skewed reach velocity profile (peak reach velocity skewed towards the start of the reach) is indicative of a conservative motor control strategy, possibly in response to transitory or endpoint accuracy demands. Alternatively, negative velocity profile skew results in a shorter deceleration period. This strategy is appropriate for reach movements with lower accuracy demands, but it could also be the result of a failure or inability to modify a reach movement to meet task demands. An examination of the segmentation of the velocity profile also provides information about the integrity of the motor control acting on a reach. A more segmented velocity profile (multiple peaks and troughs, prolonged plateau region around maximum velocity) suggests increased reliance on ongoing corrective control to modify movement sequencing. Segmentation (or 'submovement') frequency counts have been used to characterize task accuracy constraints on reaching among neurologically normal [Jagacinski et al., 1980], developing [Fallang, Saugstad, & Hadders-Algra, 2000; von Hofsten, 1991] and pathological [Doan et al., 2006; McRea & Eng, 2005] populations. In the current

study, qualitative comparison of group-averaged time-normalized velocity profiles was used to check pathological and contextual characteristics of standing reach.

Pertinent CoP and CoM measures were also calculated for each phase. These included net displacement in the anterior-posterior (AP) dimension, peak AP velocity, and relative and absolute time to peak AP velocity. In addition, peak posterior CoP displacement (PREP) was identified as a component of the REACH phase, and absolute and relative phase times for peak PREP CoP velocity were also calculated with reference to the duration of the REACH phase.

Three separate comparisons were conducted on the data, using GROUP (PD OFF vs CTRL (between-group comparison); PD OFF vs. PD ON (within-group comparison); PD ON vs. CTRL (between-group comparison) x CONTEXT (LOW vs. HIGH) analyses of variance with level of significance set at $\alpha = .05$.

Table 3.2. Segment endpoint definitions and CoM segment parameters [from Winter, 2005].

Segment	Mass Fraction	Segment endpoint definition
Head and trunk	0.5780	(dHIP + sHIP)/2; (dSHLD + sSHLD)/2 ;
Reach Upper Arm	0.0280	dSHLD; dELB
Non-reach Upper Arm	0.0280	sSHLD; sELB
Reach Lower Arm	0.0220	dELB; dWrU
Non-reach Lower Arm	0.0220	sELB; sWrU
Reach Thigh	0.1000	dHIP; dKNEE
Non-reach Thigh	0.1000	sHIP; sKNEE
Reach Shank	0.0465	dKNEE; dANK
Non-reach Shank	0.0465	sKNEE; sANK
Feet	0.0145 (2)	dANK; dTOE
Total	1.0000	

Note: 'd' signifies endpoint positions defined by dynamic displacement data, while 's' signifies endpoint positions defined by static position data. Static position data were the mean of the first 10 collection samples (static sample times = 1/120 s to 10/120 s).

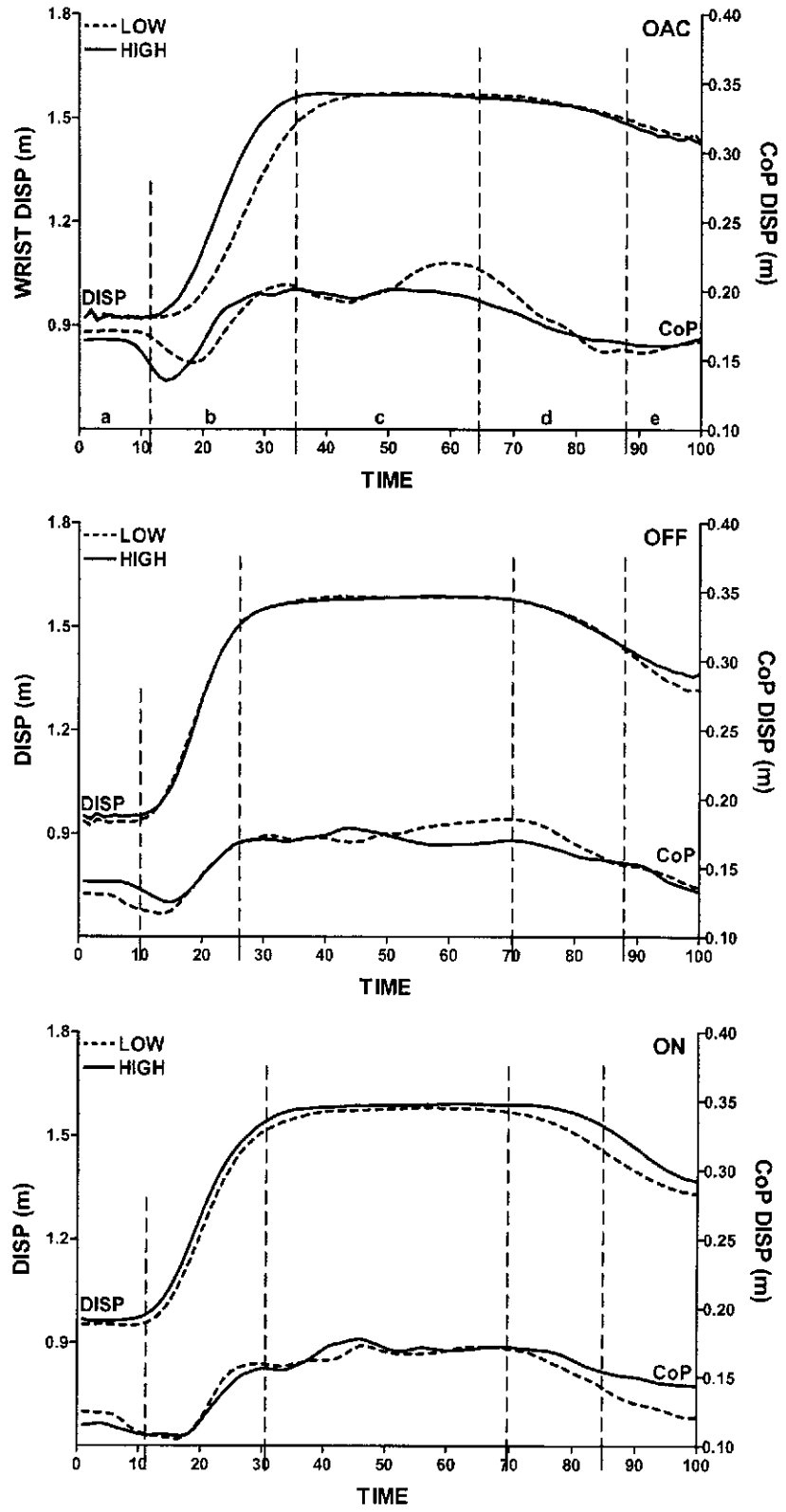

LOW
HIGH
OAC
WRIST DISP (m)
CoP DISP (m)
DISP
CoP
a
b
c
d
e
TIME
OFF
ON

Figure 3.2. Sample reach wrist and centre of pressure displacement patterns, with event onset times.

Reach wrist displacement (resultant) and centre of pressure displacement for representative control (top), non-medicated PD (middle), and medicated PD (bottom) patient. LOW context reaches are shown in broken lines, with sold lines marking HIGH context reaches. Broken vertical lines indicate reach phase boundaries for LOW context reaches. Phases (labeled on top figure) are: a) response time (RT), b) REACH, c) HANDLE, d) return to mouth (TRANSPORT), and e) time at mouth (MOUTH).

3.4 RESULTS

3.4.1 PREPARATORY POSTURAL KINETICS

A significant CONTEXT effect existed within the CTRL/PD OFF group comparison for CoP displacement ($F(1, 14) = 4.582$, $p = .050$), with both groups exhibiting greater posterior displacement in HIGH context conditions. PREP CoP velocity was non-significantly smaller and slower for OFF compared to either CTRL or PD ON participants. PREP CoP displacement measures are available in Table 3.3, while exemplar CTRL, PD OFF, and PD ON resultant CoP signals can be compared in Figure 3.2.

3.4.2 REACH MOVEMENT

3.4.2.1 REACHING SUCCESS

Among the 8 PD OFF participants (32 total trials), there were 5 mistrials (anticipation of GO signal, delay (>3 s) after GO signal, non-reaching hand seeking support on safety rail) in LOW context and 8 in HIGH context. PD ON ($n = 8$; $trial_n = 32$) had one mistrial in each of the LOW and HIGH conditions (delay and anticipation, respectively), while CTRL ($n = 8$; $trial_n = 32$) had one mistrial (anticipation) in the HIGH condition (Figure 3.3). Participants were allowed up to 2 repeat attempts for any mistrial, and no subject made three mistrials in a single trial opportunity. All subject quantitative results were the mean of two successful trials.

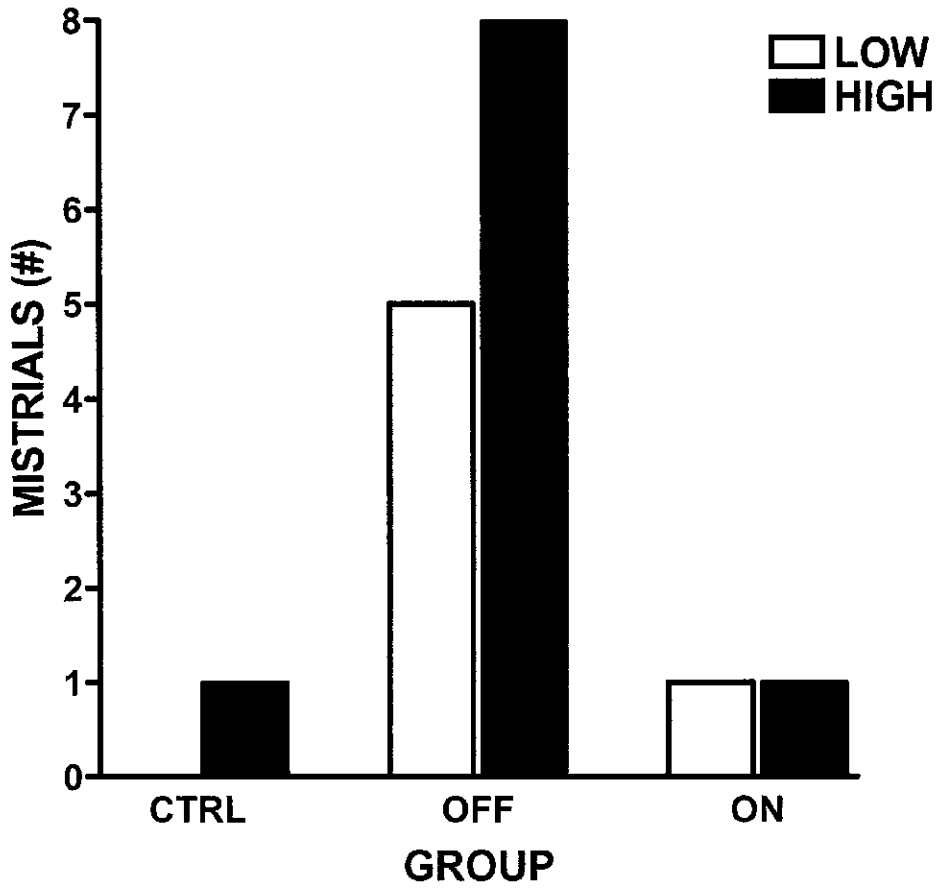


Figure 3.3. Error trials in standing reach task.

Tally of mistrials for CTRL, PD OFF, and PD ON standing reach trials. A reach attempt was classified as a mistrial if investigators observed any reach limb movement prior to audio GO signal (anticipation), if reach movement was delayed for >3s after GO signal (delay), or if the subject needed support from the safety rail and/or harness during the course of the reach (misfire).

3.4.2.2 GROUP EFFECTS

Group differences in reach kinematic parameters have been well-documented in studies comparing non-medicated PD patients, medicated PD patients, and neurologically normal older adults [Alberts et al., 2000; Bennett et al., 1995; Castiello et al., 2000; Doan et al., 2006; Negrotti et al., 2004]. In the current study, non-medicated PD patients exhibited pathology-typical bradykinesia in REACH (Figure 3.5) and TRANSPORT (Figure 3.6) phases. Specific group differences are highlighted in subsequent sections.

3.4.3 REACH WRIST KINEMATICS

3.4.3.1 KINEMATIC PROFILES

Figure 3.4 shows the time-normalized GROUP average reach wrist resultant velocity profiles in each CONTEXT condition. The CTRL group exhibited a non-segmented velocity profile peak, with a minimal, context-appropriate positive skew (skewed toward movement onset) to said profile in the HIGH context condition. In contrast, OFF exhibit more segmented velocity profiles in both CONTEXT conditions, with a long peri-maximal velocity plateau instead of a defined maximal velocity. This plateau is extended in the HIGH context condition, with the velocity profile peak being negatively skewed as compared to reaches in the LOW context condition, or reaches in either condition among CTRL participants. ON also exhibit these longer peri-maximal velocity plateaux in reaches in both conditions, along with a negative skew in the HIGH context reach.

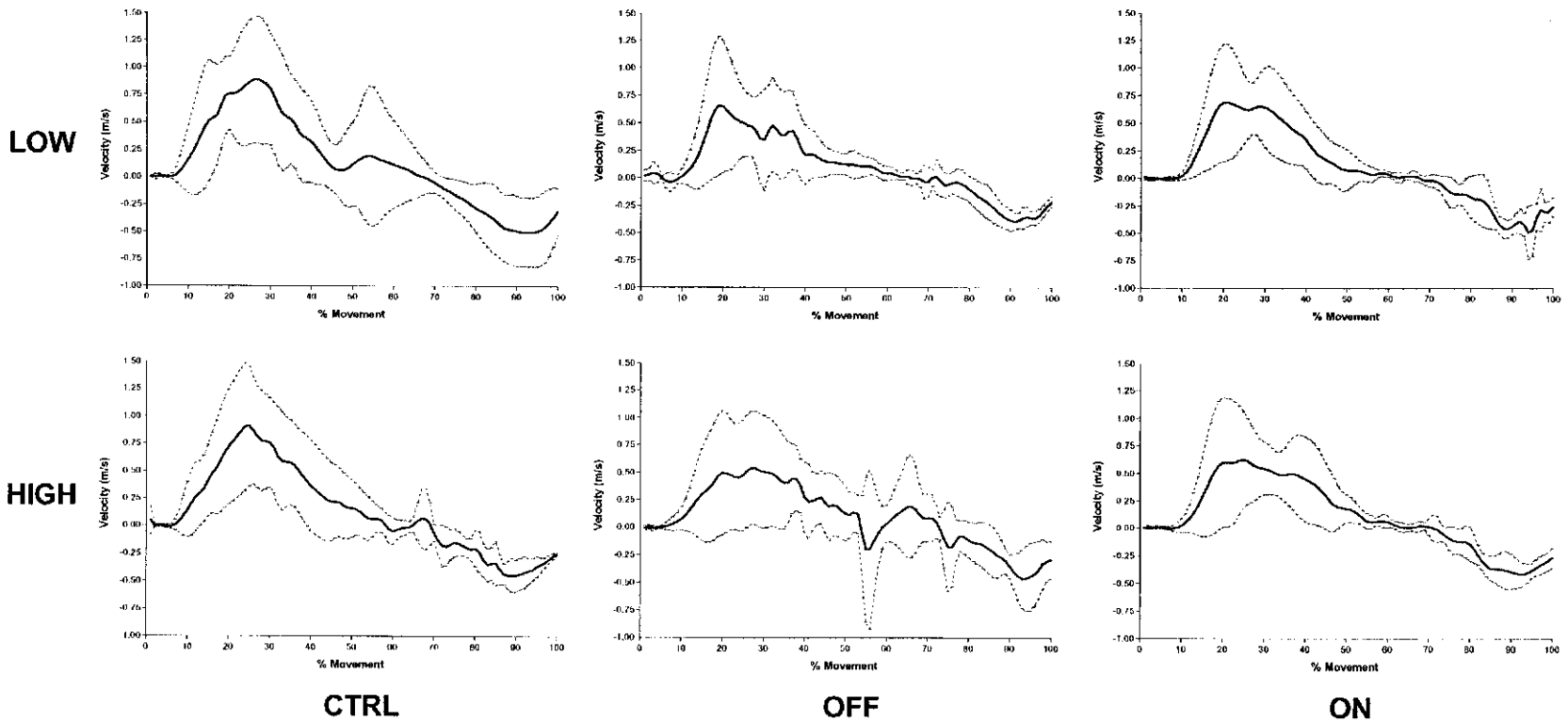

LOW
HIGH
Velocity (m/s)
% Movement
CTRL
OFF
ON

Figure 3.4. Kinematic profiles of wrist velocity in standing reach trials. Reach wrist resultant velocity profiles normalized to movement time and averaged within GROUP and CONTEXT. PD OFF exhibit a more segmented profile in both CONTEXTs, with a negative profile skew (peak shifted away from movement initiation) and a flattened peri-maximal peak. PD ON exhibit less segmentation, but similar flattened velocity peaks.

3.4.3.2 PHASE TIMES

PD OFF and PD ON were both significantly slower on absolute REACH in the HIGH context condition compared to the LOW context condition ($F(1,7) = 6.905$, $p = .034$). HIGH context condition also lead to shorter REACH phase times in the CTRL/OFF comparison ($F(1, 14) = 6.278$, $p = .025$). A significant interaction existed in relative TRANS phase time for the PD ON/PD OFF comparison ($F(1,7) = 5.811$, $p = .047$), with PD ON reducing TRANS time in the HIGH context condition (20.2 ± 1.4 % versus 24.2 ± 1.4 % in LOW context) while PD OFF increased TRANS time for HIGH context movement (22.6 ± 2.6 % versus 20.2 ± 1.7 % for LOW context). CTRL also decreased relative TRANS phase duration (26.0 ± 1.7 % in LOW versus 25.3 ± 0.9 % in HIGH). All absolute and relative phase time values are available in Table 3.3.

3.4.3.3 REACH phase

HIGH context condition led to longer relative time to peak REACH velocity among PD OFF and CTRL (($F(1, 14) = 8.887$, $p = .010$), driven by an relative increase among the PD OFF group (Figure 3.5A; 45% LOW versus 59% HIGH). This context-associated delay resulted in a GROUP x CONTEXT interaction ($F(1, 14) = 6.334$, $p = .025$), as CTRL showed minimal change in relative time to peak velocity between context conditions (Figure 3.5A; 53% LOW versus 54% HIGH). This interaction did not exist between CTRL and PD ON, who exhibited no relative temporal change between context conditions (Figure 3.5A; 51% LOW versus 51% HIGH). The longer REACH acceleration phase used by PD OFF for HIGH context reaching was not accompanied by any significant change in mean or peak REACH wrist velocity (Figure 3.5B), a constancy that is shared with the other experimental groups.

Table 3.3. Phase times for complete reach task.

		CTRL		*PD OFF*		*PD ON*		**GROUP EFFECTS**	**CONTEXT EFFECTS**
		LOW	HIGH	LOW	HIGH	LOW	HIGH		
RT	(ms)	429 ± 42	515 ± 104	594 ± 57	579 ± 108	715 ± 104	846 ± 133		C
	(%)	*12.9 ± 1.0*	*13.7 ± 2.0*	*12.3 ± 1. 3*	*12.4 ± 2.1*	*15.4 ± 3.2*	*19.4 ± 3.0*	*B*	*C*
REACH	(ms)	772 ± 85	728 ± 65	1138 ± 125	957 ± 96	922 ± 77	796 ± 55	A, B	A, B
	(%)	*23.0 ± 1.8*	*20.1 ± 1.4*	*23.0 ± 2.3*	*21.7 ± 2.8*	*20.1 ± 1.6*	*18.7 ± 0.9*	*B*	
HANDLE	(ms)	993 ± 54	1262 ± 113	1870 ± 193	1737 ± 164	1552 ± 103	1564 ± 121	A, B, C	
	(%)	*30.2 ± 1.5*	*34.8 ± 2.1*	*38.2 ± 3.4*	*38.2 ± 2.8*	*34.6 ± 2.7*	*36.6 ± 2.5*	*A*	
TRANS	(ms)	849 ± 38	914 ± 59	970 ± 65	1076 ± 155	1128 ± 170	853 ± 50		
	(%)	*26.0 ± 1.7*	*25.3 ± 0.9*	*20.2 ± 1.7*	*22.6 ± 2.6*	*24.2 ± 1.4*	*20.2 ± 1.4*		*B x B*
MOUTH	(ms)	263 ± 42	201 ± 39	314 ± 69	228 ± 65	258 ± 35	223 ± 30		
	(%)	*7.9 ± 1.2*	*6.0 ± 1.4*	*6.4 ± 1.6*	*5.1 ± 0.9*	*5.6 ± 0.9*	*5.1 ± 0.6*		

All values are mean ± SE.
[A] PD OFF/CTRL, $p<0.05$; [B]PD OFF/PD ON, $p<0.05$; [C]PD ON/CTRL, $p<0.05$; X x X indicates GROUP x CONTEXT interaction ($p<0.05$)

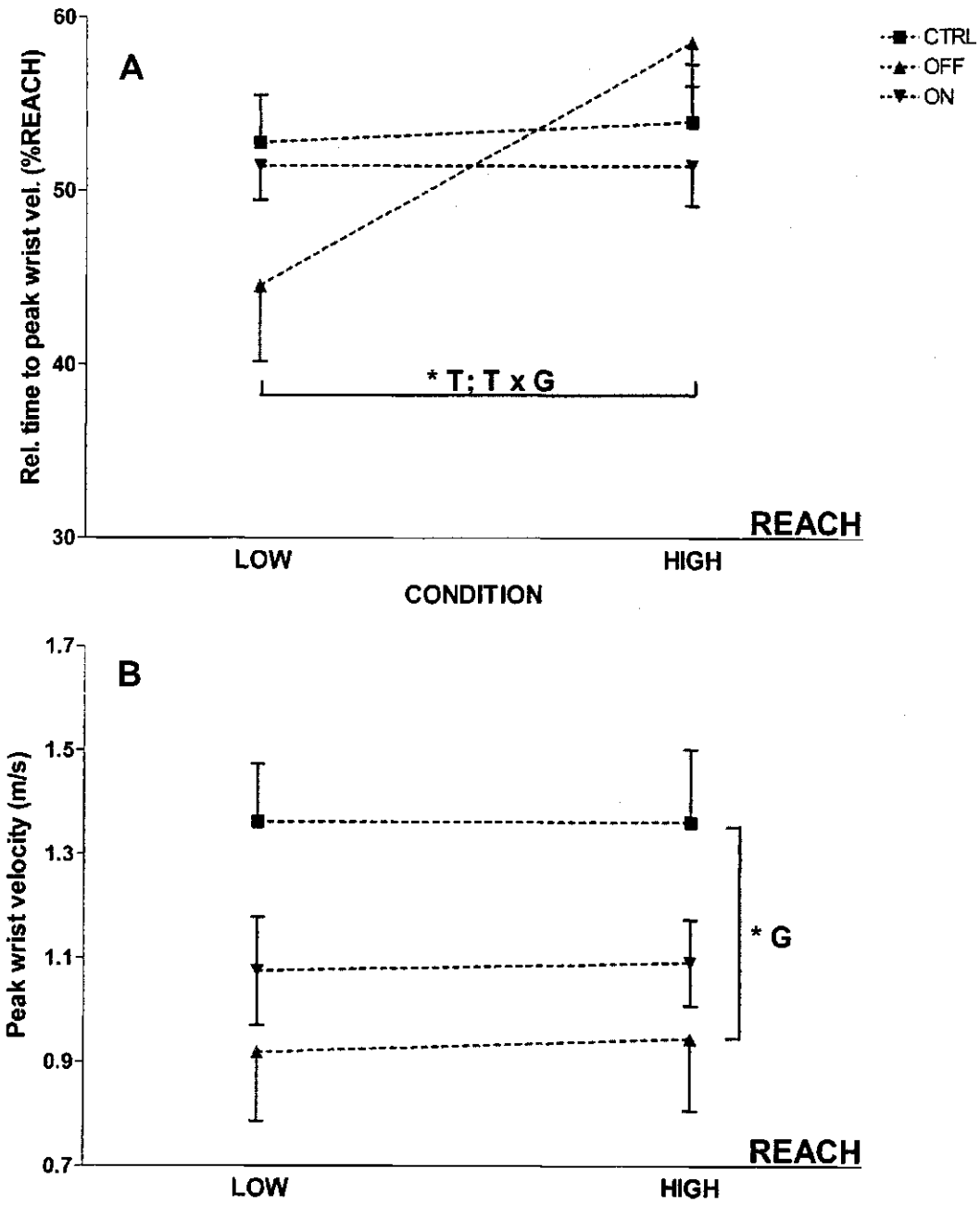


Figure 3.5. Wrist kinematics during standing REACH phase.

Relative time to peak resultant wrist velocity (A) and magnitude of peak resultant wrist velocity (B) are shown for the REACH phase.

3.4.3.4 TRANSPORT phase

PD OFF and CTRL exhibited reductions in relative time to peak velocity between the LOW and HIGH context conditions for the TRANSPORT phase (Figure 3.6A; 54% versus 42% for CTRL, 60% versus 50% for OFF). PD ON exhibited no change in the HIGH context condition (47% versus 50%). Both PD ON and CTRL reached higher peak resultant wrist velocity in TRANSPORT than PD OFF (Figure 3.6B; $F(1, 7) = 9.236$, $p = .019$ and $F(1, 14) = 5.830$, $p=.030$, respectively).

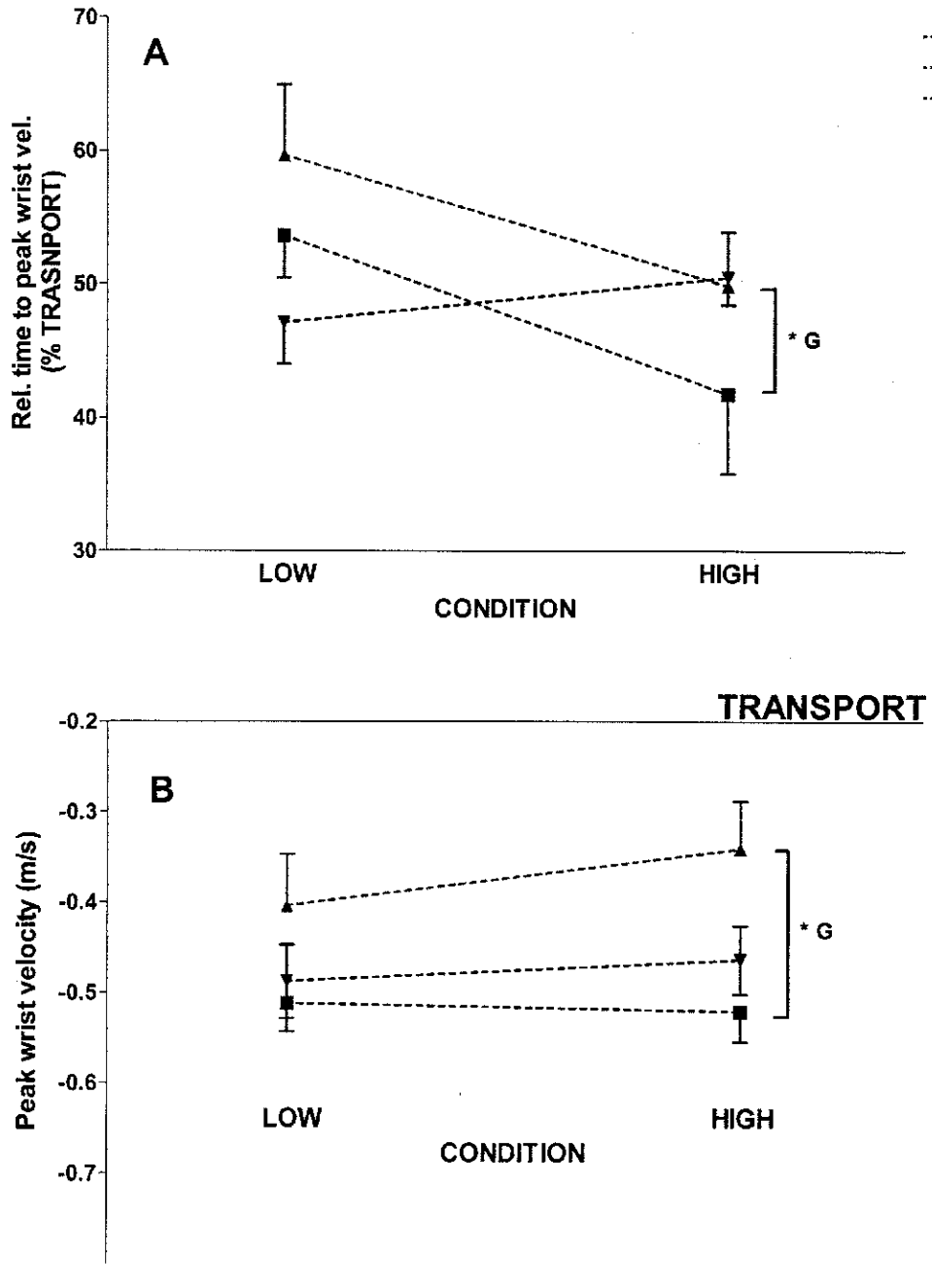


Figure 3.6. Wrist kinematics during standing TRANSPORT phase.

Relative time to peak resultant wrist velocity (A) and magnitude of peak resultant wrist velocity (B) are shown for the TRANSPORT phase.

3.4.4 WHOLE BODY KINEMATICS

3.4.4.1 SEGMENT CONFIGURATION

CTRL used flexion at the shoulder (mean angular displacement of +50.0°) combined with slight extension at the hip (+2.7°) and knee (+5.3°) to complete the REACH phase in the LOW context condition. This movement strategy was not changed in the HIGH context condition (angular displacements of +53.5°, +1.3°, and +2.4°, respectively), as shown in Figures 3.7A, 3.7B, and 3.7C. PD ON used a similar range of shoulder flexion in both LOW and HIGH context REACH (+53.0° and +51.3°, respectively), but used smaller hip angular displacement (-0.4° extension and +0.0° flexion, respectively) and knee angular displacement (+1.8° extension and +0.6° extension, respectively) in either REACH condition. PD OFF participants used a smaller shoulder flexion (+46.9°) and negligible knee extension (+0.2°), combined with hip flexion (-2.0°) to REACH at LOW threat. PD OFF exhibited similar mean joint angle displacements as PD ON in the HIGH REACH condition (+50.6° flexion at shoulder, +1.1° extension at knee, and -0.1° flexion at hip for PD OFF), again shown in Figures 3.7A through 3.7C. PD OFF did use significantly less knee extension than CTRL across context conditions for the REACH phase ($F(1,14) = 4.699$, $p = .048$). Greater proportion of hip angle displacement among PD was delayed compared to the CTRL group, with PD OFF using significantly more shoulder flexion than CTRL in the HANDLE phase (Figure 3.7F; $F(1, 14) = 4.955$, $p = .043$). This delayed movement strategy among PD OFF patients also emerged at the hip, where the magnitude of flexion in the HANDLE phase was larger among PD OFF patients than CTRL. This difference approached significance (Figure 3.7D; $F(1, 14) = 3.949$, $p= .067$). No interaction effects were observed in the joint angle measures.

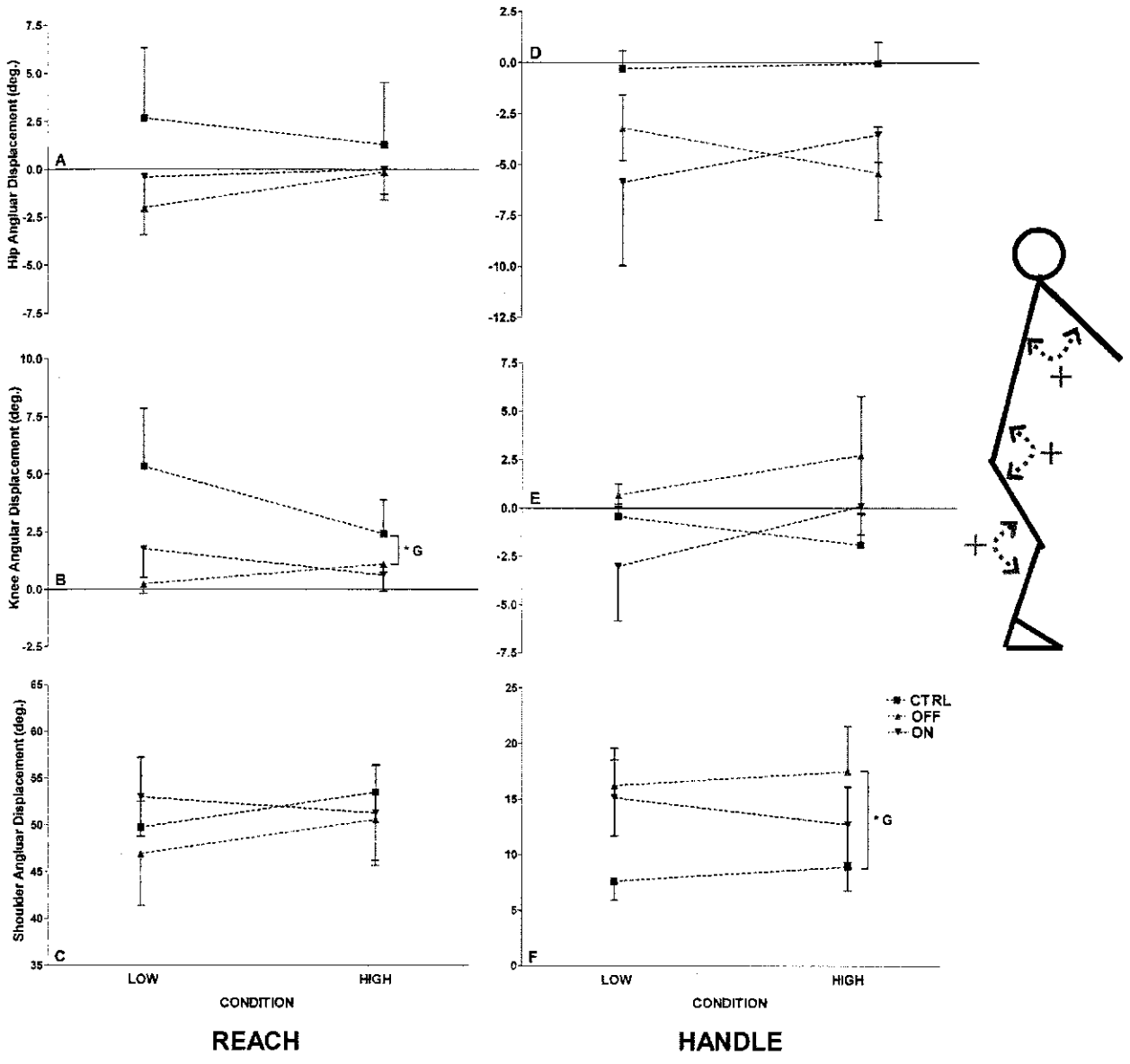


Figure 3.7. Mean joint angular displacements for REACH and HANDLE movement phases. Sign convention is as shown on stick figure on right.

3.4.4.2 COM KINEMATICS

PD OFF exhibited smaller CoM A/P displacement during the REACH phase than CTRL, across both standing conditions ($F(1, 14) = 5.958$, $p = .029$). No GROUP difference in CoM displacement was observed between PD ON and CTRL ($F(1,14) = 4.179$, $p=.060$). CTRL participants achieved greater peak CoM velocity in the REACH phase than either PD group ($F(1, 14) = 11.913$, $p = .004$ compared with PD OFF; $F(1, 14) = 6.135$, $p = .027$ compared with PD ON). PD OFF were also lower in peak CoM REACH velocity than PD ON ($F(1, 7) = 6.529$, $p = .038$). The lower magnitude CoM velocities achieved by PD OFF also occurred later in the relative REACH phase than those generated by CTRL ($F(1, 14) = 4.479$, $p = .053$). Positive A/P CoM displacement in the HANDLE phase was similar in magnitude across all groups, while peak A/P CoM velocity was smaller among PD OFF than PD ON ($F(1, 7) = 11.233$, $p = .012$). GROUP x CONTEXT interactions for CoM kinematics existed only in the TRANS phase, where CTRL participants increased peak velocity in the HIGH context condition, while PD OFF decreased peak CoM velocity during HIGH context reaches ($F(1, 14) = 4.498$, $p = .050$). PD OFF and CTRL also exhibited a THREAT effect in relative time to peak TRANS CoM velocity, with both groups using a longer acceleration phase to return from reach in the HIGH context condition ($F(1, 14) = 4.812$, $p = .046$). Conversely, TRANS CoM kinematics revealed a GROUP x CONTEXT interaction between PD OFF and PD ON for the relative timing of peak velocity, with PD ON decreasing the relative time to peak CoM velocity under HIGH context conditions ($F(1, 7) = 9.045$, $p = .020$). CoM kinematic data are presented in Table 3.4.

Table 3.4. Centre of mass kinematics for REACH, HANDLE, and TRANSPORT phases.

		CTRL		*PD OFF*		*PD ON*		**GROUP**	**CONTEXT**
		LOW	HIGH	LOW	HIGH	LOW	HIGH	**EFFECTS**	**EFFECTS**
REACH									
Displacement	(cm)	5.0 ± 0.7	4.6 ± 0.4	2.9 ± 0.6	3.0 ± 0.7	3.5 ± 0.6	3.2 ± 0.6	A	
Peak Velocity	(cm/s)	11.5 ± 1.9	10.1 ± 1.0	4.9 ± 1.1	5.8 ± 1.1	7.0 ± 1.1	6.4 ± 1.3	A, B, C	
Time to Peak Velocity	(%)	64.5 ± 6	67.9 ± 4	76.6 ± 5	76.7 ± 4	70.8 ± 5	75.6 ± 3	A	
HANDLE									
Displacement	(cm)	1.8 ± 0.2	2.1 ± 0.3	2.7 ± 0.5	2.6 ± 0.5	2.3 ± 0.4	2.4 ± 0.4		
Peak Velocity	(cm/s)	6.7 ± 0.8	7.3 ± 0.7	4.3 ± 0.9	4.8 ± 1.0	5.9 ± 0.9	6.1 ± 1.0	B	
Time to Peak Velocity	(%)	1.8 ± 1	3.5 ± 3	13.0 ± 6	17.3 ± 8	4.9 ± 3	7.9 ± 4		
TRANSPORT									
Displacement	(cm)	5.1 ± 0.3	5.0 ± 0.4	4.0 ± 0.7	3.5 ± 0.8	3.8 ± 0.6	4.2 ± 1.0		
Peak Velocity	(cm/s)	1.6 ± 0.5	2.6 ± 0.7	1.8 ± 0.8	1.1 ± 0.8	1.5 ± 0.9	1.9 ± 0.7		A X A
Time to Peak Velocity	(%)	30.3 ± 13	42.2 ± 15	25.2 ± 16	59.8 ± 15	51.1 ± 15	43.8 ± 14		A, C X C

All values are mean ± SE.
[A] PD OFF/CTRL, $p<0.05$; [B]PD OFF/PD ON, $p<0.05$; [C]PD ON/CTRL, $p<0.05$; X x X indicates GROUP x CONTEXT interaction ($p<0.05$)

3.4.5 REACH MOVEMENT POSTURAL KINETICS

PD OFF produced significantly smaller CoP velocity than CTRL during REACH for both context conditions ($F(1, 14) = 5.672$, $p = .032$), yet both groups achieved higher positive A/P CoP velocity during REACH in the HIGH condition when compared to LOW ($F(1, 14) = 5.897$, $p = .029$). In contrast, PD ON used reduced CoP velocity during REACH for the HIGH condition, providing a significant GROUP x CONTEXT interaction between PD groups ($F(1, 7) = 9.184$, $p = .019$). This interaction was significant in the PD ON/CTRL comparison as well ($F(1, 14) = 4.900$, $p = .044$). A CONTEXT effect also existed for the relative timing of maximum anterior/posterior CoP velocity in the HANDLE phase, with PD ON and CTRL both taking less time to achieve their maximum forward CoP velocity in the HIGH threat condition ($F(1,14) = 5.217$, $p = .038$). Both PD groups used significantly greater peak CoP velocity in HANDLE phase under HIGH threat condition ($F(1, 7) = 14.935$, $p = .006$), though peak CoP velocity values for the PD OFF group in the HANDLE phase were smaller than those of PD ON ($F(1, 7) = 11.372$, $p = .012$) or CTRL ($F(1, 14) = 7.035$, $p = .019$) participants across conditions. No significant differences were observed for postural kinematic measures from the TRANSPORT phase. Anterior/posterior CoP measures for REACH, HANDLE, and TRANSPORT phases are provided in Table 3.5.

Table 3.5. Centre of pressure measures for PREP, REACH, HANDLE, and TRANSPORT phases.

		CTRL		*PD OFF*		*PD ON*		GROUP	CONTEXT
		LOW	HIGH	LOW	HIGH	LOW	HIGH	EFFECTS	EFFECTS
PREP									
Net -ve Disp.	(cm)	0.5 ± 0.1	0.7 ± 0.2	0.3 ± 0.1	0.3 ± 0.1	0.4 ± 0.0	0.5 ± 0.1		A
Peak Velocity	(cm/s)	5.3 ± 1.7	6.9 ± 2.2	2.4 ± 0.4	2.4 ± 0.5	2.5 ± 1.0	3.2 ± 0.8		
Time to Peak Vel.	(%)	22.2 ± 6.8	15.9 ± 6.8	33.9 ± 11.8	30.4 ± 11.9	20.4 ± 11.7	18.8 ± 5.5		
	(ms)	218 ± 89	151 ± 79	483 ± 222	511 ± 274	185 ± 103	132 ± 39		
REACH									
Net +ve Disp.	(cm)	3.3 ± 0.5	3.2 ± 0.5	2.0 ± 0.5	2.5 ± 0.6	3.2 ± 0.7	2.4 ± 0.7		
Peak Velocity	(cm/s)	13.4 ± 1.5	15.2 ± 2.6	6.9 ± 1.8	9.0 ± 1.9	12.3 ± 2.9	9.6 ± 2.2	A, B	A,BXB, CXC
Time to Peak Vel.	(%)	62.5 ± 6.6	73.8 ± 6.1	73.8 ± 7.6	85.4 ± 3.8	68.6 ± 8.1	71.7 ± 8.2		
HANDLE									
Net +ve Disp.	(cm)	1.2 ± 0.3	1.3 ± 0.6	2.8 ± 0.7	1.8 ± 0.5	2.4 ± 0.6	2.4 ± 0.6		
Peak Velocity	(cm/s)	9.3 ± 0.7	12.5 ± 2.5	5.8 ± 0.8	7.5 ± 1.0	8.5 ± 1.2	9.6 ± 1.3	A, B	B
Time to Peak Vel.	(%)	29.0 ± 9.7	10.0 ± 4.1	29.2 ± 7.7	34.1 ± 10.0	29.4 ± 5.0	17.7 ± 3.6		C
TRANSPORT									
Net –ve Disp.	(cm)	3.5 ± 0.7	3.3 ± 0.8	3.5 ± 0.9	2.8 ± 0.8	3.5 ± 0.5	2.7 ± 0.4		
Peak Velocity	(cm/s)	10.8 ± 0.8	11.8 ± 1.5	9.3 ± 2.4	6.8 ± 1.6	9.6 ± 1.4	8.8 ± 1.5		
Time to Peak Vel.	(%)	42.5 ± 11.9	49.5 ± 9.7	45.3 ± 10.0	41.2 ± 8.8	43.5 ± 5.5	44.5 ± 5.8		

All values are mean ± SE.
[A] PD OFF/CTRL, $p<0.05$; [B]PD OFF/PD ON, $p<0.05$; [C]PD ON/CTRL, $p<0.05$; X x X indicates GROUP x CONTEXT interaction ($p<0.05$)

3.5 DISCUSSION

The purpose of this study was to compare the control and execution of standing reach between PD patients and neurologically normal older adults during a reach task performed in a threatening environmental context. Our results showed that PD patients were able to perform functional standing reaches in either a low or high context task environment, with limited context-induced kinematic or kinetic deficits. However, the deficits that were observed may be disruptive to the function and stability of standing reach in PD patients. Specifically, non-medicated PD patients took significantly longer than age-matched control participants to achieve peak reach velocity under high context conditions, and exhibited a decrease in horizontal centre of mass velocity for the transport (return to upright) phase of the reaching movement.

One suggested mechanism for the frequent falls observed among PD can be drawn from the finding that non-medicated PD patients were observed to move the arm at the same speed but with a longer acceleration phase during the reach and transport phases in the high threat condition. These focal arm movements were coupled with diminished preparatory displacement of the CoP, delayed peak anterior velocity of the CoM, and increased flexion at the hip during the latter stages of forward movement. With delayed peak anterior momentum of the arm and whole body CoM, the relative time available for arresting forward momentum is reduced. Deficient recruitment of musculature to arrest this momentum could also reduce the time available for arrest. Both of these outcomes have been identified in PD patients [Aruin et al., 1996; Frank, Horak, & Nutt, 2000; Latash et al., 1995]. In a standing reaching movement, the extreme possibility is a reduction of relative time for anterior CoM momentum arrest below a critical level, such that the CoM could

translate outside of the base of support in the anterior direction, leading to a fall [Kozak et al., 2003].

The general (GROUP) movement deficits observed in this task agree with clinical and experimental assessments of parkinsonian dysfunction. Slowness in reaching is a common experimental finding for PD movements [Alberts et al., 2000; Bennett et al., 1995; Doan et al., 2006; Negrotti et al., 2004]], typically combined with dysfunctional sequential movement patterns in targeted reach [Rand et al., 2000; Whishaw et al., 2002]. The adoption of a hip flexion-dominant strategy has also been previously identified for PD patients during the sit-to-stand task [Inkster and Eng, 2004]. In all examples, partial explanation for the dysfunction may be placed on the bradykinesia and joint rigidity that are symptomatic of PD. Our exploration of task performance in challenging context allows for further insight by demonstrating exacerbated disease symptomology and compromised pharmacological efficacy under increased context. Interpretation of our findings can be extrapolated from earlier research, which has shown that motor performance of PD patients is susceptible to attentional interference. Attentional interference has been defined as the need for two or more concurrent tasks to make use of the same, limited processing capacity [Abernethy, 1988]. Typically, this interference manifests as diminished performance on one or both tasks [Woollacott and Shumway-Cook, 2002]. Dual task paradigms using either a cognitive [Brown and Marsden, 1991; Morris et al., 2000]] or motor [Bond and Morris, 2000; Canning, 2005; Rochester et al., 2004] concurrent task result in a deficit of performance on a primary motor task among non-medicated PD patients. It is possible that the exacerbated movement deficits that emerged for non-medicated PD patients in the high context condition reflect the result of attentional interference between the heightened perceptual processing of challenging context and the increased attention generally used by PD to

implicitly cue and control movement [Canning, 2005; Morris et al., 2000]. Support for this notion comes from previous work from our laboratory, confirming that attentional strategies for motor performance changed in threatening environmental contexts, requiring more information processing resources than in the low threat condition [Gage et al., 2003]. Our current work is directed at identifying interventions and attentional strategies that can decrease attentional interference among PD patients.

Pharamacotherapeutic effects

Medicated PD patients exhibited improvements in the magnitude and timing of reach arm and whole body kinematics for the reach and handle phases. The positive effect of levodopa medication on movement kinematics has been previously identified for walking and reaching tasks [Blin et al., 1991; Castiello et al., 2000; Doan et al., 2006; Ferrarin et al., 2004; Negrotti et al., 2004]. However, despite medicated improvements in movement kinematics, dopa-resistant aspects of movement have been observed, including disrupted postural kinetics [Horak, Frank, and Nutt, 1996] and multi-joint segment movements [Melvin et al., 2005; Negrotti et al., 2004]. In the current study, medicated PD patients still produced smaller peak wrist velocities for the reach and transport phases, compared to neurologically normal older adults. Differential effects of levodopa medication in PD, specifically improvements on movement kinematics and deficits in movement kinetics and postural configurations, suggest separate neural processing of these functions [Frank, Horak, and Nutt, 2000; Melvin et al., 2005].

Limitations

Relatively few trials per subject-condition combination were performed in this study. While this under-sampling may fail to completely capture the variability of the standing reach task among PD patients, previous studies have found a general kinematic constancy in various targeted reaching tasks [Marteniuk et al., 1987, Whishaw et al., 2002]. In this study, trial number was intentionally limited to minimize any repeated trial effects on response to threat, which have been evidenced as a partial extinction of compensatory standing postures under threatened conditions [Adkin et al., 2000].

3.6 CONCLUSIONS

Our findings show that the control and execution of standing reach among PD patients is functional in a challenging context, though some deficits were observed. Specifically, non-medicated PD patients exhibited a longer duration of hand acceleration during the reach, in combination with a smaller and slower preparatory (posterior) shift of centre of pressure and a later peak anterior centre of mass velocity. We suggest that attentional interference between the increased processing required for threatening context and the attention used by PD patients to access neural representations of movements may be the cause of increased dysfunction in the co-ordination of posture and reach among PD patients. This hypothesis presents a basis for further critical study, comparing quantitative measures of parkinsonian movement deficit and established PD symptom assessment measures (e.g. UPDRS) as correlates of motor performance in tasks constrained by ecologically-valid contextual levels identified for activities of daily living. Threatening contexts lead to both increased fear of and increased frequency of falls among PD patients [Adkin et al., 2003; Stolze et al., 2004]. Both of these factors can contribute to a long-term

downward activity spiral, resulting in increased anxiety and depression, and a decreased quality of life [Ashburn et al., 2001]. Developing therapeutic strategies that allow patients to identify and control attentional interference may help maintain a functional level of activity and improved quality of life among Parkinson's disease patients.

4.0 OBSTACLE AVOIDANCE IN PARKINSON'S DISEASE PATIENTS IS LIMITED BY THREATENING CONTEXT

4.1 ABSTRACT

We examined whether people with Parkinson's disease (PD) have difficulty stepping over a gait obstruction in a high threat context (gait path and obstacle raised above floor level) compared to a low threat context (gait path and obstacle at floor level). 10 PD patients were tested in a non-medicated and medicated state, along with 10 age-matched control subjects. Participants completed 18 obstructed gait trials, walking 5.0 m at a self-selected speed while attempting to cross an obstacle 0.15 m in height that was placed near the centre-point of the walkway. Kinematic parameters relevant to obstacle negotiation were measured through three-dimensional motion analysis and three expert judges independently recorded obstacle crossing strategies and errors from trial videos. Results indicated that PD patients in both medication states made more obstacle contacts (errors) than neurologically normal older adults in the high threat context. Successful crossings by PD patients in both threat conditions also exhibited deficits, with non-medicated PD groups making shorter preparatory and crossing steps, and using decreased crossing velocity of the lead foot. The findings from this study support a theory of cortical movement control among Parkinson's disease patients and provide indication that the motor improvements provided by current PD pharmacotherapy may be limited by contextual interference. In everyday contexts, these maladaptive movement patterns may be placing PD patients at an increased risk of obstacle contact, postural instability, and falling.

4.2 INTRODUCTION

Epidemiological investigation indicates that Parkinson's disease (PD) patients experience more falls than either neurologically normal adults or individuals with other neuropathologies [Stolze et al., 2004]. For patients with PD, fall occurrences and increased fear of falling are most frequent in situations with complex or threatening context, a finding that is reinforced by case histories and qualitative assessments of fall occurrences [Gray and Hildebrand, 2000; Macht and Ellgring, 1999; Strubel, Jacquot, Martin-Hyundai, 2001]. These reports suggest contact with an obstacle leading to tripping as a major cause of falls among PD [Stolze et al., 2004; Bloem et al., 2004] and among healthy elderly [Tinetti and Speechley, 1989]. In this study, we have adopted obstacle negotiation as an activity that is representative of everyday challenges for PD patients, and thus suitable for the investigation of context-specific movement disturbances [Czaja and Sharit, 2003; Morris, 2000; Teasdale and Stelmach, 1988]. This ecological relevance is supported by previous studies indicating that movement disturbances and motor blocks among PD patients are identified as resulting from constrained movement requirements [Alemida, Wishart, Lee, 2003; Fahn, 1995; Nieuwboer et al., 2001; Vaugoyeau et al., 2003] a task demand construct that would include obstacle crossing.

Specific task demands, such as the inherent characteristics of the obstacle to be crossed, as well as constraints imposed by the environment, contribute to situational context [Dunn, Brown, McGuigan, 1994]. In general, context provides a modulatory influence on motor performance, such that actions must be structured in agreement with context to be successful [Marteniuk et al., 1987]. Previous studies have shown that neurologically normal adults adopt conservative strategies for standing [Adkin et al., 2000], standing reaching [Kozak, Ashton-Miller, Alexander, 2003], walking [Brown et al., 2002; Marigold and Patla,

2002], and obstacle crossing [McKenzie and Brown, 2004] when concurrently challenged by a context that directly threatens stability, or that threatens increased consequence as a result of instability. In contrast, PD patients have exhibited decreased postural stability [Morris et al., 2000] and increased disturbance of gait [Hausdorff, Balash, Giladi, 2002; Rochester et al., 2004] when concurrently challenged with a cognitive or motor demand. It is probable that threatening context may exacerbate any obstacle negotiation deficits that exist for PD patients, though this relationship has not been previously explored in non-medicated or medicated PD patients.

Pharmacological PD treatments are found to provide a reduction in parkinsonian symptoms [Mercuri and Bernardi, 2005; Vokaer, Abou-Azar, Zegers de Beyl, 2003] and an increased quality of life [Montgomery, 2005; Quittenbaum and Grahn, 3004; Schrag, Jahanshashi, Quinn, 2000]. Nevertheless, the specific sensitivity of parkinsonian movements to amelioration through dopamine replacement is not invariant [Blin et al., 1991; Melvin et al., 2005; Negrotti, Secchi, Gentilucci, 2004; Saleniius et al., 2002]. Furthermore, the relative mobility improvements enabled by PD medication can still be compromised by task or environmental context [Doan et al., 2006; Schaafsma et al., 2003]. This compromise could lead to instability during standing and deterioration in gait performance, consequently increasing the risk of falls. This phenomenon has been well documented in previous studies [Ashburn et al., 2001; Bond and Morris, 2000]. Indeed, the potential for limitations of PD medication efficacy in a threatening context makes targeted rehabilitation strategies an elusive goal [Montgomery, 2004]. One solution to this difficulty is to identify specific PD movement deficits within naturalistic environmental contexts, so that context-targeted strategies and therapies can be developed [Gage and Storey, 2004].

The purpose of this study was to investigate changes in obstacle avoidance and obstacle crossing kinematics among medicated and non-medicated Parkinson's disease patients in response to task context. To this end, we had PD patients in medicated and non-medicated states step over a walking-surface obstacle in two contexts: at floor level, presumably a context providing little threat to posture; and on a raised platform, previously identified as sufficient to elicit movement pattern modification among healthy older adults [McKenzie and Brown, 2004]. The expectation was that non-medicated PD patients would exhibit movement deficits, but functional success, in crossing an obstacle while walking at floor level. Furthermore, we expected that dopamine replacement would improve the kinematics of obstacle crossing for PD patients in situations with limited threatening context. We further hypothesized that high threat context would have a stronger overall influence on obstacle crossing than dopamine replacement, resulting in similar, dysfunctional obstacle negotiation kinematics for medicated and non-medicated PD patients in the threatening context.

4.3 METHODS

4.3.1 PARTICIPANTS

Ten participants with idiopathic PD (PD; mean age: 69.7 ± 10.3 years) and ten age-matched controls (CTRL; mean age: 68.8 ± 8.4 years) served as subjects. All participants were informed on the nature of the study and provided written consent. The Human Research Ethics committee of the University of Lethbridge had previously approved all procedures in the study.

All PD patients were receiving dopaminergic and associated medication as PD management (Table 4.1), and each PD subject was tested OFF (>12 h removed from last oral drug dose) and ON (between 1h and 2 h following regular medication) pharmacological treatment in the same laboratory visit (same day). All patients were tested in the OFF then ON order for patient practicality and comfort. Quality of ON condition was confirmed both by patient self-report and qualified clinical assessment, and ON and OFF scores for each patient on the Unified Parkinson's Disease Rating Scale [Motor Subsection] (UPDRS-III: questions 18 through 31) are provided in Table 4.1.

4.3.2 APPARATUS

For all trials, participants were initially in a standing posture at the start of a 4.7 m long, 0.6 m wide walkway. Threatening context for gait was inferred from the potential result of postural instability in each condition, as established in previous studies of gait [Brown et al., 2002] and obstacle crossing [McKenzie and Brown, 2004]. In the highly threatening condition (HIGH), this walkway was solidly supported 0.7 m above the ground and the force platforms were raised on a hydraulic lift (Pentalift, Guelph ON) such that the

horizontal surfaces of the walkway and the platforms were at equal height. In the low threat condition (LOW), the walkway was outlined on the laboratory floor with continuous tape borders. A ramp (0.9 m length, 5.5 ° angle of declination) was positioned at the start of the walkway, flush with the anterior edge of the force platforms, to allow for gradual vertical displacement from force platform height (0.09 m) to LOW walkway height (0.0 m). Gait initiation parameters measured on force plate transducers were explored in a separate study [Kurek et al., 2005]. Figure 4.1 provides a visual comparison of the HIGH and LOW threat walkway configurations. The obstacle was a small rigid foam block (0.15 m high, 0.60m wide (perpendicular to gait path), 0.15 m long). The height and width of the obstacle were approximately equal in height to a North American concrete parking curb [Alberta Transportation and Utilities Document CB-6, 1998].

All subjects wore a whole body safety harness for all trials. During trials in the HIGH threat condition, the harness was tethered to a rolling coupling on an overhead track. Subjects also wore vision-occluding goggles (PLATO, Translucent Technoliges, Toronto, ON) that initially concealed the presence or absence of the gait obstacle, to control for pre-planning as an adaptation in obstacle negotiation strategy. During practice trials, all participants were familarised with the preparatory stimulus (opening of the goggles), followed by the imperative stimulus (audio GO signal). In experimental trials, the goggles were initially set to closed, occluding vision. Once the investigator had either placed the obstacle (for obstructed trials) or feigned placing the obstacle (non-obstructed trials), a second investigator informed the participant that a new trial was set to begin. At a random interval following this instruction, the goggles were opened using the data collection computer. The audio GO signal sounded 0 ms, 500 ms, or 1000 ms after goggles opening, with all subjects receiving the same number of trials at each latency (n=3) in the same

random order. Variable audio GO latencies were included as a manipulation of pre-planning and gait initiation, as part of a larger study.

4.3.3 PROCEDURE

Subjects walked at a self-selected speed along the walkway in each of the HIGH and LOW imposed threat conditions, performing a block of 18 trials in each condition (36 trials total). Order of threat condition (LOW/HIGH versus HIGH/LOW) was counter-balanced between subjects. Obstacle trials were further randomized in each threat condition, such that 9 of 18 trials in each threat condition involved obstacle negotiation and nine were control trials, without obstacle. All subjects performed two practice trials with obstacle prior to the start of each threat condition. For all experimental trials, the primary investigator placed the obstacle or feigned placing the obstacle after the participant's vision-occlusion goggles were closed, such that any sensory stimuli related to obstacle placement would not be consistently congruent. Obstacle position was chosen at a point on the walkway greater than three strides from the point of gait initiation, as determined from practice trials. Participants kept their arms loosely crossed in front of the body for all trials, to minimize inadvertent disruption of motion capture.

4.3.4 DATA COLLECTION AND MEASURES OF INTEREST

Participants were outfitted with passive, lightweight infrared-reflective markers, temporarily affixed to either skin surface or overlying clothing at the following anatomical locations: bilaterally, at the most anterior end of the shoe (toe), the lateral malleolus, the posterior end of the shoe (heel), the lateral epicondyle of the femur, the greater trochanter, the ulnar styloid, the lateral epicondyle of the humerus, and the acrominon process; and

unilaterally at the sternal notch and at the centre of the forehead at the browline. A single marker was also placed in the center of one anteroposterior face of the obstacle. Positional data were collected using a 6-camera infrared motion analysis data collection system (Peak Motus 2000, Peak Performance Technologies, Englewood, CO), with a collection frequency of 120 Hz. Digital video recordings of each trial were made in the sagittal and frontal planes, for qualitative scoring of obstacle crossing success and strategy. Kinetic data for gait initiation were also captured through the Peak analog-to-digital interface, at a rate of 600 Hz.

Behavioural coding of obstacle crossing was completed from sagittal plane video separately by three judges. Frontal plane video was used to confirm responses as required. Judges coded number of pre-obstacle gait cycles, obstacle contact frequency, and obstacle crossing step length. Crossing step length was coded as shortened, lengthened, or same, based on subjective comparison of the steps prior to obstacle crossing. Specifically, a crossing step was coded as 'shortened' if the preparatory to crossing step was shorter than previous steps, or 'lengthened' if the crossing step was longer than previous steps [McKenzie and Brown, 2004]. These qualitative assessments, to our understanding, provide the first experimental characterization of obstacle crossing for PD patients.

Kinematic and kinetic data were processed using custom written programming (MATLAB, The Mathworks, Natick, MA, USA). Raw displacement data were visually inspected and interpolated as required then filtered using a 4^{th} order Butterworth low pass digital filter with a cut-off frequency of 10 Hz. Velocity data were calculated through differentiation by finite differences. Pertinent kinematic measures assessing obstacle negotiation in both the lead limb (first limb across obstacle) and the trail limb (second limb across obstacle) are fully described in Table 4.2, and illustrated in Figure 4.2.

4.3.5 STATISTICAL ANALYSIS

For the video analysis data, intra-class correlations were performed to ensure adequate agreement between judges. Subsequently, event frequency counts were averaged across judges, and separate χ^2 analyses were used to examine GROUP and THREAT effects in the video analysis data. Three separate comparisons were conducted on 5 kinematic measures, using GROUP (PD OFF vs CTRL; PD OFF vs. PD ON; PD ON vs. CTRL) x THREAT (LOW vs. HIGH) ANOVAs with a Bonferroni-corrected level of significance of $\alpha = .017$ for all comparisons. Post-hoc planned comparisons were made where significant differences existed.

Table 4.1. Clinical information of Parkinson's disease patient group.

Patient	Age (yr)	*Disease* Duration	Sex	UPDRS – III*		*Symptoms (OFF)*			*Medication*
				ON	OFF	Bradykinesia	Action Tremor	Resting Tremor	
1	80	15	M	28	45	Y	Y	Y	Levodopa Levodopa (sustained release)
2	69	4	M	18	40	Y	Y	Y	Levodopa
3	76	8	M	6	24	Y	Y	N	Levodopa Levodopa (sustained release) Pramipexole
4	75	1	M	6	17	Y	N	Y	Levodopa
5	81	7	M	16	33	Y	Y	Y	Levodopa Pramipexole
6	54	10	F	5	14	Y	N	Y	Levodopa Pergolide mesylate Amantadine
7	54	22	F	21	43	Y	Y	Y	Levodopa Pramipexole
8	80	2	F	38	54	Y	Y	Y	Levodopa Amantadine
9	63	2	F	22	58	Y	Y	Y	Levodopa
10	65	11	F	21	34	Y	Y	N	Levodopa Pramipexole
Mean (SD)	69.7 (10.3)	8.2 (6.6)		18.1 (10.5)	36.2 (14.7)				

Unified Parkinson's Disease Rating Scale – III (motor component – questions 18-31), with higher scores indicative of greater motor deficit.

Table 4.2. Measures of interest in obstacle negotiation, with variable name and description.

Measure		Variable name	Description of measure
		D_{PRE}	Horizontal distance from rear edge of obstacle to trail toe off (pre-crossing)
Crossing clearance	(m)	D_{VERT}	Vertical distance between top of obstacle to lead toe (crossing)
		D_{POST}	Horizontal distance from lead heel contact to front edge of obstacle (post-crossing)
Crossing length	(m)	CL	Mean length of lead and swing crossing steps
Crossing velocity	(m/s)	CV_{COM}	Horizontal velocity of whole body centre of mass during obstacle crossing step

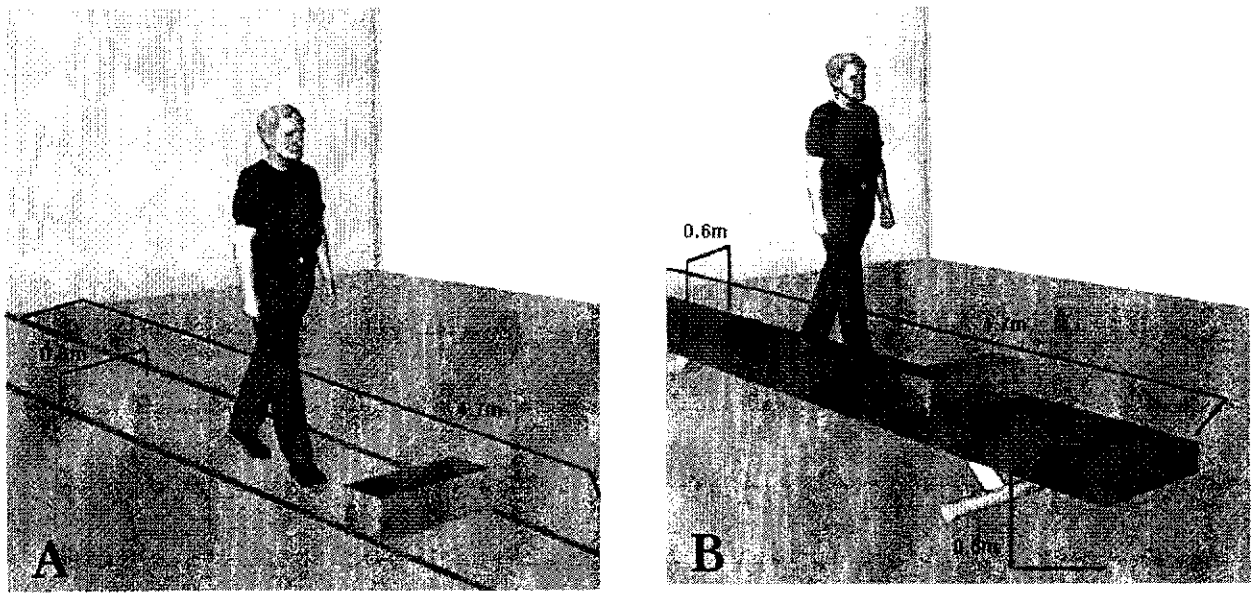


Figure 4.1. Conditions of environmental threat for gait trials.
(A) LOW postural threat, (B) HIGH postural threat. Subjects wore a full-body safety harness in all trials. In HIGH threat trials, the harness was attached to a rolling coupling on an overhead track (not shown).

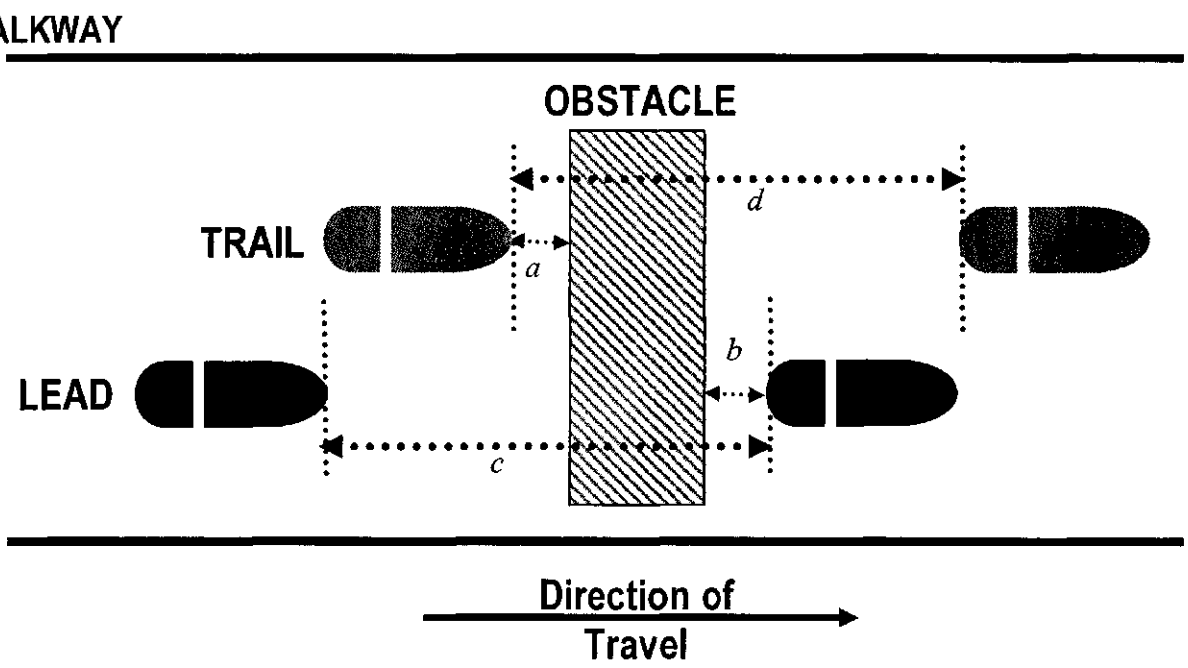


Figure 4.2. **Top-down view illustration of obstacle crossing, with horizontal spatial measures of interest.**

Obstacle is marked in diagonal lines, while lead and trail feet are indicated by black and gray ovals respectively. Measures shown are: (a) trail foot pre-crossing clearance [D_{PRE}]; (b) lead foot post-crossing clearance [D_{POST}]; (c) lead foot crossing step length [CR_{LEAD}]; and (d) trail foot crossing step length [CR_{TRAIL}]. Not shown is horizontal centre of mass crossing velocity [CV_{COM}].

4.4 RESULTS

4.4.1 OBSTACLE CROSSING

4.4.1.1 VIDEO ANALYSIS

Intra-class correlation revealed high consistency between judges (ICC(1,3) = -37.59, p = .9744), and video coding scores were subsequently collapsed across judges. PD OFF had a higher than expected frequency of obstacle contacts in the HIGH condition; in total, 21.3% of trials, compared to 9.9% observed in LOW (χ^2(1,1, N=162) = 4.05, p<05). PD ON also made more frequent obstacle contact in HIGH (observed in 18.3% of trials) than in LOW (5.9% of trials) (χ^2(1,1, N=156) = 5.49, p<05). Conversely, CTRL had fewer than expected obstacle contacts in the both the HIGH (8.5% observed) and LOW (6.3% observed) threat conditions, though these differences did not reach significance (χ^2(1,1, N=180) = 0.32, p>.05). Obstacle contact frequencies are presented in Figure 4.3.

Chi-square tests also indicated that obstacle crossing preparation step length differed between groups and heights. PD ON made frequent use of a LONG strategy in the LOW threat condition (23.7% of trials), but significantly reduced this frequency in the HIGH threat condition (2.8% of trials), replacing step lengthening with a step shortening strategy (26.8% of trials) in HIGH (χ^2(1,1, N=156) = 16.21, p<05). PD OFF made more frequent use of step shortening strategies (SHORT) in both LOW (27.2 % of trials) and HIGH (35.4% of trials) conditions, though the observed frequencies of preparation step lengths did not differ with threat (χ^2(1,1, N=162) = 1.41, p>.05). Conversely, CTRL participants favoured preparatory steps of SAME length (74.0% and 77.0% of LOW and HIGH trials, respectively), with no differences resulting from the threat manipulation. Figure 4.4 provides

full comparison of obstacle crossing step length for all conditions, as a percentage of completed trials.

4.4.1.2 KINEMATIC ANALYSIS

All kinematic data and identification of significant differences are presented in Table 4.3.

4.4.1.3 PD OFF VERSUS CTRL

PD OFF were significantly slowed in obstacle crossing velocity compared to CTRL (CV_{COM}; $F(1, 18) = 11.317$, $p = .003$), regardless of threat condition. In addition, both PD OFF and CTRL reduced CV_{COM} ($F(1, 18) = 14.481$, $p = .001$) while negotiating the obstacle in the HIGH threat condition. PD OFF used a smaller pre-crossing clearance margin (D_{PRE}; $F(1, 18) = 10.941$, $p = .004$) than CTRL, combined with a smaller crossing step (CL; $F(1, 18) = 10.993$, $p = .004$) in both testing conditions. PD OFF and CTRL both tended to reduce D_{PRE} in the HIGH threat condition ($F(1, 18) = 3.897$, $p = .064$). In contrast, CTRL increased post-obstacle horizontal clearance of the lead heel in the HIGH threat condition (D_{POST}; 33 ± 8 cm, as compared to 23 ± 5 cm in LOW), where PD OFF produced horizontal heel clearance values of similar magnitude in either threat condition (15 ± 2 cm in LOW, 14 ± 2 cm in HIGH). Both groups slightly decreased vertical obstacle clearance in the HIGH threat condition.

4.4.1.4 PD ON VERSUS CTRL

PD ON and CTRL used similar obstacle crossing velocities (CV_{COM}; $F(1, 18) = 5.230$, $p = .035$) in crossing the obstacle, and both groups decreased crossing velocity in the HIGH threat condition ($F(1, 18) = 25.988$, $p = .000$). PD ON used smaller crossing steps

than CTRL (CL; $F(1, 18) = 45.247$, $p = .000$), but both groups decreased crossing step length in the HIGH threat condition ($F(1, 18) = 12.671$, $p = .002$). In contrast, PD ON used a smaller pre-obstacle trail limb toe horizontal clearance than CTRL in both threat conditions (D_{PRE}; $F(1, 18) = 9.510$, $p = .006$). Post-obstacle lead heel horizontal clearance approached a GROUP X THREAT interaction ($F(1, 18) = 5.130$, $p = .036$), with PD ON leaving smaller lead heel clearance in HIGH threat (11 ± 2 cm, compared to 16 ± 2 cm in LOW), while CTRL increased lead heel clearance in HIGH obstacle crossing (33 ± 8 cm, compared to 23 ± 5 cm in LOW).

4.4.1.5 PD OFF VERSUS PD ON

PD OFF and PD ON used significantly slower whole body CoM obstacle crossing velocity (CV_{COM}; $F(1, 9) = 10.252$, $p = .010$) in the HIGH threat condition. PD patients also used a smaller crossing step in the HIGH threat condition (CL; $F(1, 9) = 17.663$, $p = .002$), with PD ON using smaller crossing steps than PD OFF in both conditions ($F(1, 9) = 30.111$, $p = .000$). Both groups exhibited non-significant decreases in pre-crossing horizontal trail toe clearance, mid-crossing vertical lead toe clearance, and post-crossing horizontal lead heel clearance in the HIGH threat condition.

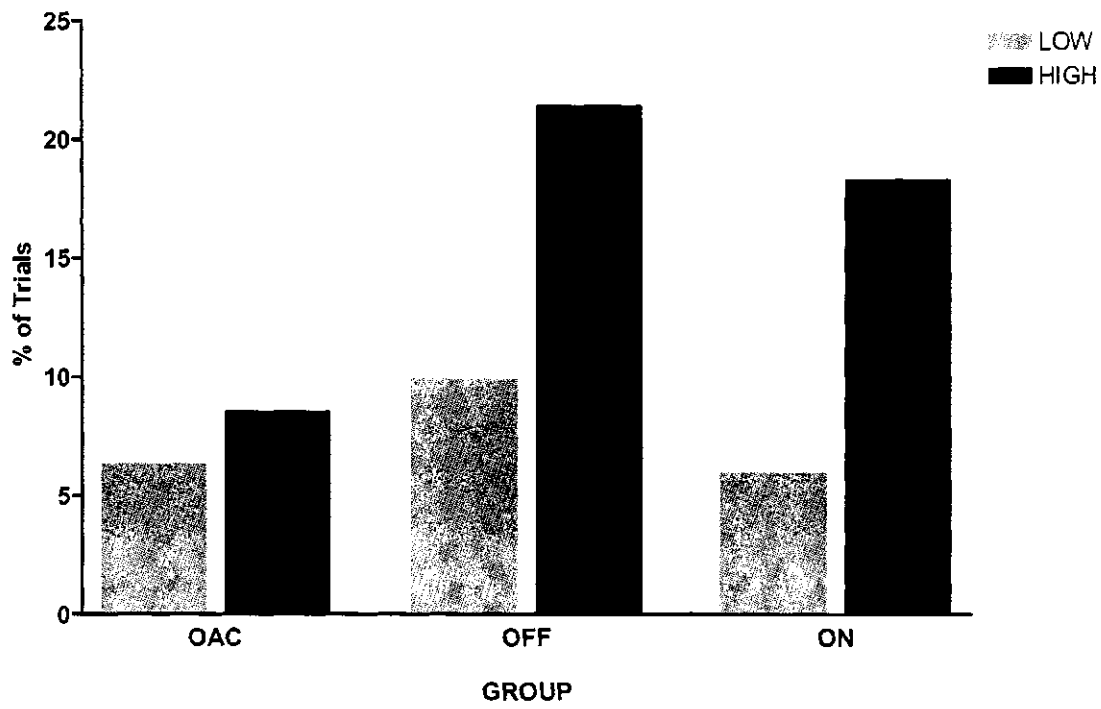


Figure 4.3. Obstacle negotiation error rates for participants.
Multiple gait trials from neurologically normal older adults (OAC; n = 10), non-medicated Parkinson's disease patients (OFF; n = 10), and the same patients with normal medication levels restored (ON; n = 10). In both the LOW and HIGH environmental threat conditions, the obstacle dimensions were identical.

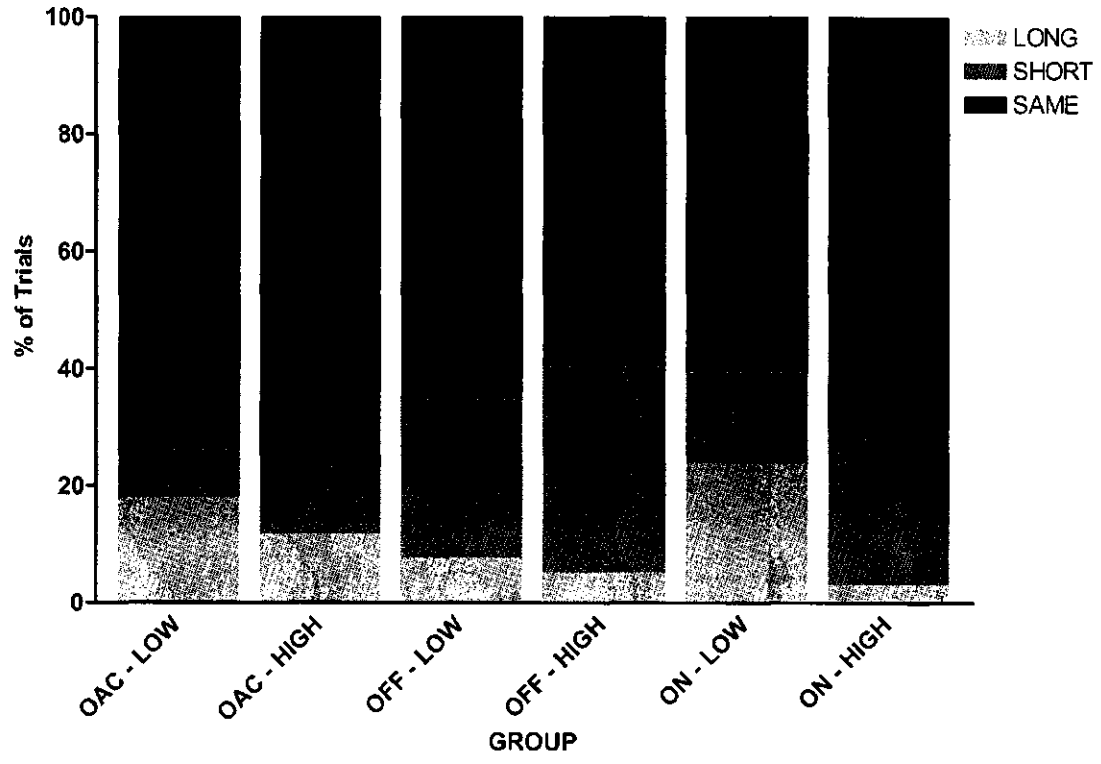


Figure 4.4. Distribution of observed step crossing behaviours.
Frequency counts were made for step lengthening (LONG), step shortening (SHORT), and same step length (SAME) strategies for successful trials among all groups.

Table 4.3. Summary of kinematics (mean [SEM]) for obstacle negotiation.

MEASURE	CTRL		PD OFF		PD ON		G	T	G X T
	LOW	HIGH	LOW	HIGH	LOW	HIGH			
D_{PRE} (m)	0.57 [0.05]	0.44 [0.06]	0.36 [0.05]	0.32 [0.04]	0.35 [0.07]	0.27 [0.06]	A, B		
D_{VERT} (m)	0.21 [0.05]	0.19 [0.01]	0.19 [0.05]	0.15 [0.02]	0.17 [0.03]	0.16 [0.01]			
D_{POST} (m)	0.23 [0.05]	0.33 [0.08]	0.15 [0.02]	0.14 [0.02]	0.16 [0.02]	0.11 [0.02]			
CL (m)	0.87 [0.06]	0.81 [0.04]	0.69 [0.02]	0.66 [0.04]	0.57 [0.03]	0.40 [0.03]	A, B, C	B, C	
CV_{COM} (m/s)	0.68 [0.05]	0.54 [0.03]	0.49 [0.04]	0.39 [0.03]	0.52 [0.06]	0.40 [0.05]	A	A, B, C	

A - CTRL/OFF, $p < .01$
B - CTRL/ON, $p < .01$
C - OFF/ON, $p < .01$

4.5 DISCUSSION

The purpose of this study was to investigate how medicated and non-medicated PD patients adapted motor output in a threatening situational context. Parkinson's patients were asked to negotiate a walking surface-level obstacle during gait trials in both non-threatening and threatening environmental context. The results agreed with our hypotheses, indicating that obstacle crossing errors were aggravated among PD patients during threatened context trials. In addition, the level of motor improvement potentiated among PD patients through conventional pharmacotherapy was not maintained in the threatening environmental context. We suggest that motor improvements among medicated PD patients can be compromised by context, and postulate that the contextually-exacerbated deficits observed in both PD groups may be predicated by cognitive processes.

Previous studies have established that parkinsonian motor deficits are manifest in multiple aspects of gait, including initiation [Atchison et al., 1993; Halliday et al., 1998], steady-state gait parameters [Lim et al., 2005; Morris et al., 2005; Schubert et al., 2005], turning [Stack, Jupp, Ashburn, 2004], stride variability and falls [Hausdorff, Balash, Giladi, 2002; Nieuwbower et al., 2001; Schaafsma et al., 2003; Bartels et al., 2003], and termination [Bishop et al., 2003]. However, no previous studies could be found investigating parkinsonian deficits with on-ground obstacle negotiation during gait. In that respect, we feel our work provides a valuable contribution to understanding the functional result and kinematics adopted in an everyday scenario that is responsible for many falls among PD patients [Stolze et al., 2004]. Specifically, we suggest that the deficits in obstacle avoidance and negotiation kinematics uniquely observed among PD patients in the threatening environmental context may be the result of the psychological constraint induced when attention is directed toward a threatening environment [Gage et al., 2003; McKenzie and

Brown, 2004]. Weerdesteyn and colleagues [2003] used a dual task paradigm to induce a similar obstacle avoidance negotiation deficit among neurologically-normal participants, but this study is the first, in our review, to investigate PD obstacle negotiation strategies, and the possible existence of attentional interference in obstacle avoidance for PD patients.

4.5.1 POTENTIAL CONTRIBUTING NEURAL MECHANISMS

The main finding of this study is that threatening environment appears to be particularly detrimental for PD patients. In neurologically normal adults, perception and classification of threat requires attentional resources, and increasing threat requires increasing resources [Koster et al., 2004]. For PD patients, the diversion of attentional resources to threatening context may lead to an attentional resource conflict, as previous studies have suggested that patients have adapted to use directed attention to initiate and control movement [Camicioli et al., 1998; Morris et al., 2000; Rochester et al., 2004]. The combination of attention to environment and attention to task may exceed available attentional capacity, especially among moderate to severe PD patients, who have been shown to have decreased executive function [Firnberger, Frith, Jahanshashi, 2005]. This attentional interference may lead to dysfunction in movement initiation, movement sequencing, or set switching [Brown and Marsden, 1991; Marsden, 1982; Woodward, Bub, Hunter, 2002]. It follows that a similar instance of attentional interference, resulting from high task demands during an activity of daily living, may result in a motor block or disequilibrium event for a PD patient. Additional work in our laboratory will be addressed at further investigating these events.

It is possible that the observed errors and kinematic changes in the HIGH threat condition are the result of arousal and anxiety induced by the threatening context. Previous

studies, from our laboratory [Brown, Polych, Doan, in press; Gage et al., 2003; McKenzie and Brown, 2004] and others [Adkin et al., 2000; Carpenter et al., 2001], have shown that anxiety-provoking contexts can lead to kinematic changes in previously stable behavioural patterns. Furthermore, previous research has shown that Parkinson's disease patients exhibit higher levels of anxiety [Walsh and Bennett, 2001] and a heightened fear of falling in threatening contexts [Adkin et al., 2003]. While it is possible that the deficits observed among PD patients completing threatened trials in this study are a partial result of anxiety, we did not observe changes in success rates between the LOW and HIGH threat conditions for neurologically normal adults. This finding contradicts previous research that has identified threat-induced modifications to stable behaviours among neurologically-normal participants, and suggests that the threat manipulation imposed in this study was not sufficient to invoke performance-inhibiting anxiety, at least among non-Parkinson participants. It is possible that both attentional interference and increased anxiety contribute to the deficits observed among PD patients in the threatening context, and that some portion of the diverted attention is consumed by perceptions and emotions related to the contextual threat [Rochester et al., 2004]. Given this hypothetical detrimental combination, one possible suggestion is that the deficits in obstacle avoidance and negotiation kinematics uniquely observed among PD patients in the threatening context may be the result of interference that arises when attentional resources are directed toward the perception and interpretation of a relevant and challenging environment.

4.5.2 CURRENT PHARMACOLOGICAL MANAGEMENT OF PARKINSON'S DISEASE

Our results show that current pharmacological treatment of PD, namely through exogenous dopamine replacement, allows PD patients access to more conventional obstacle crossing strategies, both in terms of obstacle avoidance and crossing step kinematics. However, these improvements failed to reach levels equal to control participants. Furthermore, threatening environment appeared to have the capacity to limit medication benefits, reducing obstacle crossing kinematics and obstacle crossing success rates for medicated PD patients to similar levels as non-medicated PD patients. Previous work has indicated that temporal aspects of gait (e.g., stride cadence, stride event durations) are less sensitive to dopamine replacement [Blin et al., 1991; Morris et al., 1994]. Given the critical importance of gait cadence and response timing in obstacle avoidance [Chen et al., 1994], it follows that this activity would still be deficit for medicated PD patients, if cadence and timing show only moderate improvements with medication. It is possible that the increased deficits observed for medicated PD in the threatening environment reflect a situational dysfunction in the non-dopaminergic neural processes at work in this environmental context. We believe that executive attentional resources are the non-dopaminergic assets that are being overloaded by concurrent attentional demands from perceived environmental threat and directed focus on task control. Other researchers have previously observed executive attentional dysfunction among PD patients, both in motor [Hocherman, Moont, Schwartz, 2004] and cognitive [Woodward, Bub, Hunter, 2002] tasks.

4.6 CONCLUSION

Our findings show that obstacle negotiation among PD patients is compromised in a threatening context. Specifically, PD patients exhibited more obstacle contacts, decreased obstacle crossing clearance, and decreased crossing velocity of the lead foot when walking on a raised platform. Furthermore, conventional PD pharmacotherapy failed to reduce obstacle contacts or increase obstacle clearance in the threatening context. We suggest that attentional interference between the increased processing required for perceived threatening context and the directed attention used by PD patients to access neural representations of movements may be the cause of increased dysfunction in obstacle negotiation among PD patients. Developing therapeutic strategies that incorporate and investigate real-world movements and activities (e.g., falls diaries, naturalistic tasks) will allow patients and practitioners to identify specific situations where task and context combine to increase attentional interference and exacerbate movement deficits. In turn, these therapies can help patients anticipate and manage threatening environmental contexts, minimizing motor dysfunction and improving quality of life among Parkinson's disease patients.

5.0 DISCUSSION

To summarize the main findings of this thesis:

5.0.1 PD patients exhibit spatial and temporal movement deficits during the completion of stable tasks with limited contextual challenge, but complete said tasks with similar relative sequencing and success rates as neurologically normal older adults.

5.0.2 PD patients exhibit exacerbated spatial and temporal movement deficits during the completion of stable tasks with increased contextual challenge. These deficits extend to the relative spatiotemporal structuring of movement events, the ongoing corrective control of focal movements, and the ultimate success rate of functional tasks. These deficits do not appear to be an alternative functional modification (i.e. permitting successful completion of task) or an intentional protectionist response (i.e. avoiding personal or target disequilibrium). Rather, the deficits suggest an attentional resource sharing conflict between attention dedicated to the selection, initiation, and control of motor output (a proposed adaptive response resulting from PD that may enable both unstable and stable tasks) and attention diverted to task or environmental context, a contextual processing bias that may be higher among PD patients.

5.0.3 PD medication can reduce spatial and temporal movement deficits during stable tasks with limited contextual challenge, but pharamcotherapeutic improvements can be superceded by increased contextual challenge.

The following subsections will discuss the pertinence of these findings to the understanding of context and sequence deficits in the PD form of BG dysfunction.

5.1 PD MOTOR DEFICITS IN CONTEXT

5.1.1 TASK-INSTRINSIC CHALLENGE

While bradykinesia is a common symptom of moderate to severe PD patients [Uitti et al., 2005], the bradykinesia observed among the PD participants in this study was more severe when the intended movement was being made towards a target with increased context, or threat. This result was manifest in both manipulations of task-intrinsic context in this study, as non-medicated PD patients were slower to initiate both a seated reach towards a high context (full) glass (as compared to the low context (empty) glass) and a series of steps towards an obstacle (as compared to a similar step path to no obstacle).

Furthermore, this context-induced latency was also found to delay motor excitation in the increased task-instrinsic challenge condition, indicating that the deficit was not primarily a problem of appropriately scaling muscle force magnitude after the arrival of a 'normal' activation signal, but rather a disruption in the fundamental neural signal to initiate muscle force production. Similar slowed muscle depolarization has been observed in postural tasks [Dick et al., 1986; Frank, Horak, Nutt, 2000].

The most prevalent evidence of a similar contextual initiation deficit among PD patients in everyday tasks comes from investigations of PD motor blocks, or 'freezing'. Motor blocks of movement initiation are common among PD patients at either advanced disease duration or clinical stage [Giladi et al., 1992]. Motor blocks are also exacerbated by

pharmacotherapy fluctuations, adding to their unpredictability and increasing their association with falls and injury, lost independence, and decreased quality of life among PD patients.

5.1.2 TASK-EXTRINSIC CHALLENGE

Increases in task-extrinsic contextual challenge, specifically the increase of postural threat and injurious consequences that could follow an episode of postural disequilibrium, also induced increased bradykinesia, along with subsequent decreases in rate of task success. Again, this was true in both task-extrinsic context paradigms, specifically the standing reach to a full glass with a horizontal gap between participant and target and obstacle crossing during gait trials on a raised platform.

These task-extrinsic context paradigms were chosen with similar rationale as the task-intrinsic manipulations – existence of an ecological parallel, anecdotal and/or experimental evidence of PD deficits in the ecological parallel, and a foundation of quantified movement analysis for neurologically-normal older adults in a version of the experimental paradigms. Of these developmental criteria, the ecological parallel and evidence of PD deficits were of prime importance. Contextual motor disturbances among PD patients often result in falls, with more than 60% of PD patients falling one or more times per year [Stolze et al., 2004]. The direct results of falls, specifically injury and health care cost, combined with the secondary results of falls, which include decreased independence, decreased activity, and increased depression, may be major contributors to the increased depression and decreased quality of life reported by clinically moderate to

severe PD patients [Chapuis et al., 2005].

5.2 PD MOTOR DEFICITS IN SEQUENCE

5.2.1 TASK-INSTRINSIC CHALLENGE

Task-intrinsic contextual challenge was also found to induce movement structure and sequencing deficits among non-medicated PD patients. For seated reaches, non-medicated PD patients were observed to use an axially-segmented reach profile in the threatening task context, a result previously observed by Alberts et al. [2000] for skilled reaches to non-ecological targets among PD patients. This uniaxial approach may represent a disco-ordination of motor control and a compromise to the typically invariant spatial path of reaching [Haggard and Richardson, 1996]. Alberts et al. [2000] have previously suggested that movements with increased task performance requirements (either speed or accuracy) were susceptible to this axial disc-ordination, due to the challenge of sequenced movement parameterization. The reduction of these unaxial reach constructs following dopaminergic treatment has been previously reported for a non-ecological reaching task [Castiello et al., 2000], a finding which is supported by the current study.

Closer examination of reaching paths revealed that non-medicated PD patients used more corrective submovements during the threatened reach to control movement trajectory, as compared to either reaches in the low context conditions or non-neuropathological participants reaching in either context condition. These submovements were distinct from tremor, and again, indicate an on-going attention to and control of movement sequencing not observed among neurologically normal older adults, or among reaches to low context targets. Furthermore, non-medicated PD patients used an unique, delayed relative timing of

peak acceleration in both reach and transport of the full drinking glass, a sequencing approach not observed among neurologically normal older adults, and partially ameliorated among medicated PD patients. The situational sequencing deficits evidenced among PD patients have the potential to be as disruptive to daily activity as the over-riding cardinal symptoms of PD. For example, inappropriate sequencing of a single element in a multi-element sequence can lead to endpoint errors, either in task accuracy [Rand et al., 2002] or margin of safety [Frank, Horak, & Nutt, 2000].

5.2.2 TASK-EXTRINSIC CHALLENGE

As previously established, a strict biomechanical interpretation of task-extrinsic contextual response would suggest that no changes in movement pattern should be observed, as no changes had been made to the physical constraints specific to successful completion of the task between the two contextual conditions. Despite this potential for redundancy between the motor behaviours that would successfully meet the goal in each threat condition, quantitative and qualitative differences were observed for each group. For PD patients, many of these sequencing modifications in the threatening context movements did not result in safer or more successful movements. For example, PD patients were observed to delay peak velocity of effector endpoint during reaches to the full glass target in the standing position with the compensatory step platform removed. This context strategy change was accompanied by a late peak CoM velocity and larger CoP translation. This pattern of motor response produces a strategy with high potential for disequilibrium.

A similar threat response was observed in the threatened obstacle crossing, where PD patients used smaller post-obstacle clearance and obstacle crossing CoM velocity in the high threat condition, leading to an increased frequency of obstacle contacts among both PD

groups. Longitudinal studies have indicated that obstacle contacts in true ecological tasks are responsible for many of the falls experienced by PD patients [Ashburn et al., 2001].

In both task-extrinsic paradigms from this study, successful completion of the low threat task indicates that the appropriate movement response can be produced by PD patients. Disrupted or unsuccessful completion of the high threat task indicates that some aspect of increased task threat is leading to an inappropriate adaptation or execution of that functional movement response. In combination, these results suggest that functional motor mechanisms persist among PD patients, and further suggest that rehabilitative strategies that tap these mechanisms while limiting interference from task and/or environmental context may be helpful in maintaining independent activity for PD patients.

5.3 PD MOTOR DEFICITS IN MEDICATED STATE

Our results indicate that serial dopaminergic replacement, through oral dose of synthetic dopamine, was able to restore some biomechanical aspects of everyday movements for PD patients. This response can be viewed as a partial re-automatization, as per Fattaposta and colleagues [2002], wherein a 'smoothness' is restored to movements. This smoothness was evidenced in decreased duration of initiation motor blocks in seated and standing reaching, improved relative sequencing of wrist movement parameters, and improved mean movement velocity for reaches. Interestingly, medication appeared to provide less functional benefit for actions of the lower-limb, as evidenced by persistent deficits in obstacle clearance parameters among medicated PD patients. This deficit may reflect a proximal-to-distal degradation of motor performance among PD patients, a result which has been previously observed for skilled reaching tasks [Melvin et al., 2005; Whishaw et al., 2002].

Despite these variable improvements, context continued to oppose positive movement consequences among medicated PD patients. Specifically, we observed medicated PD patients making as many obstacle contact errors as non-medicated PD patients in a threatening context. Medicated PD patients also used more hip flexion later in the anterior movement to reach and grasp the glass in the posturally-threatening context, though this difference did not reach significance. It has been suggested that the persistence of deficits in segment positional control among medicated PD patients may reflect a separate neural processing stream that is primarily non-dopaminergic [Frank et al., 2000; Melvin et al., 2005]. Furthermore, the contextual exacerbation of the motor deficits observed among medicated PD patients in this study suggests that these non-dopaminergic resources are at an executive functional level, such that they can be limited by a concurrent cognitive demand; specifically, neural resources concurrently dedicated to interpreting challenging context.

Regardless of context level, medicated PD patients were also observed to exhibit persistent deficits in peak limb movement kinematics for reaching tasks, as compared to neurologically-normal older adults. These persistent deficits may reflect a decreased magnitude of muscle activation, a result which has been previously established [Dick et al., 1986].

5.4 PD MOTOR DEFICITS AND ECOLOGICAL TASKS

For Parkinson's disease (PD) patients, motor deficits are manifest in many activities of daily living. Anecdotal examples of these deficits have been documented in various everyday situations, such as walking in crowded public spaces or crossing the street; however, a specific cause-effect relationship between task situation and motor deficit is not

known [Macht and Ellgring, 1999]. Fahn [1995] suggests that the reason for deficient movement expression in PD patients can be visual and/or cognitive input regarding an impending challenge or constraint to movement. It is well-established from the experimental setting that explicit constraints to movement influence motor expression among PD patients. For example, Sanes [1985] associated PD movement deficit to task demands for targeted movements with the upper extremity, showing that spatial constraints significantly affected the kinematics of PD motor expression at higher accuracy levels. Rand and colleagues [2000] have also demonstrated that an endpoint accuracy constraint on an upper limb aiming movement causes prolonged movement duration, especially in the deceleration phase, as well as increased corrective movement control during task execution. In another novel experimental task, Weiss et al. [1996] found that endpoint accuracy constraints in an arm flexion task led to prolonged movement times and decreased arm velocities in PD.

While the laboratory tasks defined above help to elucidate the magnitude and scope of motor deficits associated with Parkinson's disease, they may be elucidating specific task-performance relationships that are of oblique pertinence to the daily function, independence, and quality of life among Parkinson's disease patients. As previously suggested, laboratory tasks may exacerbate the nature and magnitude of PD deficits by including novel or artificial motor and cognitive challenges to task execution [Czaja & Sharit, 2003]. At a minimum, strict laboratory motor tasks typically fail to incorporate context as a critical parameter in the planning and production of movement [Dunn, Brown, and McGuigan, 1994]. On the contrary, bona fide functional tasks permit valuable understanding of motor performance within a realistic context. In addition, functional tasks provide ecologically-relevant opportunities for the representation of movement planning and expression as a function of

practical task constraints. However, the presentation and performance of functional tasks outside the laboratory setting is subject to high variability, with limited investigator control [Czaja & Sharit, 2003]. In addition, the real-world behaviours of participants under observation are often artificially modified in response to the very act of task observation, classically defined as the Hawthorne Effect and reliably reproduced in occupational, clinical, and ecological settings [Turnock & Gibson, 2001]. With these limitations in mind, the goal in the research was to combine the benefits of experimental research with the validity of real-world tasks [Dunn, Brown, & McGuigan, 1994] to investigate functional deficits and compensation in PD. To this end, laboratory tasks were designed that exhibited good face validity with real-world activities of daily living. In addition, non-ecological interference (i.e physical restrictions, effects of excessive fatigue, abundance of experimental investigators) in these tasks was limited wherever possible. Potential limitations to the ecological validity of these tasks will be discussed in the next section.

5.5 LIMITATIONS

One limitation on the research in this dissertation is the quasi-ecological status of the performance tasks. This constraint may be more pronounced among Parkinson's disease patients, given the hypotheses of this study Despite efforts to examine PD patient performance on ecologically valid tasks in this study, confounds internal and external to the task persist. The external confounds evolve from the nature of controlled experimental testing, specifically the introduction of measurement and safety to the study of human movement. Free and natural movement performance of all subjects was restricted, to some degree, by the skin surface attachments, peripheral electronic connections, and main electronic tether necessary for data collection. Conventional and consistent cable binding

techniques, along with a participant-dedicated research investigator, were used to minimize measurement electronics confusion. In addition, all participants were given an equal number of task practice trials, followed by an opportunity to adjust experimental apparatus as required. Practice trials were most critical for developing familiarity with the liquid crystal vision occlusion goggles, which may have presented the single greatest deviation from an ecological construct. For tasks that required the overhead safety harness system (Sections 3.0 and 4.0), participants wore the body harness in both the low context and high context trials of the task, to partially equalize any physical restraints.

Beyond these technical issues, the influence of observation on human behaviour can also be considered as a limitation. Any Hawthorne effect was minimised by limiting the number of research personnel involved in the study. In addition, participants were invited to bring a spouse/caregiver with them to the laboratory, to increase their comfort level. In all cases, participants were given regular practice trials, along with rest breaks when requested, in an effort to decrease laboratory anxiety. Where possible, participants were also invited to visit the lab on a day prior to their visit, to help reduce anxiety.

Trial number and trial order also present limitations to this work. For patient and caregiver practicality, all PD participants were tested first off medication, then on medication. This order could result in a learning-related inflation of on medication performance results. However, the presumed stable nature of the tasks should have limited any learning benefits. PD patient movement variability is not well captured by limited trial repeats. This confound is an acknowledged limitation of this work, but a necessary concession to the multiple research questions posed in studies conducted in a multi-investigator laboratory.

5.6 FUTURE DIRECTIONS

Several questions emerge from the current work. Primary among them is identifying the specific critical features, along with their salience, in a given context, then associating these parameters with PD movement deficits. Secondly, thorough investigation of the mechanisms responsible for disturbed motor performance should be conducted. The introduction of a dual task methodology to the examination of ecologically-valid motor tasks, with inclusion of alternative secondary tasks in the both the motor and cognitive domains, could discriminate the magnitude and locus of attentional interference [Rochester et al., 2004]. In addition, the incorporation of qualitative and quatitative anxiety measures would identify the effect of anxiety on PD motor deficits in challenging task contexts. Finally, developing concrete a priori strategies for recognizing and reducing the disruptive potential of high context situations may lead to more successful maintenance of activity, independence, and quality of life for Parkinson's disease patients.

6.0 CONCLUSION

Given the numerous multi-system loops which transverse and receive modulation from the basal ganglia and a pathologically and progressively decreased concentration of the basal ganglia's primary excitatory transmitter, the continued existence of any coordinated behaviour among Parkinson's disease patients could be cast as a remarkable scientific finding. The observations in this study indicate the persistence within PD patients of functional and flexible neural mechanisms for standing, reaching, and stepping. These programs help many PD patients in the general population maintain independent activities of daily living until later stages of their disorder. But inherent in any interaction with naturalistic daily activities is the dynamic appearance of both predictable and unpredictable

contextual challenges. From the results of this study, it can be suggested that the behaviours that persist among PD patients, and the neural mechanisms that support them, are uniquely and intrusively impaired by challenging environmental contexts. It may be these transient disruptions in challenging contexts that lead to the motor blocks, disequilibrium experiences, and eventual loss of independence that greatly impair the quality of life among PD patients. These responses, similar to those observed in this study, indicate a context-based adaptation of PD behaviour, as more stereotypical behaviour can be observed in less threatening contexts. These responses, also similar to those observed in this study, do not appear to be functionally adaptive, as they increase injury risk and possibility of error. Therefore, it can be a conclusive and novel suggestion of this study that threatening context leads to an unique and dysfunctional alteration of several naturalistic motor behaviours among PD patients. It is unlikely this context-modified sequence is a positive volitional or automatic neural response for PD patients, as it is largely dysfunctional in the observed actions. Rather, it is suggested that the dysfunctional sequence/consequence response in the threatening context is the result of attentional interference, and that corresponding functional sequence/consequence response among PD patients in less threatening contexts are possibly planned, initiated, and controlled by neural mechanisms and resources that compensate for a damaged basal ganglia, but remain susceptible to contextual interference. The evidence from this dissertation provides specific and novel illumination on the role of both task and context in deficits of movement sequence and consequence among non-medicated and medicated Parkinson's disease patients. Observations of disrupted kinematic sequencing and dysfunctional consequences suggest that challenging context can interfere with the psychomotor mechanisms that are recruited for movement by Parkinson's disease patients.

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