A Model Based Approach to Apraxia in Parkinson's Disease

by

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AUTHOR'S DECLARATION

I hereby declare that I am the sole author of this thesis. This is a true copy of the thesis, including any required final revisions, as accepted by my examiners.

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ABSTRACT

This thesis provides new insight into how learned skilled movements are affected in a disease with basal ganglia damage, within what task demands these deficits can be detected, and how this detection can occur within the constraints of primary motor symptoms. Hence the purpose of this thesis was threefold. Firstly, the aim was to take a model-based approach to apraxia in PD, in order to determine the nature of the errors in reference to other populations that experience apraxia. Apraxia by definition cannot be the product of primary motor deficits, weakness, sensory loss, or lack of comprehension, therefore the second objective of the study was to detect apraxia while remaining true to these prerequisites. The third objective was to extend the examination of apraxia beyond the upper limbs, and investigate the relationship between upper limb and lower limb apraxia, as well as the relationship between freezing (which shares similarities with gait apraxia) and upper limb and lower apraxia. Overall, the most common pattern of apraxia identified in this PD group was impairment at both pantomime and imitation, suggesting issues with executive function. However, there are other results that suggest an issue with visuomotor transformation may be superimposed on this executive function deficit, including a higher frequency of participants impaired at imitation and a very pronounced impairment at meaningless gestures. To ensure that these deficits are not the product of primary motor symptoms, correlation analyses were conducted between gestural impairment and total motor impairment, cardinal symptom impairment, and degree of asymmetry of these symptoms. While there was a significant correlation of total motor severity and gestural impairment, there were no significant correlations between cardinal motor symptoms and total gestural impairment, or limb specific gestural impairment and the degree of motor asymmetry. These results indicate that the outward manifestation of primary motor symptoms does not necessarily correspond with

gestural impairment, however the overall relationship (total UPDRS) hints to an indirect influence of the basal ganglia on healthy praxis. With regards to the third objective, the lower limb assessment turned out to be very consistent with the results yielded in the upper limb assessment. While there were similar frequencies of impairment in both pantomime and imitation, the upper limb and lower limbs assessments were found to correlate very strongly. This is a promising result, because the lower limb battery is easy to administer, there are typically less motor symptoms to deal with, and preliminary analyses show a high inter-rater reliability established. Furthermore, there was a higher proportion of freezers with apraxia compared to non-freezers, and this is the first study to reveal this. All these results taken together are evidence of similar underlying mechanisms for these impairments (upper limb apraxia, lower limb apraxia, and freezing). The model-based approach to studying apraxia in both the upper and lower limbs of PD, enables us to determine the frequencies, patterns and severities of apraxia, and better equips us to predict which systems are more susceptible to deterioration. This thesis project has hopefully created a framework for determining coping strategies and future interventions for apraxia, specifically in basal ganglia disordered populations.

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CHAPTER 1: THESIS INTRODUCTION & OBJECTIVES

Praxis is a term used to describe the planning and execution of coordinated motor behavior. Although considered an isolated function, praxis can be described by three fundamental processes: i) generating an idea for interacting with the environment, ii) organizing a program of action, and iii) executing a motor act (Gravenhorst & Walter, 2007). To accomplish this function there needs to be an integration of sensory input and motor planning processes. When an individual loses this ability to produce purposeful movement, and it cannot be explained by an elementary motor, sensory, or language comprehension disorder, we use the term "apraxia". The ability to skillfully and purposefully generate movement allows us to interact with the world, such as when we use tools to accomplish everyday activities, or using gestures to communicate with others.

Despite a century of research on the topic, it is still not well understood how the brain organizes and controls purposeful movement. However, the study of limb apraxia has generated a great deal of insight into how damage to the brain affects the control of skilled movements, which ultimately leads to inferences regarding how the healthy brain controls voluntary skilled action. By examining apraxia, the overall objective of this thesis is to expand on our current understanding of how the brain, and more specifically the basal ganglia controls purposeful skilled movement, as most of the literature regarding apraxia pertains to cortical pathologies such as right and left hemisphere stroke. Apraxia is not ordinarily associated with disorders of the basal ganglia, however some literature has suggested that many of these individuals exhibit signs of apraxia (for a review see (Zadikoff & Lang, 2005)). In order to meet this objective, my goal is to examine the nature of limb apraxia in individuals with perhaps the most common disease of the basal ganglia, Parkinson's disease (PD).

1.1 AN OVERVIEW OF LIMB APRAXIA

It is difficult to discuss apraxia without first mentioning Hugo Liepmann, who proposed the first contemporary ideas of the disorder in the early 1900s. While praxis functions occur through different neural networks, the errors that arise in voluntary movement due to apraxia will vary depending on the location of the lesion, as well as the modality and cognitive demand of the action.

Categories of Apraxia

Liepmann categorized these apraxic phenomena three ways, namely Limb Kinetic Apraxia (LKA), Ideational Apraxia and Ideomotor Apraxia (IMA).

i) Limb Kinetic Apraxia

Pathological confirmation of LKA is typically associated with cases of focal injury involving primary motor cortex(Tsuchiya, Ikeda, Uchihara, Oda, & Shimada, 1997), or frontal and parietal cortices(Fukui, Sugita, Kawamura, Shiota, & Nakano, 1996). Due to the damage of the motor cortex, the quality of the movements appear clumsy and poorly controlled, causing even very simple acts to lack precision and resemble unpracticed, novel movements (Liepmann, 1905/1988). When evaluated, regardless of the nature of the gesture (meaningful, object-related, novel, etc) all movements are coarse and distorted in those with LKA (Zadikoff & Lang, 2005). Some have questioned whether this is a true apraxia as it may reflect a deficit in primary control of movement as opposed to higher order impairment.

ii) Ideational Apraxia

For ideational apraxia, the limbs are obedient to the goal of the movement(Liepmann, 1905/1988). However, errors with this type of apraxia usually include impairment in carrying out actions in a proper sequence to obtain a goal, and it is the ideational outline that is flawed. There is often a loss of tool action knowledge such that there is difficulty associating a tool with the action it performs(L. J. G. Rothi, Mack, Verfaellie, Brown, & Heilman, 1988). No specific area of damage has been implicated, however it is typically thought to occur in the left parieto-occipital and parietotemporal regions, but may also involve left frontotemporal regions, sometimes with subcortical involvement (Heilman, Maher, Greenwald, & Rothi, 1997). This type of apraxia can be referred to as content apraxia.

iii) Ideomotor Apraxia

In contrast to LKA and ideational apraxia, motor representations are intact in thoses with IMA, however these engrams are not properly integrated with the other mental apparatus required in motor planning(Liepmann, 1905/1988). In this case, simple motion that may be effortless in one context may not be successfully performed when appropriate, desired, or requested with or without demonstration. To elaborate, there seems to be little integration between the ideational outline of the motion (a product of its perceptual and sensory elements) and the motor elements of the limbs. With IMA, the goal of a movement is usually recognizable, however a variety of spatial, temporal, and sequential abnormalities may occur in the production of this act (L. Rothi, Mack, L., Verfaillie, M., Brown, P., & Heilman K.M., 1988). Spatial errors are common including abnormal amplitude of the movement, substituting a body part as part of the object, or abnormal orientation of the body part performing the action. Errors of a temporal nature may demonstrate an increase or decrease from normal rate of gesturing. Finally, sequencing errors may involve a transposition, addition, or deletion of aspects, however the

overall goal of the action is still recognizable. These errors are partially remedied with imitation(Schnider, Hanlon, Alexander, & Benson, 1997) and or the use of the actual tool(Clark et al., 1994). Unlike LKA which does not discriminate between gestures, IMA usually affects gestures that involve the use of tools or objects, more than symbolic or communicative gestures (Watson, Fleet, Gonzalez-Rothi, & Heilman, 1986). The lesions that have IMA as a consequence are diverse but are mainly found in the left parietal association areas, as well as the white matter bundles at the fronto-parietal interface(Gross & Grossman, 2008). Less common, but certainly of interest are the lesions of the basal ganglia and thalamus, as well as the premotor and supplementary motor area (Grossman et al., 1991; Hamilton, Haaland, Adair, & Brandt, 2003; R. Leiguarda, Merello, & Balej, 2000; R. C. Leiguarda et al., 1997).

To summarize, according to Liepmann's models, kinetic engrams are lost or damaged in LKA, disconnected in IMA, and distorted in ideational apraxia. Consequently, each subtype of apraxia produces a unique array of errors and characteristics when clinically evaluated. Ideational apraxia is often described in the literature as a conceptual deficit, while IMA is more often described in the literature as a gesture production deficit. These terms are still commonly found in the literature, however, from this point on the term limb apraxia used in this paper will encompass both ideational apraxia and ideomotor apraxia. We have chosen to avoid exercising these terms due to inconsistencies regarding their use. Before we introduce the pathology of basal ganglia disorders, we will briefly outline some influential models of apraxia which have helped to refine assessment and discussion of apraxia.

1.2 MODELS OF APRAXIA

With respect to skilled movement, apraxia may be defined as demonstrating varying combinations of disturbances, classified by both the characteristics of the errors made and the

means by which they are produced. Various models have been proposed to explain limb apraxia and the combination of deficits that arise, and the following section will outline some of the major contributions to understanding the neuropsychological basis for apraxia.

The most logical place to start is with Leipmann's original description of apraxia and build chronologically from there. He described healthy praxis as a left hemisphere dominant phenomenon, stating that movement formulae contained a space-time representation stored in the left parietal lobe(Liepmann, 1905/1988). To carry out a skilled movement, this plan needs to be retrieved and associated via cortical connections with a corresponding innervatory pattern stored in the precentral and postcentral gyri, and the middle and inferior frontal convolutions (R. C. Leiguarda & Marsden, 2000; Liepmann, 1905/1988). For actions of the left arm, information must cross the corpus callosum to the right premotor area and then to the primary motor areas of the right side of the cortex.

Lesion studies further support these assertions, demonstrating how unilateral lesions of the left hemisphere in right-handed people produce bilateral deficits, usually less severe in the left than in the right limb. These studies are in reference to those who are right-handed, as it is well documented that the neurological organization of those who are left-handed is distinct(Kim, 1994; Kimura, 1983; Rasmussen & Milner, 1977) (further comment on the topic of lefthanders is beyond the scope of this paper).

Subsequently, and much later, Geschwind's model of apraxia(Geschwind, 1975) describes a disconnection between motor and posterior language areas, specifically the superior longitudinal fasciculus connecting the left frontal cortex with Wernicke's area. This is of the notion that lesions in this pathway would spare comprehension but compromise action

performance. This would only apply specifically to pantomime in which there are verbal commands, however Geschwind accounted for imitation by proposing that visual association areas and premotor cortex are connected via the same white matter tracts as the language and motor areas. This claim is highly disputed, and some have argued that while these pathways both involve the corpus callosum, the visual pathways seem to involve the splenium(L. J. Rothi, Heilman, & Watson, 1985).

Subsequently, several authors have put forth models of praxis with their respective advantages and disadvantages, however the common denominator between them is the concept of two separate systems for controlling movement. Rothi and Heilman describe praxis function by dissociating roles of the anterior and posterior regions as execution-production and conceptual-representational components respectively(L. J. G. Rothi & Heilman, 1997). Thus, they proposed knowledge and representations of objects and actions are stored in the parietal lobe, transformed by the premotor cortex, and used by the motor cortex. This very influential hypothesis gained much of its support from lesion studies(Heilman, Rothi, & Valenstein, 1982), though was scarcely evidenced by imaging studies(Kareken, Unverzagt, Caldemeyer, Farlow, & Hutchins, 1998).

A recent proposal by Buxbaum and colleagues involves a model that employs a frontal-parietal information processing system, responsible for transforming motor acts in space(Buxbaum, Kyle, Grossman, & Coslett, 2007). According to this model internal representations of movements and body part location are processed by the inferior parietal lobe processes. The study of meaningless gestures has helped to improve models with the notion of distinct processing routes for meaningful (requiring stored semantics) and meaningless (requiring visuospatial mediation of body part relationships). Therefore, an important development for

characterizing apraxia is the use of meaningless gestures in imitation. While it is not clear that impairment at these gestures represent apraxia(as these gestures are not learned skilled actions), it is likely they share a neural substrate with transitive movements, as impairments in both gesture types are often found to co-occur(Buxbaum et al., 2007; R. Leiguarda, 2005). These two distinct pathways have been demonstrated in functional MRI studies in which a particular part of the parietal lobe was implicated in processing of object/tool based gestures but not meaningless gestures(Buxbaum et al., 2007; Goldenberg & Hagmann, 1997; L. J. Rothi, Raymer, Maher, Greenwald, & Morris, 1991).

While these models have their distinctive advantages and disadvantages, the common denominator for these models is the concept of two separate systems for the control of movement. This cognitive model for limb praxis originally defined by Roy et al (Roy, 1996), employs i) a conceptual system, which stores knowledge of tools and gestures, and ii) a production system responsible for the execution of a gesture or action, including the organization, response selection, working memory and control thereof. These authors later added a sensory-perceptual level to this model to account for modality specific dissociations, such as visuogestural information (crucial for imitation), auditory or verbal command/information, and visual tool/object information such as tactile cues. This model is depicted in figure 1.1.

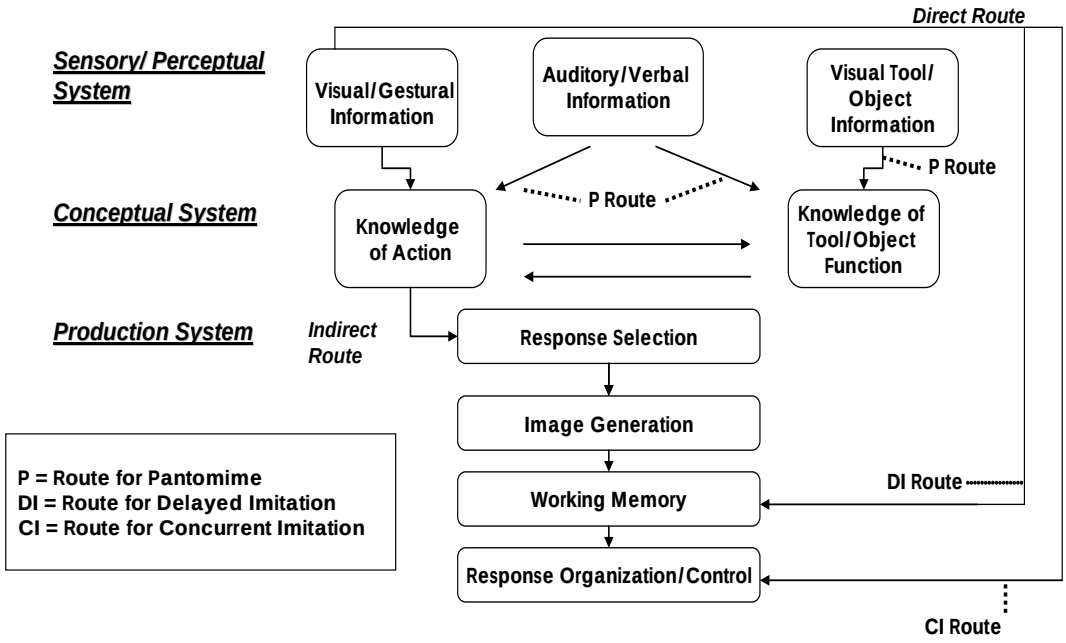

Figure 1.1 Roy and Square's Conceptual-Production System of Apraxia(Roy, 1996)

In terms of the whole process, dysfunction of any combination of the three systems (sensory, conceptual, and production) will elicit a distinct pattern of errors. Table 1.1 describes eight patterns outlined by Roy(Roy, 1996). Although this model of apraxia does not account for all empirical evidence, it provides a good framework for discussing the wide variety of performance patterns in the population of interest.

Table 1.1 The Eight Patterns of Deficits Described by Roy (Roy, 1996)		
Apraxia Performance Pattern	**System Affected**	**Nature of Disruption**
"Sensory-Perceptual" (P+/DI-/CI-/ID-)	Sensory/Perceptual	Impaired ability to analyze visual gestural and tool/object information
"Conceptual" (P-/DI+/CI+/ID-)	Conceptual	Impaired knowledge of action and tool/object function
"Production Response Selection" (P-/DI+/CI+/ID+)	Production	Impaired response selection and/or image generation
"Production Encoding" (P+/DI-/CI+/ID+)	Production	Impaired encoding of visual gestural information into working memory
"Production Working Memory" (P-/DI-/CI+/ID+)	Production	Impaired working memory
"Production Conduction" (P+/DI-/CI-/ID+)	Production	Impaired ability to use visual information in the control of movement
"Production Ideomotor" (P-/DI-/CI-/ID+)	Production	Impaired response organization and control
"Global" (P-/DI-/CI-/ID-)	Production & Conceptual	Impaired knowledge of action and tool/object function + Impaired response organization and control.
P=Pantomime, DI= Delayed Imitation, CI=Concurrent Imitation, ID=Gesture Identification (+) denotes normal performance (-) denotes impaired performance		

Assessment of Limb Apraxia

A thorough examination of gestural performance across various modalities and task demands is required in order to infer the specific pattern of apraxia. In pantomime, participants are asked to perform an action from either a verbal command or based on the picture of an object, such that the person needs the interplay of their knowledge of tools and the actions associated with them in order to successfully translate this information into an actual movement. In the imitation task, the examiner demonstrates a gesture to the participant, and then requires them to replicate after the demonstration is complete (delayed imitation) or while the examiner is

still performing the demonstration (concurrent imitation). Gesture types fall into three categories; i) transitive which are meaningful gestures involving the use of objects or tools, (eg. fork) ii) intransitive which are meaningful gestures not using tools, but conveying a message of some sort(e.g. a thumbs up), and iii) nonrepresentational gestures which carry no meaning and are novel to the person being tested (eg. open hand moving in sagittal plane).

Verified by many, and according to Roy's model (Figure 1.1) there are two routes a person can use to accomplish the imitation task; i) an indirect route, in which the individual recognizes the gesture and transforms an existing representation into an appropriate gesture, and ii) a direct route, where the individual relies solely on vision (their sensory-perceptual system) to complete the task(Heilman, Gonyea, & Geschwind, 1974; Tessari, Canessa, Ukmar, & Rumiati, 2007). This direct route to action is the only option when the gestures being copied are meaningless or novel. Aside from the pantomime and imitation conditions, it is also important to include real-life use of objects particularly because it is the most true to life condition and perhaps best demonstrates the impact apraxia has on everyday lives. Roy's model, with its knowledge of objects focus, is more conducive to describing deficits in transitive gestures, however, it can easily be adapted to other gesture types. Various studies have suggested that each gesture type may have different neuroanatomical correlates(Buxbaum et al., 2007; R. Leiguarda, 2001). This point emphasizes the need to have a wide range of tasks and gesture types in an apraxia battery.

Finally, all apraxia assessments should include an examination of the conceptual praxis system including tasks such as object identification, and gesture identification, recognition, and matching tasks. Much of the currently published apraxia research did not establish these kinds of conceptual baselines.

The greatest downfall of most apraxia investigations is that the analysis of gestural performance can be insensitive to subtle apraxic impairments. This is a major reason for inconsistencies in the literature, and perhaps what could be an underestimation of apraxia frequency, but also severity of apraxia across individuals in a number of clinical populations. The main advantage to the approach outlined by Roy et al(Roy, Black, Blair, & Dimeck, 1998) is the use of a composite score across several dimensions of the movement. This helps to define the presence and degree or severity of apraxia relative to healthy controls more precisely.

This thesis includes the collection of a large comprehensive limb apraxia battery, called the Waterloo-Sunnybrook Limb Apraxia Battery, a collection of tasks encompassing all the aforementioned task demands and modalities. Despite collecting all the data, there is a primary focus on pantomime, imitation (transitive, and intransitive non-representational), and the group of conceptual tasks.

1.3 AN OVERVIEW OF PARKINSON'S DISEASE

The basal ganglia refers to the striatum (collectively the caudate nucleus and putamen), globus pallidus (internal and external), subthalamic nucleus, and substantia nigra(Nolte, 2002). Parkinson's disease is the most well-known disorder associated with damage to the basal ganglia and has several distinct outward symptoms. This motor disease is often classified by a resting tremor, akinesia (difficulty initiating movement), hypokinesia (small amplitude movement), bradykinesia (slowness of movement), rigidity and postural instability. Secondary impairments in Parkinson's disease include disturbance of the spatiotemporal aspects of gait such as step length and cadence, cognitive impairments, micrographia (small writing), decreased speech volume, sleep disorders, and mood fluctuations(Guttman, Slaughter, Theriault, DeBoer, & Naylor, 2003; Leung & Mok, 2005; Wolters & Francot, 1998). These symptoms are the result of

a pronounced degeneration of dopamine producing neurons in the substantia nigra(pars compacta), leading to a loss of dopamine in the striatum (Wolters & Francot, 1998). Unfortunately, the outward symptoms of PD only become visibly apparent after an estimated 60% of the available dopamine has been lost and neural pathways through the basal ganglia have been severely impaired. The loss of dopamine in the striatum affects two pathways through the basal ganglia to the thalamus that facilitate cortical output(please see figure 1.2)(Pahwa & Lyons, 2007). The direct pathway begins with input from the cortex to the striatum, which then sends an inhibitory signal to the globus pallidus internal (GPi). The output from the GPi to the thalamus is subsequently decreased, however, as the role of the GPi is to inhibit thalamic output, decreased input to the thalamus results in increased thalamic output to the cerebral cortex. In Parkinson's disease, a lack of dopamine in the striatum, inhibits the direct pathway leading to decreased striatal output, increased globus pallidus output, and ultimately decreased thalamic output. The decreased thalamic output leads to diminished cortical activity, and is likely the root cause of characteristic symptoms of Parkinson's disease including bradykinesia and hypometria (small movements)(Nolte, 2002).

An indirect pathway also passes through the basal ganglia to affect cortical output. The striatum sends an inhibitory signal to the globus pallidus external (GPe), which thereby decreases output from the GPe to the subthalamic nucleus. The GPe is inhibitory, and thus a decreased output from the GPe leads to increased output from the subthalamic nucleus to the GPi. The subthalamic nucleus is excitatory, and it increases the output from the GPi to the thalamus. As the GPi inhibits the thalamus, this increased output results in decreased output from the thalamus. In Parkinson's disease, the lack of dopamine increases the activity of the indirect

pathway, ultimately leading to decreased thalamic output and diminished cortical activity(Nolte, 2002).

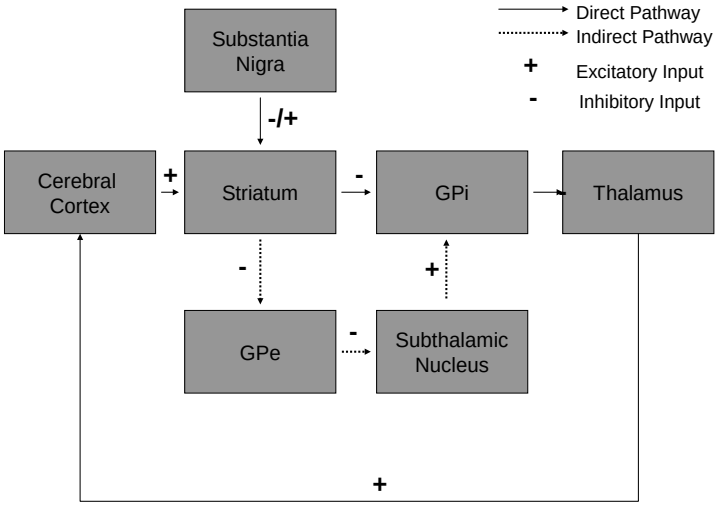

Figure 1.2 Direct and Indirect Pathways of the Basal Ganglia (Nolte, 2002)

The end stage of both pathways is thalamus, and therefore in Parkinson's, the generation of excitatory cerebral cortex projections in diminished. As such, therapeutic interventions have been aimed at identifying chemical messengers or neurotransmitters that improve transmission along these pathways to restore proper thalamo-cortical output.

The primary assessment for Parkinson's disease is the Unified Parkinson's Disease Rating Scale, herein referred to as the UPDRS(Fahn, 1987). It is the gold standard used by researchers and clinicians to track the disease progression in PD. It is divided into four sections including i) the UPDRS-I, a self report on mood, mentation and behaviour, ii) the UPDRS-II, a self report on activities of daily living, iii) the UPDRS-III, a clinical motor examination, and iv) the UPDRS-IV, a description of any complications of therapy such as side effects from the

medication. For the purpose of this project, the primary focus is on the motor section of the UPDRS (III), with some brief mention of the UPDRS-II.

1.4 THE ROLE OF THE BASAL GANGLIA IN PRAXIS

Finally the discussion is turned to the role of basal ganglia in praxis, and how pathology thereof may adversely affect motor control in general. As discussed in the previous section, basal ganglia nuclei are intricately interconnected with the cortex, thalamus and brainstem. The striatum is the main area for input from other brain areas, mainly from the motor and prefrontal cortices. From a developmental perspective it is known that during early phases of learning, the parietal association cortex, premotor cortex, and primary motor and sensory cortices are highly active regions. However, as an everyday skill becomes well-established or 'over-learned', its execution becomes largely processed in the supplementary motor area, primary motor cortex, basal ganglia and cerebellum (Grafton et al., 1992; Roland, 1984). Given the aforementioned outward symptoms of basal ganglia disorders, it is evident these nuclei are involved in controlling or influencing motor output. However, considering the abundance of reciprocal connections from the basal ganglia to cortical structures, some might argue for the involvement of these nuclei in higher sensory processes in addition to motor processes. The purpose of this section is to touch on roles of the basal ganglia as they relate to the execution of skilled movement. Here we describe evidence for the role of the basal ganglia in the selection of kinematic parameters, the linking of sequential motor acts, the transformation of sensory information into motor acts, and the sensorimotor integration that must occur to do so.

Several authors describe the role the basal ganglia may possibly play in selection of kinematic parameters for a voluntary movement(R. Leiguarda, 2001; R. Leiguarda, Merello, Balej et al., 2000; Rosenbaum, 1991). This point is supported by the fact that some neurons in

the globus pallidus (GPi and GPe) and the substantia nigra increase their firing rates with changes in amplitude and peak velocity during a movement, while pallidal and putaminal cells discharge relative to movement direction (R. Leiguarda, 2001). Furthermore, recent work by Leiguarda found individuals with Parkinson's disease exhibited kinematic deficits in the spatial precision and velocity of movement(R. Leiguarda, Merello, Balej et al., 2000). Therefore, when scaling the amplitude of skilled movements, a dysfunctional basal ganglia loop could result in disruptions of size, speed, and timing. In studies in which the putamen was deactivated, movements had large, abnormal fluctuations in amplitude and velocity, and this was particularly the case in tasks that required multiple steps(Kato & Kimura, 1992).

Thus, it is not surprising that several studies have indicated difficulty for those with basal ganglia disease in linking together multiple motor commands(Martin, Phillips, Iansek, & Bradshaw, 1994; E. A. Roy, J. Saint-Cyr, A. Taylor, & A. Lang, 1993; Sharpe, Cermak, & Sax, 1983). During two phases of sequential movements, some neurons in the basal ganglia have a double firing pattern such that the first discharge occurs after the first movement, and the second discharge precedes the second movement as evidence for the role of this structure in learning sequences(Brotchie, Iansek, & Horne, 1991). As further evidence of this role, activation of the caudate/anterior putamen occurred during new and complex sequences, activation of the middle putamen during performance of automatic sequences, and activation shifted back to caudate/anterior putamen when attention was paid to the over-learned actions (R. Leiguarda, 2001). Additionally, within this network there are many potential subsystems subserving functionally separate cognitive functions related to motor sequencing (i.e. timing, motor attention, selection of limb movements, and object oriented responses). For example, pallidal neurons display strong activation during planning and use of spatial working memory, and the

SMA-basal ganglia system is recruited preferentially when a sequence is well-known or automated. These functional substrates may be selectively damaged by the pathological process seen in Parkinson's disease (among other basal ganglia disorders), and therefore produce the many different error patterns exposed in apraxia evaluations.

It is a possibility that errors observed in apraxia mostly arise from the inability to transform sensory information into action. Our ability to adapt action based on stimuli in the environment relies on the integration of sensation and motor commands. Several authors suggest that damage to parietal cortices and striato-parietal circuits may interfere with sensory prediction processes used to guide movement (Sirigu et al., 1996; Wolpert & Ghahramani, 2000) and hinder the ability to estimate environmental and body states (Wolpert, Goodbody, & Husain, 1998). Therefore, many accounts of apraxia have described the disorder as essentially being a "disconnection syndrome" (Geschwind, 1965), wherein white matter tracts connecting cortical areas involved in sensory and motor processing are interrupted (for review see (R. C. Leiguarda & Marsden, 2000)). Damage to these circuits, namely the parietofrontal circuit and its subcortical connections, may result in faulty grasping and reaching, and production of incorrect finger and hand postures, abnormal orientation of tools/objects, inappropriate configuration or coordination of the arms, and faulty movement trajectories. Observation of ideomotor apraxia in Parkinson's disease has led to the consensus in the literature that the basal ganglia is an integral part of these aforementioned parallel circuits devoted to sensorimotor integration. This line of thinking can be further supported by reaching tasks, in which PD groups are largely more dependent on vision than healthy groups, to compensate for disruptions in sensory feedback (Flash, Inzelberg, Schechtman, & Korczyn, 1992; Flowers, 1976; Klockgether & Dichgans, 1994). Studies by Adamovich & Poizner have shown when vision of a limb is available (by putting a light on the

finger tip), the accuracy of individuals with PD is similar to healthy controls. When vision of the limb is removed, participants perform dramatically worse even when vision of the target is available throughout the trial. Therefore they argued that the dependence on vision with PD may be explained by a specific role of the basal ganglia in integrating vision and proprioception (Adamovich, Berkinblit, Fookson, & Poizner, 1998, 1999). This theory can be expanded on through the work of Almeida et al, who propose that through feed-forward processes, direction and amplitude of movements toward a stationary target are programmed in advance based on visual information about target and start positions(Almeida, Wishart, & Lee, 2003). The role of the basal ganglia is thought to modulate cortical output that guides the execution of the movement as a whole.

Furthermore, recent work by Leiguarda found individuals with Parkinson's disease exhibited kinematic deficits in the spatial precision and velocity of movement, as well as failure to maintain proper joint amplitudes. Interestingly, spatial disruption of wrist trajectories was more apparent in those characterized with apraxia. The results from the study, in terms of inter-joint coordination are also consistent with the suggestion that there may be defective cue production in the basal ganglia, leading to impaired preparation for sub-movements performed in sequence.

1.5 APRAXIA IN DISEASE OF THE BASAL GANGLIA

While basal ganglia lesions commonly accompany the apraxia attributed to left and right hemisphere strokes(Roy et al., 1998), several authors have maintained that apraxia rarely arises from the isolated disruption to the basal ganglia as opposed to dysfunction corresponding with damaged cortical regions (R. Leiguarda, Merello, Balej et al., 2000; R. C. Leiguarda et al., 1997; Pramstaller & Marsden, 1996; Roy, 2000). The greatest challenge in this field of study is the

diagnostic dilemma of differentiating the elementary motor and sensory deficits characteristic of these diseases (such as weakness, bradykinesia, ataxia, tremor, rigidity, or dystonia) and higher order deficits in skill performance. This is where it becomes crucial for praxis errors to be well-defined clinically and kinematically, such that they can be superimposed on primary movement impairments. This predicament, and the approach used in this study to address it is the primary focus of chapter 3. Ideomotor apraxia has been described in Parkinson's disease by a number of researchers, in which kinematic deficits of spatial and temporal precision are demonstrated (Goldenberg, Wimmer, Auff, & Schnaberth, 1986; Grossman et al., 1991; R. C. Leiguarda et al., 1997; E. A. Roy, J. Saint-Cyr, A. Taylor, & A. E. Lang, 1993; Sharpe et al., 1983). In the most comprehensive study to date, Leiguarda et al looked at praxis in individuals with Parkinson's disease, and showed that deficits did not differ between ON and OFF states in levodopa responsive patients, nor did apraxia scores correlate with motor disability(R. C. Leiguarda et al., 1997). These findings re-emphasize the point that limb apraxia can be examined in the presence of, yet is not necessarily explained by classic Parkinsonian symptoms.

1.6 PROPOSED RESEARCH

Although a number of research groups have looked into the manifestation of apraxia in Parkinson's disease, there are still several outstanding questions to study and current theories in need of expansion. The first area of focus for this project is a model-based approach to praxis impairments in Parkinson's disease, using the well-established model of apraxia described by Roy et al(Roy, 1996) (please see figure 1.1. The sensory level of praxis is represented by performance on pantomime and imitation with both eyes open and eyes closed. The conceptual level is represented across meaningful and meaningless gestures as well as a battery of naming and identification tasks. The production system is represented through a comparison of

pantomime and imitation, and the use of the detailed scoring system described by Roy et al (Roy, 2000; Roy et al., 1998). Rarely have these two tasks been studied systematically and compared within a PD group.

The second area of focus is to absolve some of the criticisms that surround testing a population with an elementary motor disorder. We can use the asymmetrical framework of Parkinson's disease to discern motor symptoms from performance on gestural tasks on each hand separately.

The final component to this project is a novel and systematic evaluation of apraxia in the lower limbs in Parkinson's disease. As a neurodegenerative disease that typically begins in the upper limbs and then progresses to the lower limbs, it would be interesting to see if apraxia can manifest itself in the lower limbs in the same nature and frequency that it does in the upper limbs. This is an ambitious proposal as the lower limbs are more limited than the upper limbs in their repertoire for complex movement, and there are currently no multimodal approaches for evaluating apraxia in the lower limbs. The current document is a collection of three studies, and there is some repetitious material in terms of the introduction and methods sections.

Ultimately the big picture objective for this project is to use the information processing approach of the conceptual-production model to evaluate performance levels, study brain asymmetries and discern patterns of deficits in the Parkinson's disease population. This thesis will provide insight into how both a healthy and diseased basal ganglia control purposeful movement.

CHAPTER 2: A MODEL-BASED APPROACH TO APRAXIA IN PARKINSON'S DISEASE

2.1 INTRODUCTION

Apraxia is a complex movement disorder that frequently occurs following stroke, such that individuals are unable to execute or control voluntary movements(Liepmann, 1988). It has also been reported, albeit less often, in diseases of the basal ganglia such as corticobasal degeneration, progressive supranuclear palsy, and Parkinson's disease(Zadikoff & Lang, 2005). Apraxia by definition cannot be accounted for by weakness, sensory loss, or poor comprehension of or attention to commands, thus it is challenging to work around the manifestation of primary motor deficits common to basal ganglia diseases including akinesia, rigidity, and tremor(L. J. G. Rothi & Heilman, 1997). Poeck asserts that it is possible to distinguish between these elementary motor deficits and the higher order apraxia errors, such that an apraxic diagnosis is made when someone is impaired in the proper sequence of motor elements that constitute a gesture or movement(Poeck, 1982).

Examining Apraxia in Parkinson's Disease

Several studies have used Parkinson's disease as a framework for observing the role of the basal ganglia in praxis. Apraxia has been described in Parkinson's disease by a number of researchers, in which kinematic deficits of spatial and temporal precision are demonstrated(Goldenberg et al., 1986; Grossman et al., 1991; R. C. Leiguarda et al., 1997; E. A. Roy et al., 1993; Sharpe et al., 1983). Furthermore, in a comprehensive study of PD by Leiguarda and colleagues, apraxia scores did not correlate with motor disability(R. C. Leiguarda et al., 1997). These findings help suggest that limb apraxia can be examined in the presence of,

yet is not necessarily explained by classic Parkinsonian symptoms, however there is still a great deal of ambiguity regarding the relationship between apraxia and basal ganglia dysfunction.

Leiguarda et al. propose that the basal ganglia is an integral part of the network directly involved in praxis(R. Leiguarda, Merello, Balej et al., 2000), but argue that pathology restricted to the basal ganglia may not disrupt the limb trajectory enough to be observable clinically. Rather, they argue that when basal ganglia pathology is coincident with cortical damage, timing, sequencing errors and other kinematic abnormalities become severe enough to be observable. Roy asserts that a more quantitatively based observational system in the clinical examination of apraxia would be a more accurate reflection of the deficit at hand(Roy, 2000). The approach used by others in examining apraxia typically involves recording different types of errors (e.g spatial, temporal, etc) when gesturing, and then either assigning a cutoff or comparing the number of correct gestures relative to healthy controls. One of the other major pitfalls of past examinations of apraxia is the insensitivity to frequency and degree of apraxia(Roy, 2000). The main difference and advantage to the scoring system used in this study is that a composite score is derived in the form of a percentage accuracy across several dimensions of movement. Therefore, the presence and severity of apraxia can be defined more precisely by looking at this performance relative to healthy control performance. Moreover, this composite score is used to calculate a Z score relative to the performance of healthy participants, rather than just comparing the deviation from the number of correct gestures.

Comparing Pantomime and Imitation in Parkinson's Disease

There are several reciprocal connections between the basal ganglia and the cortex, constituting multiple circuits that act in parallel, many of which are thought to be involved in

sensorimotor integration or translation of sensory input into movement output(R. C. Leiguarda & Marsden, 2000; Marsden, 1998; Zadikoff & Lang, 2005). The circuit activated depends on the nature and complexity of the task at hand in terms of cognitive demand, and one of the earliest observations in the apraxia literature is the distinction between pantomime and imitation. Liepmann, who proposed the first contemporary ideas of apraxia, differentiated between the two tasks suggesting that pantomime impairment reflected a disruption in the motor program or 'praxicon' for the action, while poor imitation may be indicative of an inability to implement, execute, or control the gestures(Liepmann, 1988). A number of studies have compared performance in pantomime versus imitation, and there have been strong dissociations between these two tasks in stroke populations(Halsband et al., 2001; Poeck, 1982; Roy et al., 2000). Two studies by DeRenzi (Barbieri & De Renzi, 1988; De Renzi, Motti, & Nichelli, 1980) also showed that performance on pantomime and imitation were not correlated which supports the notion that the two tasks engage different processes in praxis. Roy (Roy, 1996; Roy et al., 1998; Roy et al., 2000) suggested that the combination of impairment across pantomime and imitation could reflect a disruption at a particular stage in performing an action. Individuals may be considered apraxic under three circumstances; those who are impaired i) at both pantomime and imitation, ii) at only pantomime, or iii) at only imitation. When apraxia is present in pantomime but not imitation, there may be a disruption in the conceptual system pertaining to their knowledge of tool function or actions or in the early stages of the production system involving response selection. In those who are apraxic in solely the imitation condition, there may be a deficit in the ability to analyze visual gestural information or to translate this information into movement. Roy suggests that when individuals are found to have apraxia for both pantomime

and imitation, it may hint at a selective impairment at a later stage in gestural production involving movement execution(Roy, 2000).

Rarely has both pantomime and imitation been systematically investigated in people living with Parkinson's. In Leiguarda et al.'s examination of 45 individuals with PD(R. C. Leiguarda et al., 1997), participants were found to be most impaired on pantomime and improve on imitation, with nobody selectively impaired at imitation. However, the gestural analysis leaves much to be desired in terms of detail and also the pantomime and imitation conditions did not compare the same gestures. Also, despite being a large sample of participants, the majority of PD had a mild severity of disease as per average UPDRS(Fahn, 1987), which leaves room to expand on the current literature for apraxia in PD.

The present study was designed to examine the frequency and severity of apraxia in PD, employing the same detailed analysis system as Roy et al(Roy et al., 1998) to better understand the nature of these deficits. Further, the participants will be assessed in both pantomime and imitation to compare the frequency of apraxia across the three patterns of deficits described above. One might expect that in opposition to what was demonstrated in the previous study by Leiguarda et al(R. C. Leiguarda et al., 1997), the more detailed analysis may be more sensitive to subtleties in both tasks. That said a more global impairment across pantomime and imitation might be expected, hinting towards a predominantly executive disorder. While a flawed production system has been hypothesized as the culprit in these instances of apraxia across both tasks, there may be an issue further upstream regarding the sensory-perceptual and conceptual inputs, or the integration of this information. Therefore, it is important to evaluate the roles of sensory and conceptual inputs as described by Roy's model(Roy et al., 2000).

The Conceptual System

Pantomime requires access to the conceptual system of praxis, in other words, knowledge of actions and tools/objects. Imitation of gestures can be accomplished with an indirect route, through which a participant recognizes the conceptual basis of the gesture being performed by the examiner, and thus employs a route similar to pantomime. However, in imitation, it is possible to bypass the conceptual system and use a direct route based on visual encoding of the gesture as performed by the examiner. For most gestures, unless one system is faulty, one might assume there are contributions of both routes in imitation. Imitation of meaningless gestures is the only way to be certain there are no contributions of the conceptual system, as there is no lexical support for the gestures being performed. Imitation of meaningless gestures has been included in many descriptions of apraxia, however it is controversial as to whether a deficit thereof would represent apraxia as it is classically defined (as these postures are novel and not learned actions). Despite coexisting with apraxia, it has been considered that these movements may have a different, but partially shared neural substrate more associated with visuospatial mediation of body part relationships(Buxbaum et al., 2007). The notion that the routes for performing meaningful versus meaningless gestures are dissociable is supported by functional MRI work, in which a region of the parietal lobe showed activation during tool-use gestures but not meaningless gestures(Moll et al., 2000). Therefore, while it may not be accurate to refer to someone who is impaired at meaningless gestures as ‘apraxic’, these gestures isolate the quality of the visual analysis and the ability to translate this information into movement.

The Sensory-Perceptual System

A complete model of praxis includes the addition of the sensory-perceptual level. Our ability to adapt action based on stimuli in the environment relies on the integration of visual and proprioceptive inputs with motor commands. Many authors have suggested that damage to parietal cortices and striato-parietal circuits may interfere with integrative processes used to guide movement(Sirigu et al., 1996; Wolpert & Ghahramani, 2000) and this ultimately hinders the ability to estimate environmental and body states(Wolters & Francot, 1998). Damage to these circuits, particularly, the parietofrontal circuit and its subcortical connections, may result in apraxia because of faulty reaching trajectories, production of incorrect finger and hand postures, abnormal orientation of tools/objects, and inappropriate configuration of the limbs. This line of thinking can be further supported by reaching tasks, in which individuals with Parkinson's disease are largely dependent on vision to compensate for disruptions in somatosensory feedback (Flash et al., 1992; Flowers, 1976; Klockgether & Dichgans, 1994). These studies have shown when vision of a limb is available the accuracy the PD group is similar to healthy controls. However, when vision of the limb was removed, the PD group performed dramatically worse even when the target was visible throughout a whole trial. Therefore dependence on vision with PD may be explained by a specific role of the basal ganglia in integrating vision and proprioception (Adamovich et al., 1998, 1999). This theory can be expanded on with the work of Almeida et al, who propose that through feed-forward processes, direction and amplitude of movements toward a stationary target are programmed in advance based on visual information about target and start positions(Almeida et al., 2003). Therefore, the role of the basal ganglia is thought to modulate cortical output that guides the execution of the movement as a whole.

Study Objectives & Predictions

In summary, this chapter seeks to expand on the current findings regarding apraxia in Parkinson's disease in several ways. Firstly, a systematic comparison of pantomime and imitation will be conducted, and the frequency of apraxia therein calculated. A higher frequency of PD with apraxia than previously identified(R. C. Leiguarda et al., 1997) is predicted due to a more detailed scoring system used in the current study. Secondly, the contribution of the conceptual system will be evaluated through both a series of naming and identification tasks, as well as through the comparison of meaningful and meaningless gestures. It is predicted that apraxia in Parkinson's disease is primarily due to an executive disorder, and not pervasive to the conceptual system, therefore no difficulties are expected with naming or identification tasks. As seen in groups of healthy participants, a decline in performance of meaningless gestures is expected. Thirdly and finally, the contribution of the sensory-perceptual system is examined in terms of the role of visual feedback for performing gestures. This will be accomplished by comparing no vision and vision conditions for performance of the same task. It is predicted the PD group will demonstrate the most difficulty in no vision conditions across all tasks, consistent with past observation that PD are heavily reliant on vision to guide movement.

2.2 METHODS

Participants

The experimental group for this study consisted of 48 individuals meeting strict clinical criteria of idiopathic Parkinson's disease. PD participants were assessed after an average withdrawal of 14.9 ± 4.3 hours from their anti-Parkinsonian medication. Only those with a minimum score of 80 on the Modified Mini Mental State Examination were included, and all were right handed. In addition, performance of 16 age-matched healthy community volunteers, who were right handed, and had no history of neurological diseases comprised a control group.

The mean age for this group was not statistically different from the PD group [t(1,62)=0.9807, p > .3307]. Basic demographics can be found in Table 3.1 (further detail available in Appendix A).

Table 2.1 Study Participant Demographics

Group	Age (Mean ± SD)	UPDRS-III (Mean ± SD)	Disease Duration (Mean ± SD)
PD (n=48)	69.2 ± 8.9 years	32.9 ± 9.6	7.9 ± 6.2 years
Healthy (n=16)	68.3 ± 6.7years	n/a	n/a

Conceptual Tasks

All participants completed a battery of verbal conceptual tasks. These included tool naming tasks, tool identification, and gesture identification tasks. Tool naming had the participant provide the name of a tool from a picture (eg. “What would you call the object in this picture?”), from a description of an action (eg. “Which object would you use to pull out a splinter?”), and from a gesture performed by the examiner (eg. “Which object am I holding in my hand when I perform this action?”). There were two tool identification tasks, both of which involved choosing the correct picture from a choice of four pictures. There was tool identification (eg. “Point to the spatula”), and tool identification by function (eg. “Point to the object you would used to pound a nail”). There were three tasks for gesture identification in which participants watched a video of a man performing sequences of gestures and all answers were in the form of ‘yes’ or ‘no’. The first identification task asked participants to identify if the performer was using a certain object (eg. “Does it look like he is using a comb to style his hair?”). For the second identification task, the examiner held up an object with each segment of video footage and asked the participant to identify if the performer was using that object (eg. “Does it looked like he is using this object?”). The final identification task was a gesture

matching test in which the examiner performed gestures alongside the video footage and the participant had to identify if the performer and the examiner were performing the same gesture (eg. “Is he performing the same gesture as I am?”).

Conceptual Task Analysis

Scores were calculated on the conceptual battery of tests as percentage accuracies, including total scores for tool naming, tool identification, and gesture identification. As well, a composite score was calculated for these three task categories, for both healthy control participants and Parkinson’s disease participants. An independent samples t-test was performed between the healthy participants and the PD participants for the composite scores.

Gestural Tasks and Performance Scoring

Participants were required to pantomime and imitate eight transitive gestures, with both their eyes open and their eyes closed. In the pantomime condition participants were asked to pretend how to use an object to perform a particular action. For example, a command would be “Show me how you would use a knife to slice a piece of bread”. The imitation condition had participants copy the examiner’s performance of the same eight gestures. In the eyes closed condition, participants first watched the examiner perform a gesture, then they were asked to close their eyes and replicate what they saw. Therefore there was a delay between their observation of the examiner and their performance. Pantomime was always performed first to avoid cueing the participants as to how each gesture was properly performed. In both pantomime and imitation, eyes-closed gestures were always performed first to avoid any visual feedback that might influence subsequent performances. All gestures were performed with both right and left hands. Each participant was videotaped for later analysis by a trained rater.

Analysis

Each gesture was assessed based on five dimensions, namely location, posture, action, plane, and orientation, each given a score of 0, 1, or 2, as clearly defined by a criteria (Appendix B). Each dimension was then given a score out of 16 and calculated as percentage accuracy. The mean percentage accuracy collapsed across the five dimensions represented the composite score. Scores for the right hand and left hand were pooled together for both the PD group and the healthy control group.

The first analyses pertained to the healthy control group in which three one-way ANOVAs were performed including a comparison of performance across each of the five dimensions (location, posture, action, plane, and orientation) in pantomime and imitation, as well as a comparison of composite scores between pantomime and imitation. Subsequently a preliminary analysis was conducted for the composite scores of the healthy control group versus those of the PD group, across both pantomime and imitation.

From herein, percentage accuracy of gesture performance for each individual with PD was converted to a Z-score with reference to the mean and standard deviation of the healthy participants. This allowed evaluation of the performance of the participants in each task and each dimension relative to healthy controls. Two cutoff scores were developed based on the average composite scores of the healthy control participants such that individuals with PD could be classified into apraxic, borderline apraxic, or non apraxic groups[20, 33]. The first and second cutoff scores were one and two standard deviations below the mean of the healthy controls respectively (-1.00 and -2.00). Individuals with PD who scored greater than the first cutoff were considered to be the non-apraxic group (> -1.00). Individuals with PD who scored between the

first and second cutoff were classified as borderline apraxic (-1.00 to -1.99), while those scoring below the second cutoff from the mean of the healthy group were classified as apraxic (< 2.00).

The first task was to look at the frequency of PD participants that were categorized into each grouping for apraxic, borderline apraxic, and non-apraxic, for both tasks of pantomime and imitation. Those belonging to the borderline group were excluded from all subsequent analyses.

Performances for pantomime and imitation were examined separately to see the occurrence of errors within each task. Two separate 2X5 ANOVAs were performed for group (apraxic, nonapraxic) by dimension (location, posture, action, plane, orientation) for pantomime and imitation respectively. Tukey's post hoc analyses were performed to compare performance across the dimensions.

PD participants were then classified into four patterns of performance based on whether they were impaired on pantomime, imitation, both or neither. To evaluate the performance of gestures from a conceptual standpoint, a 3X2 ANOVA was conducted for task (pantomime of gestures, imitation of meaningful gestures, and imitation of meaningless gestures) and group (apraxic and non-apraxic). To test the contributions of visual feedback, three separate ANOVAs were conducted for performance on the three aforementioned tasks with no vision and vision conditions for the composite scores of the healthy controls. This was repeated with the PD group, but with apraxic and non-apraxic groupings as an independent variable, while z-scores were the outcome measure used instead of the composite scores.

2.3 RESULTS

Performance of Healthy Control Participants

Healthy control participants exhibited lower overall accuracy in the pantomime relative to the imitation condition as reflected in significantly lower composite scores[F(1,15)=9.11; p<.0086]. There were no significant differences revealed in pantomime performance across all dimensions [F(4, 60) 5.43, p < .0132], imitation performance across all dimensions [F(4,60)=.97; p<.4282], and the aforementioned reduced accuracy demonstrated in pantomime was seen across all dimensions. Table 2.2 presents the performance accuracy by task and dimension.

Table 2.2 Gestural Performance Accuracy of Healthy Control Participants

DIMENSION	Pantomime		Imitation	
	%	SD	%	SD
Location	88.75	6.12	92.09	6.00
Posture	92.08	7.17	96.26	6.16
Action	90.21	6.77	94.67	4.67
Plane	89.65	10.46	94.34	3.82
Orientation	91.04	9.59	94.89	4.59
Composite	90.35	6.12	94.45	3.06

In an analysis of composite scores for the healthy controls versus the individuals the PD group, across pantomime and imitation, there was a main effect of group and a main effect of task. As such, the PD as a group performed worse than the healthy (F[1,62]=5.32; p<.0244), while both groups performed better at imitation than they did pantomime (F[1,62]=43.86; p<.0001).

Apraxia Frequency

Based on cutoff scores, frequency of apraxia category by task is shown in Table 2.3. Apraxia was identified more frequently in the imitation task versus the pantomime task, for both the borderline and apraxic groups.

Table 2.3 Frequency of Apraxic Category by Task

	Pantomime	**Imitation**
Apraxic	25.00% (n=12)	29.00% (n=14)
Borderline	8.33% (n=4)	18.75% (n=9)
Non-Apraxic	66.6% (n=32)	52.1% (n=25)

Comparing Apraxic PD Groups Across Task and Dimension

Table 2.4 displays the percentage accuracy of the PD group, but also their Z score in reference to the performance on pantomime of the healthy control participants.

Table 2.4 Pantomime Performance Accuracy of PD

DIMENSION	**APRAXIC**			**NON-APRAXIC**		
	%	SD	Z	%	SD	Z
Location	72.40	13.71	-2.67	85.13	7.60	-0.59
Posture	80.21	11.72	-1.66	97.22	4.28	0.72
Action	66.78	10.61	-3.46	88.28	7.06	-0.28
Plane	66.67	12.31	-2.20	88.69	6.93	-0.09
Orientation	74.17	12.87	-1.76	86.16	8.78	-0.51
Composite	72.04	6.85	-2.98	89.10	3.95	-0.20

With participants in their apraxic and non-apraxic groupings, a 2X5 ANOVA was performed on pantomime Z scores, revealing a significant interaction of group by dimension ($F[4,180]=3.82$; $p<.0004$). Tukey's post hoc analyses revealed significantly more impairment in the action dimension for those categorized as apraxic. Figure 2.1 depicts these results.

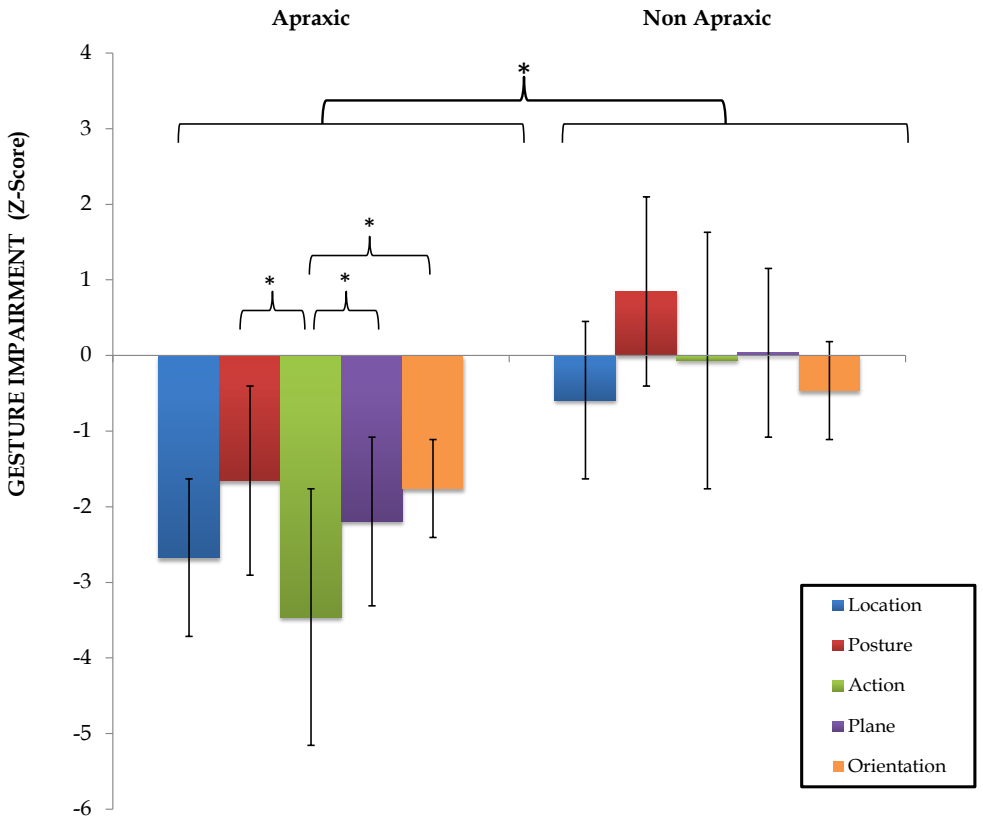

Figure 2.1 Results for pantomime show a more impaired action dimension in the apraxic group

Table 2.5 displays the percentage accuracy of the PD group, but also their Z score in reference to the performance on imitation of the healthy control group.

Table 2.5. Imitation Performance Accuracy of PD

DIMENSION	APRAXIC			NON-APRAXIC		
	%	SD	Z	%	SD	Z
Location	84.15	5.57	-1.50	92.31	6.11	-0.13
Posture	87.95	8.84	-1.35	95.89	6.69	-0.05
Action	76.79	10.19	-3.33	93.97	6.26	0.06
Plane	75.67	8.87	-3.73	92.70	7.77	-0.33
Orientation	85.49	8.68	-2.04	94.57	5.33	-0.07
Composite	82.03	5.22	-4.05	93.89	4.48	-0.18

There was a significant interaction of group by dimension (F[4,180]=11.07; p<.0001). Figure 2.2 depicts these results. Post hoc analysis revealed a greater impairment in the action and plane dimensions specifically within the apraxic groups.

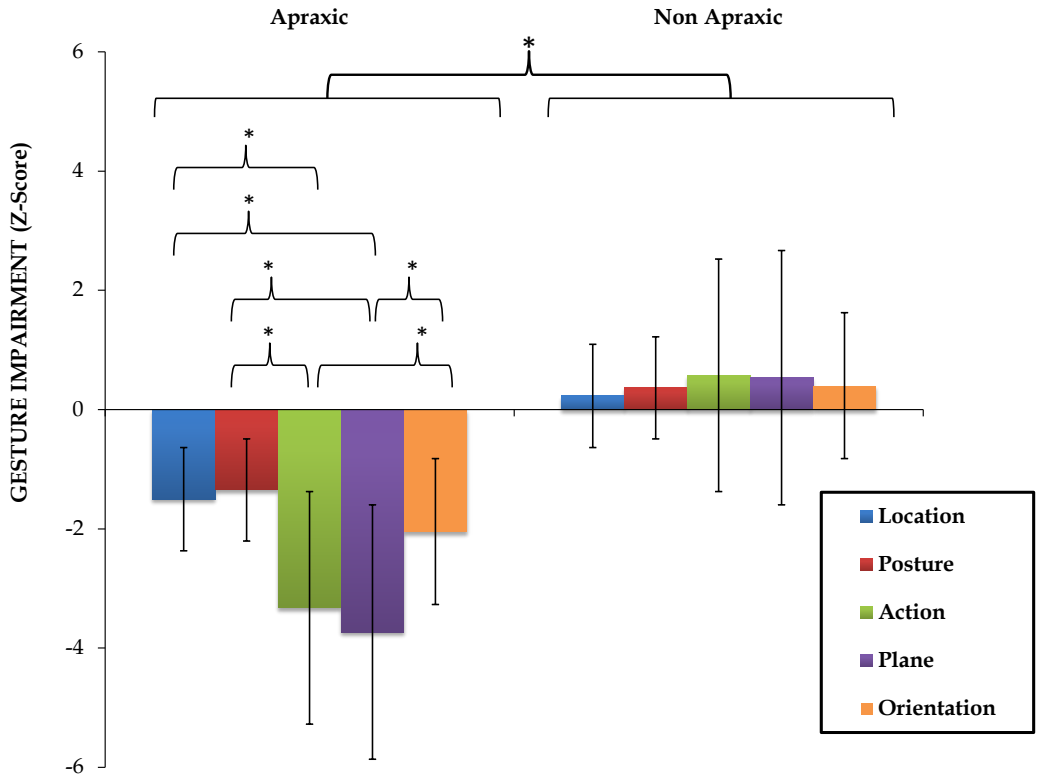

Figure 2.2 – Imitation results show impaired action and plane dimensions for the apraxic group

Patterns of Apraxia

The following final analyses evaluate performances on pantomime relative to imitation. Table 2.6 displays the frequency of PD participants that fall into each pattern of apraxia namely i) P_NI_N: non-apraxic at both pantomime and imitation, ii) P_AI_N: apraxic at pantomime only, iii) P_NI_A: apraxic at imitation only, iv)P_AI_A apraxic at both pantomime and imitation.

Table 2.6 Gestural Performance Accuracy of PD Grouped by Pattern of Apraxia								
Pattern	**Frequency**		**Pantomime Accuracy**			**Imitation Accuracy**		
	N	%	%	SD	Z	%	SD	Z
P_NI_N	32	33.33	89.86	3.62	-0.08	95.10	3.04	0.21
P_AI_N	3	6.25	75.83	3.44	-2.37	89.37	0.63	-1.65
P_NI_A	5	10.41	84.38	2.34	-0.98	83.88	4.43	-3.44
P_AI_A	9	18.75	70.78	7.36	-3.20	80.97	5.23	-4.39

The most severely apraxic participants end up being impaired at both pantomime and imitation. Figure 2.4 displays this relationship below, however results must be considered carefully given the statistical power of the selective impairment groups (P_NI_A, P_AI_N).

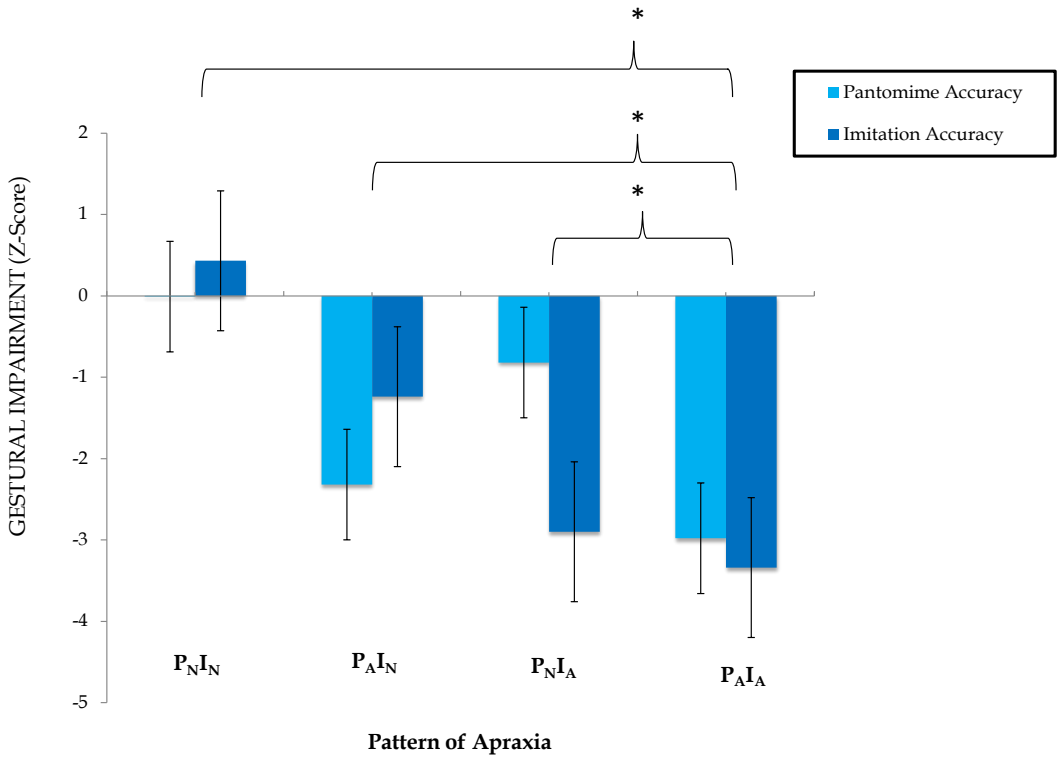

Figure 2.4 Grouped by pattern of apraxia, composite scores for both pantomime and imitation are most impaired in the P_AI_A group.

The Conceptual System

No significant differences were revealed in an independent sample t-test for composite scores of healthy control participants versus PD ($t_{(62)}$=1.69, p<.0958). Means and standard deviations for this conceptual task component of the apraxia battery are found in Table 2.7 below.

Table 2.7 Conceptual Battery Scores

Task Grouping	**Healthy Controls (n=16)**		**PD (n=48)**	
	Score	SD	Score	SD
Tool Naming	93.63	7.5	92.99	8.7
Tool Identification	100	0	98.27	4.3
Gesture Identification	100	0	93.44	6.7
Composite	96.82	3.4	95.24	4.4

For the ANOVA conducted of group (apraxic, non-apraxic) and task (pantomime, meaningful imitation, and meaningless imitation), results showed a significant interaction for (F[2, 86]=4.98, p<.0090). Tukey's Post hoc analysis revealed a significantly greater impairment in non-representational gestures for the apraxic group. There was no difference across tasks for the non apraxic group, and no difference between pantomime and imitation for either group.

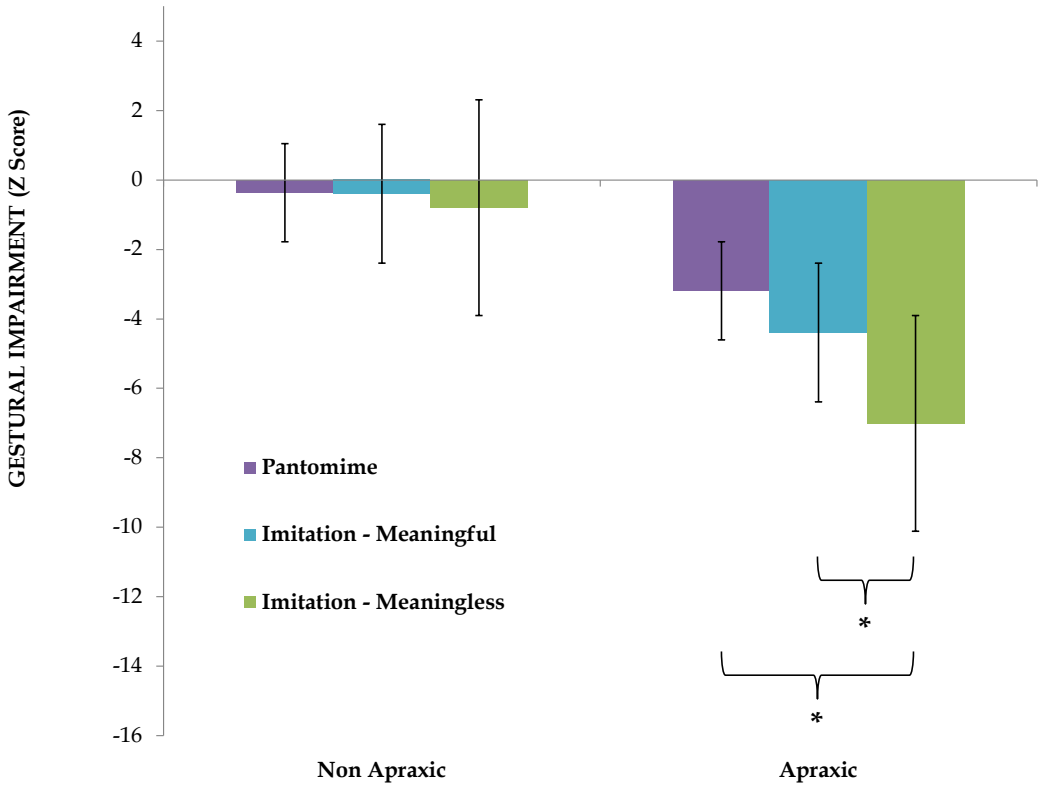

Figure 2.5 – Gestural performance by task and group

The Sensory-Perceptual System: Contributions of the Visual System to Praxis

Three separate one way ANOVAs were performed to examine the effect of visual feedback on pantomime, imitation of meaningful gestures, and imitation of meaningless gestures within the healthy control participants, and there were no significant effects revealed.

Three separate 2 x 2 ANOVAs were performed for pantomime, imitation of meaningful gestures, and imiation of meaningless gestures for group (non-apraxic, apraxic) and visual feedback (eyes closed, eyes open).In pantomime, results showed a significant main effect for visual feedback ($F[1,184]=17.50$, $p<.0001$). Figure 2.6 displays these results.

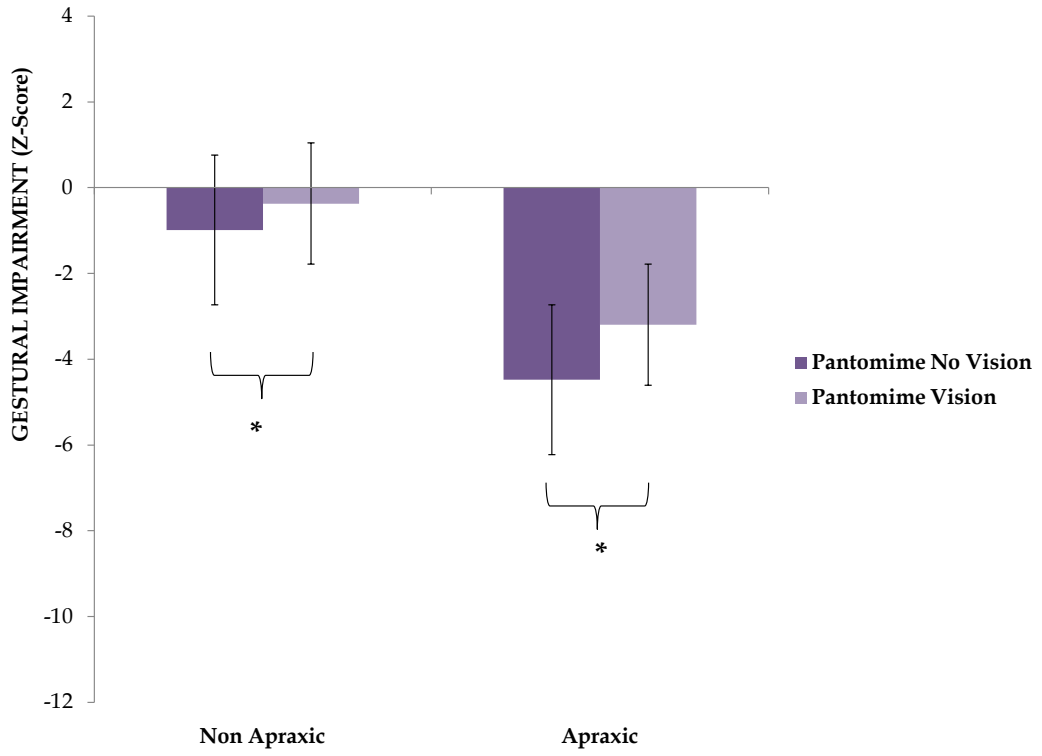

Figure 2.6 PD Participants are more impaired in the pantomime task when visual feedback is withdrawn

In imitation of meaningful gestures, a significant interaction of vision and group ($F[1,45]=8.61$, $p<.0052$), revealed that visual feedback largely hinders performance in the apraxic group, but not the non-apraxic group (please see Figure 2.7).

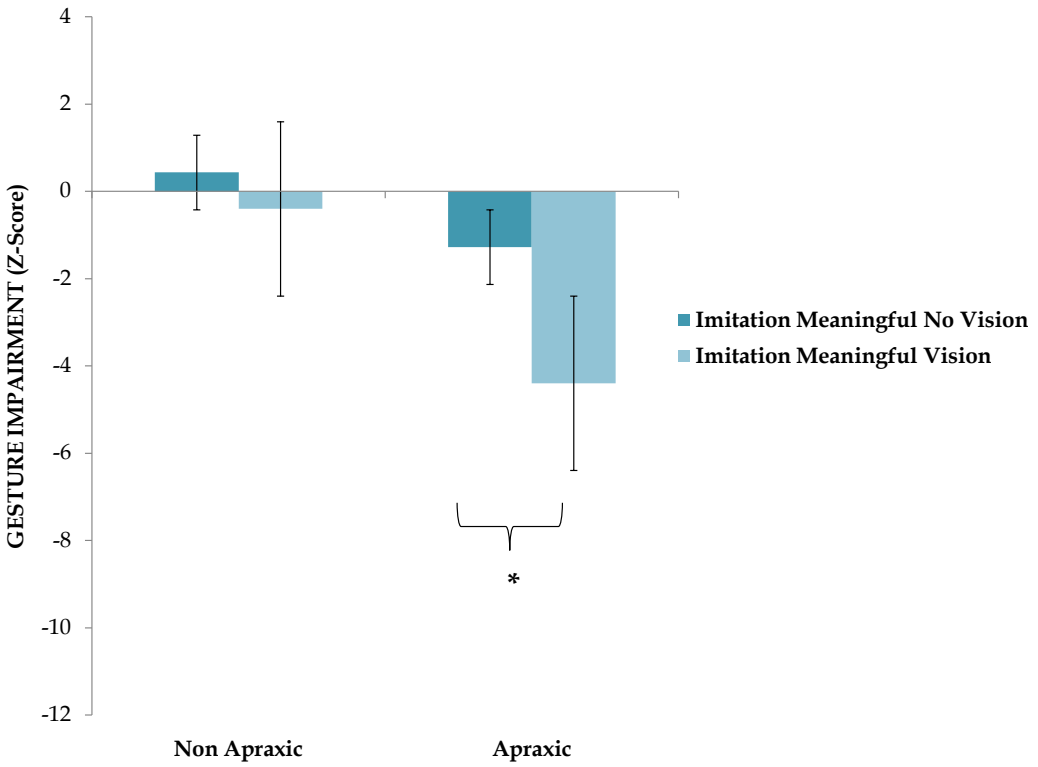

Figure 2.7 PD participants are less impaired when vision is withdrawn in the meaningful imitation task.

In imitation of meaningless gestures, results showed a significant main effect for vision ($F[1,42]=3.80$, $p<.0508$), such that regardless of group, availability of visual feedback impacted performance. Please see figure 2.8 for more information.

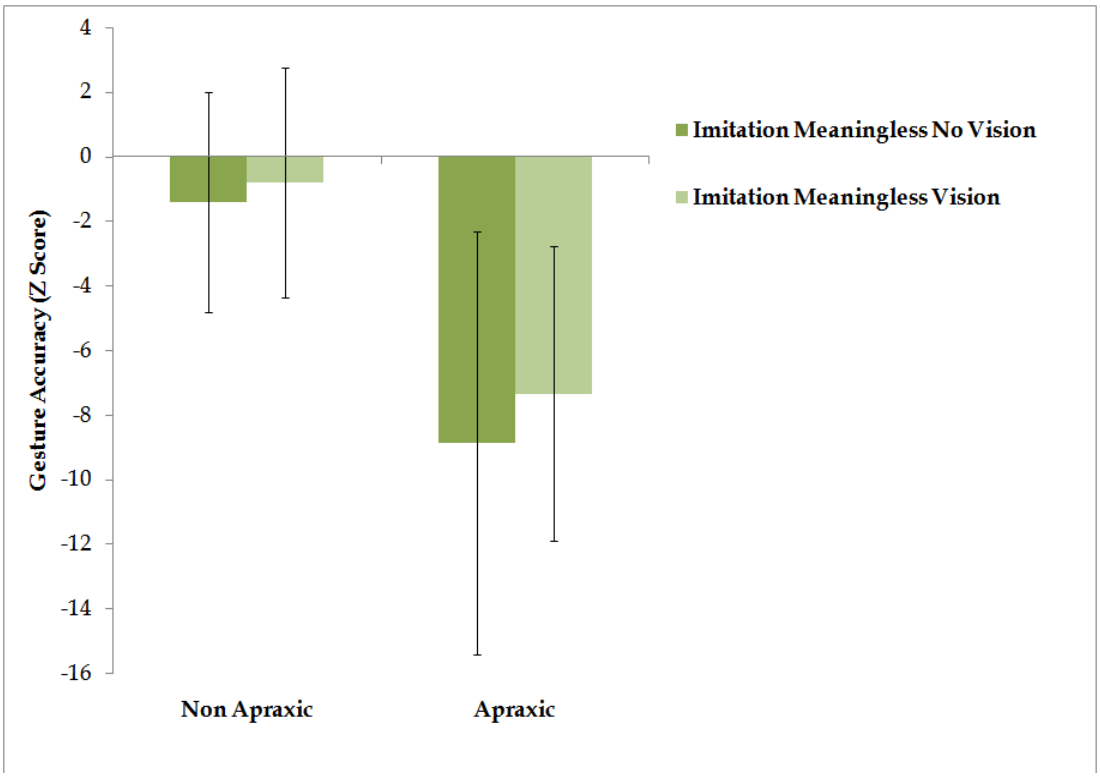

Figure 2.8 PD participants are more impaired for imitation of meaningless gestures when vision is withdrawn

A summary of means and standard deviations for these analyses can be found in Table 2.8.

Table 2.8. Gestural Impairment for PD by Task and Condition

Task/Condition		APRAXIC		NON-APRAXIC	
		Z	SD	Z	SD
Pantomime	Eyes Closed	-4.48	1.38	-0.99	1.76
	Eyes Open	-3.19	1.20	-0.37	0.86
Meaningful Imitation	Eyes Closed	-1.27	1.59	0.43	1.51
	Eyes Open	-4.39	4.82	-0.40	1.63
Meaningless Imitation	Eyes Closed	-8.86	6.56	-1.38	3.40
	Eyes Open	-7.34	4.56	-0.80	3.57

2.4 DISCUSSION

The Model-Based Approach

The goal of the present study was to examine the presence of apraxia in Parkinson's disease, using a comparison of pantomime and imitation as the framework for describing the deficits. The literature for healthy individuals has widely suggested that imitation can be more accurately performed than pantomime (Liepmann, 1988; Roy et al., 1998; Roy et al., 2000; Schnider et al., 1997), and this is true for the group of healthy control participants in this study. Referring to Roy's model, the improvement on imitation of meaningful gestures compared to pantomime is likely because there are contributions from both sensory (visual information) and conceptual systems (action and tool knowledge)[19]. In terms of composite scores, this was also the case for the PD group, however they performed much less accurately than the healthy control participants which was all the more justification to examine the performance on these two tasks more closely.

The current examination was the first time pantomime and imitation were compared in Parkinson's disease using a systematic method for which gestures in both tasks were the same (and thus comparable). Using this direct comparison, a higher frequency of impairment was revealed in imitation compared to pantomime, but there were no differences in overall accuracies (Z scores) across the two tasks. Consistent with the work of Leiguarda(R. C. Leiguarda et al., 1997), a similar proportion of individuals with Parkinson's disease exhibited apraxia. In the current sample of 48 individuals, 12 were found to be apraxic (25%) with respect to pantomime, 14 with respect to imitation (29%).

There seemed to be consistency with past research with respect to the types of errors committed. When specifically examining the most-affected dimensions, action scores were the most impaired regardless of whether pantomime or imitation was being observed. With pantomime there was a trend towards more impairment in the location dimension, and in imitation there was a significant impairment in plane, matching the severity of impairment in action. The errors in the action plane correspond with the difficulty the PD group had with inter-joint coordination and timing while errors in the plane dimension correspond with errors they committed with the spatial trajectory of the limb. Furthermore, errors in the location dimension correspond with the PD group's inability to perceive position of their own limbs. These types of errors are consistent with the findings that most errors in praxis shown in PD populations are of spatial and temporal nature (inter joint coordination, timing, trajectory, and visuospatial) (R. Leiguarda, Merello, Balej et al., 2000; R. C. Leiguarda et al., 1997).

The current study was the first to classify individuals with PD as apraxic at both pantomime and imitation (P_AI_A, n=9, 18.5%), apraxic at pantomime only (P_AI_N, n=3, 6.25%), or apraxic at imitation only (P_NI_A, n=5, 10.4%). This is an important consideration because normally these tasks are not evaluated separately, yet hypothetically have the potential to represent two distinct mechanisms. In Leiguarda's study of PD, the majority of those identified as apraxic were impaired at both pantomime and imitation, but none were selectively impaired at imitation(R. C. Leiguarda et al., 1997). The link between these findings and the severity of the PD progression will be discussed in the following chapter.

Traditionally, impairment on both pantomime and imitation is predominantly attributed to a deficit in executive function, and this was the most common pattern of apraxia found in PD. Interestingly this was also the most common pattern exhibited in individuals with corticobasal

degeneration (CBD), another basal ganglia disorder known for executive function issues(R. Leiguarda, Merello, & Balej, 2000).

In describing the selective impairments, the thorough testing of the conceptual system becomes critical. Due to the higher frequency of PD impaired at imitation, the sensory-perceptual system is of interest because impairment at imitation suggests an impaired ability to analyze visual gestural information. However in gesture recognition and matching tasks, no deficits were revealed in the PD group. For those selectively impaired at pantomime, it could be considered that their tool and action knowledge is damaged. However no deficits were revealed in tool or action naming or identification. To understand both the selective and global impairments better, a comparison of tasks (pantomime, meaningful imitation, and meaningless imitation) was conducted as a representation of the degree to which the conceptual system contributes.

The Conceptual System

While many studies have suggested a preserved ability to identify gestures and tools in PD(Goldenberg et al., 1986; R. Leiguarda, Merello, Balej et al., 2000; R. C. Leiguarda et al., 1997), few comprehensively assess action knowledge through tasks other than gesturing. This study has confirmed that when all conceptual tasks were considered, the PD group was not impaired in knowledge of gestures and tools. The role of the conceptual system in gesture production is revealed in the analysis of pantomime, imitation of meaningful gestures, and imitation of meaningless gestures. These three tasks permit an evaluation of the extent to which the conceptual system can contribute to a skilled act. Pantomime of meaningful gestures represents one extreme in which the performer is completely reliant on their action and tool

knowledge (semantics) to produce the movement from memory. Imitation of meaningless gestures represents the other extreme in which the person is not reliant at all on semantics but must completely rely on the visual gestural information from the performance by the examiner. Thus it is reasonable to assume that imitation of meaningful gestures is the middle ground in terms of contributions of the sensory system (visual encoding and transformation) and the conceptual system (action/tool knowledge and generation of a movement from memory). To articulate what is shown in figure 2.4, when lexical support is available for a gesture as in pantomime and imitation of meaningful gestures, the PD group has less difficulty producing the required movement from memory and with the help of their action and tool knowledge. These results show a deficit in imitation of meaningless gestures suggesting that the direct route for imitation is impaired, but also that access to semantics facilitates performance rather than deters it. Thus in keeping with the notion that the role of the basal ganglia is modulating cortical output to guide execution of movement, this conceptual information (from the cortical areas) helps facilitate movement through a flawed visuomotor transformation process. Since it has been established that visual feedback is an important component in modulating coordinated movements, it is of interest to examine its role in the context of praxis.

Sensory-Perceptual System

This is the first study to investigate the role of visual feedback in gestural performance of individuals with PD. Researchers would argue that PD may result in difficulties estimating motion of their own limbs(Adamovich et al., 1998, 1999). If PD were impaired with vision withdrawn it might be evidence of the specific role of the basal ganglia making use of proprioceptive information, similar to the improvements found in gait and target-reaching when vision is available.

Pantomime of meaningful gestures (figure 2.6), and imitation of meaningless gestures (figure 2.8) were shown to deteriorate with vision withdrawn. However, the most surprising finding is the fact that visual feedback seems to hinder performance in the imitation of meaningful gestures (figure 2.7). Since PD were impaired during meaningless imitation, indicating a flawed visuomotor transformation process(direct route to action), it may be that withdrawing visual feedback promotes the use of the conceptual system(indirect route to action) for gesture production when it is available. Therefore, in most circumstances (and those applicable to everyday life), vision would be advantageous to guide a movement. In the pantomime condition, the conceptual system is the anchor for producing a quality movement, and the visual feedback of the movement provides further support. For the imitation of meaningless gestures, visual feedback provides support to movement production that is completely dependent on direct route to action through visuomotor transformation (albeit, a flawed one). The availability of visual feedback for PD during imitation of meaningful gestures may promote the use of the direct route over the indirect route, and the direct route in these individuals is demonstrably flawed.

General Discussion, Limitation and Future Directions

When assessing apraxia in disorders of the basal ganglia, there is always the dilemma of doing so independently of primary motor impairments. Consistent with other examinations of apraxia in basal ganglia disordered populations (for review please see (Zadikoff & Lang, 2005)), it is possible, through a detailed multidimensional analyses to examine higher order impairment superimposed on elementary motor deficits. This topic is the focus of the chapter to follow in which the asymmetrical onset of PD can be used as a framework to examine the relationship between motor symptoms and apraxia.

This study has several strengths compared to past research conducted in the domain of apraxia. The most notable of these strengths, is the comparison of PD participants with a group of healthy control participants. Thus labeling someone 'apraxic', or deeming their performance abnormal is a literal definition because they are actually being compared to a norm. Previous studies will simply use a cutoff system, rather than a control group. The other major advantage is the evaluation of five separate dimensions of movement, namely i) location, ii) posture, iii) action, iv) plane, and v) orientation, all of which are combined to form a composite score. This is an improvement on 'cutoff' systems, because even though frequency of apraxia is reported, rarely is there a clear description of relative severity of the apraxic group.

Another source of inconsistency in task evaluation is the nature of the tasks themselves. Most assessments of imitation do not involve gesture types that are consistent with what was performed in the pantomime condition. Many of them are a mixture of intransitive gestures or movement sequences that do not match the complexity of the transitive set of gestures performed in pantomime. While the error analysis used in the current study is considered to be very advantageous in describing apraxia, it might be argued that a kinematic analysis would provide a better description of disordered movement as in studies by Poizner et al(Poizner, Mack, Verfaellie, Rothi, & Heilman, 1990). However, these types of analyses are not without flaws, since kinematic profiles have been shown to have a very high variability amongst even the healthy people. These findings point to the need to develop new approaches that integrate a qualitative error analysis with a completely objective kinematic analysis.

A potential limitation with the analysis system used in the current study is that it may not reliably depict qualitative differences within some of the performance dimensions. For example, in the posture dimension, a person may receive a score of zero for creating a very awkward and

incorrect hand posture configuration, or they could receive a zero because they are using a body part as the object (e.g. rather than pretending to firmly grasp a comb, using fingers as the teeth of a comb to detangle their hair). While this is incorrect, it's not conceptually that far off. This is why the composite score is important as well as the sum of its parts. The significance of body part as object errors (BPAOS) has been widely debated(Goldenberg et al., 1986; R. C. Leiguarda & Marsden, 2000; Raymer, Maher, Foundas, Heilman, & Rothi, 1997) and is a topic for future investigation.

For an accurate performance in the delayed imitation condition, working memory needs to be intact, and while it seems unlikely, there is the potential for selective impairment in concurrent imitation as it can bear a resemblance to dual task paradigms. Preliminary analyses regarding the concurrent imitation task have shown no statistical differences between delayed and concurrent imitation on a small group of PD(King, Almeida, & Roy, 2009). A few other studies also support this notion that working memory is not a large contributing factor in the deficits revealed in imitation(Goldenberg et al., 1986), however to fully rule out this suggestion, concurrent imitation tasks should be analyzed in full and compared to the delayed imitation of the same gestures. However, it would not be possible to conduct this task with the no-vision condition (hence why delayed imitation was chosen as a task). Inclusion of concurrent imitation should be considered in future undertakings.

Overall Conclusions

The results of the current study highlight the value of the model-based approach to examining apraxia in Parkinson's disease in several ways. While the findings of the current study were consistent with past research in the sense that there was a similar frequency of people

with apraxia identified, the methods of the current study seemed to be more sensitive to identifying selective impairment in either pantomime or imitation. This direct comparison between pantomime and imitation allowed for evidence for an impaired direct route to action. This is revealed by poor performances for the imitation of meaningless gestures, as well as the hindrance visual feedback seems to inflict on meaningful imitation. As impairment on both pantomime and imitation is the most common pattern for impairment in this group, it may be a reasonable suggestion that apraxia in PD is driven by deficits in the general organization and control of movement. These deficits may be superimposed on an inability to translate visuomotor information into action.

CHAPTER 3: A NOVEL APPROACH FOR DISCERNING APRAXIA FROM PRIMARY MOTOR DEFICITS IN PARKINSON'S DISEASE

3.1 INTRODUCTION

Apraxia is clinically well-defined across a variety of disorders however there is debate as to whether these features can be adequately distinguished from elementary motor deficits. Critical to the definition of apraxia is that it cannot be accounted for by primary motor deficits. Primary motor symptoms are a prominent characteristic in disorders of the basal ganglia such as Parkinson's disease (PD), and include tremor, rigidity, bradykinesia, and postural instability as the most common features. Several studies have attempted to examine apraxia in PD. Sharpe (Sharpe et al., 1983) tested a group of PD on transitive pantomime and imitation of non-representational hand gestures, observing that they generally made the most spatial errors on the non-symbolic movements. Goldenberg et al (Goldenberg et al., 1986) also found impaired imitation of movement sequences in a group of PD. In another study by Grossman et al (Grossman et al., 1991), 63% of individuals with PD differed in their performance of transitive pantomime, with the most common error being using the body part as an object ("BPAO"). These studies each argued that apraxia scores did not correlate with motor severity which has helped to promote the general acceptance that apraxia can be superimposed on classic Parkinsonian motor disability.

Little is known about the relationship between the amount of basal ganglia damage and the severity of apraxia in PD. Much of what is known about apraxia is from the stroke literature in which there is a positive correlation between lesion size and the severity of apraxia(Kertesz & Ferro, 1984). The recovery process from apraxia in stroke can also be predicted based on the size and location of the lesion(Basso, Capitani, Della Sala, Laiacona, & Spinnler, 1987a, 1987b).

However, basal ganglia damage in PD is not due to a focal injury but a progressive degenerative process. Corticobasal Degeneration (CBD), characterized by the co-existence of frontal-parietal and basal ganglia degeneration, might be a better comparison for this pathology. Some of the most severe examples of apraxia are found in CBD(R. Leiguarda, Merello, & Balej, 2000), characterized by deficits in inter-joint coordination and disruptions in spatial accuracy(Merians et al., 1999). A case-based tracking of the course of apraxia in this disease revealed that gesture performance deteriorated as the disease progressed (rarely stabilizing or improving)(Vessela Stamenova, 2009). The objective of the current study is to examine the relationship between apraxia and disease severity in PD by comparing gestural performance across varying levels of motor symptoms present (as quantified by the UPDRS). As seen in CBD, it might be reasonable to predict that apraxia is more pronounced (greater severity) in individuals with PD who are in later stages of the disease (as determined by a greater presence of motor symptoms).

The current study includes a much wider range of disease severities from a larger PD group. While previous research argues that studying PD at their optimal dose of medication is effective because it minimizes the presence of motor symptoms(Roy, 2000), the current study argues that motor symptoms provide a useful framework to study apraxia as the basal ganglia should be in its "least-contributing" state to truly understand the consequences of its dysfunction for normal voluntary movement. Therefore the current investigation examines participants after a withdrawal from dopaminergic medication.

Study Objectives and Predictions

This study evaluated whether apraxia can be related to the overall severity of motor symptoms, while remaining dissociable from the cardinal motor symptoms of PD. The foremost

obstacle at this point, is finding a method to discern higher order impairment of praxis from elementary motor disability. The Unified Parkinson's Disease Rating Scale (UPDRS) is the gold standard for assessment in this population (a full version of this scale can be found in Appendix B)(Fahn, 1987). If isolated damage to the basal ganglia can cause apraxia impairments, it might be expected that the most severe individuals in terms of motor symptoms might experience the most severe apraxia. Therefore it is predicted that total UPDRS will correlate with praxis impairment as pooled between the two limbs.

The UPDRS not only quantifies total motor symptoms for an individual, but also the breakdown of symptoms for each limb. One advantage of studying PD is the characteristic asymmetrical onset of motor symptoms. Gestural impairments can also be tracked for each limb separately and may present unilaterally or bilaterally. Due to the fact that higher order praxis involves the contribution of parallel parieto-frontal circuits, and complex inter-hemispheric activity(Zadikoff & Lang, 2005), apraxia and primary motor deficits should not be present in the same proportion across limbs. For example, someone who has dominant Parkinson's symptoms in their right upper extremity may not necessarily have a greater severity of apraxia in the right hand. In other words, limb specific motor symptoms should not correlate with limb specific apraxia. Therefore, it is predicted that the degree to which the motor symptoms are lateralized, should not correlate with the degree to which the apraxia is lateralized.

Furthermore, because apraxia should not be accounted for by primary motor deficits it must be ensured that the evaluation of apraxia is not directly influenced by the common symptoms of PD including tremor, rigidity, bradykinesia, hypokinesia, and akinesia. While these symptoms may slow the gesture, delay it, or in some cases reduce the amplitude of it, it is unlikely that the quality of gestures could be sufficiently distorted or unrecognizable to deem

someone apraxic. Therefore it is predicted that these symptoms, as they are represented by their sub-scores within the UPDRS, would not correlate with performance on gestural tasks.

3.2 METHODS

Participants

The experimental group for this study consisted of 48 individuals meeting strict clinical criteria of idiopathic Parkinson's disease. These participants were assessed after an average withdrawal of 14.9 ± 4.3 hours from their anti-Parkinsonian medication (see appendix A for demographics including details regarding withdrawal times). Only those with a minimum score of 80 on the Modified Mini Mental State Examination were included, and all were right handed.

In addition, performance of 16 age-matched healthy community volunteers, who were right handed, and had no history of neurological diseases comprised a control group. The mean age for this group was not statistically different from the PD group [$t(1,62)=0.9807$, $p > .3307$]. Basic demographics can be found in Table 3.1, with more specific individual details available in Appendix A.

Table 3.1 Study Participant Demographics

Group	Age (Mean ± SD)	UPDRS-III (Mean ± SD)	Disease Duration (Mean ± SD)
PD (n=48)	69.2 ± 8.9 years	32.9 ± 9.6	7.9 ± 6.2 years
Healthy (n=16)	68.3 ± 6.7years	n/a	n/a

Gestural Tasks and Performance Scoring

Participants were required to pantomime and imitate eight meaningful gestures with both upper limbs, (for complete list please see Appendix B). In the pantomime condition participants were asked to pretend how to use or act on an object to perform a certain action. For example

"Show me how you would use a knife to slice a piece of bread". In the imitation condition participants were required to copy the examiner's demonstration of each gesture. Pantomime was always performed first to avoid cuing the participants as to how each gesture was properly performed. Each participant was videotaped for subsequent analysis.

Scoring

A composite score was formed by the average percentage accuracy within five dimensions of movement including location, posture, plane, and orientation. Each of the eight gestures were given a score of 0, 1,or 2 as clearly defined by separate criteria yielding a total out of 16 for each dimension (please see appendix A for scoring). For most analyses, scores for the right hand and left hand were pooled together within the PD and the healthy control groups, with the exception of the laterality analysis in which the limb-specific scores were used.

Analysis

Percentage accuracy of gesture performance for each PD participant was converted to a Z-score with reference to the mean and standard deviation of the healthy control group. A cutoff score was developed based on the average composite scores of the healthy control participants such that PD participants could be classified as apraxic, borderline apraxic, or non apraxic with reference to the mean of the healthy controls. PD participants who scored less than one standard deviation below the mean of the healthy controls were considered to be the non-apraxic group. Those who scored between one and two standard deviations below the mean of the healthy controls were classified as borderline apraxic, while those scoring below two standard deviations from the mean of the healthy group were classified as apraxic.

Correlations

Z-scores for gestural performance of pantomime and imitation were compared to total UPDRS score of each person in separate correlation analyses. A t-test was performed for UPDRS scores of the apraxics and non-apraxics as justification for treating them as separate groups and conducting separate correlations. An upper limb score was extracted from the UPDRS for tremor, rigidity, and issues pertaining to voluntary movement (bradykinesia, akinesia, hypokinesia). This would include UPDRS items 20 and 21, 22, and 23-25 respectively excluding scores in accordance with the head, neck, and lower extremities. Correlation analyses were between scores for apraxic and non-apraxic categories and gestural composite scores for both pantomime and imitation.

To determine how lateralized the PD symptoms were for each participant, the upper limb primary motor scores were broken into right and left side totals, and then each score was divided by overall UPDRS. This score represents the proportion to which unilateral symptoms contribute to the overall motor impairment of a participant. The resultant score for the right side symptoms was then entered in a correlation analysis with gestural impairment of the right hand, and likewise for the left side symptoms and left gestural impairment. A more detailed description of the UPDRS can be found in Appendix C.

3.3 RESULTS

The relationship between overall primary motor symptoms and gestural impairment

An independent samples t-test was conducted between UPDRS scores of apraxics and non-apraxics yielding a significantly greater severity in average UPDRS amongst the apraxic group ($t_{(46)} = 2.25$, $p < .0310$) compared to the non-apraxic group. There was a significant correlation between pantomime and total UPDRS score within the apraxic group, but not the non-apraxics. Details of the correlation analyses for pantomime and imitation are presented in Figure 3.1 and Table 3.2.

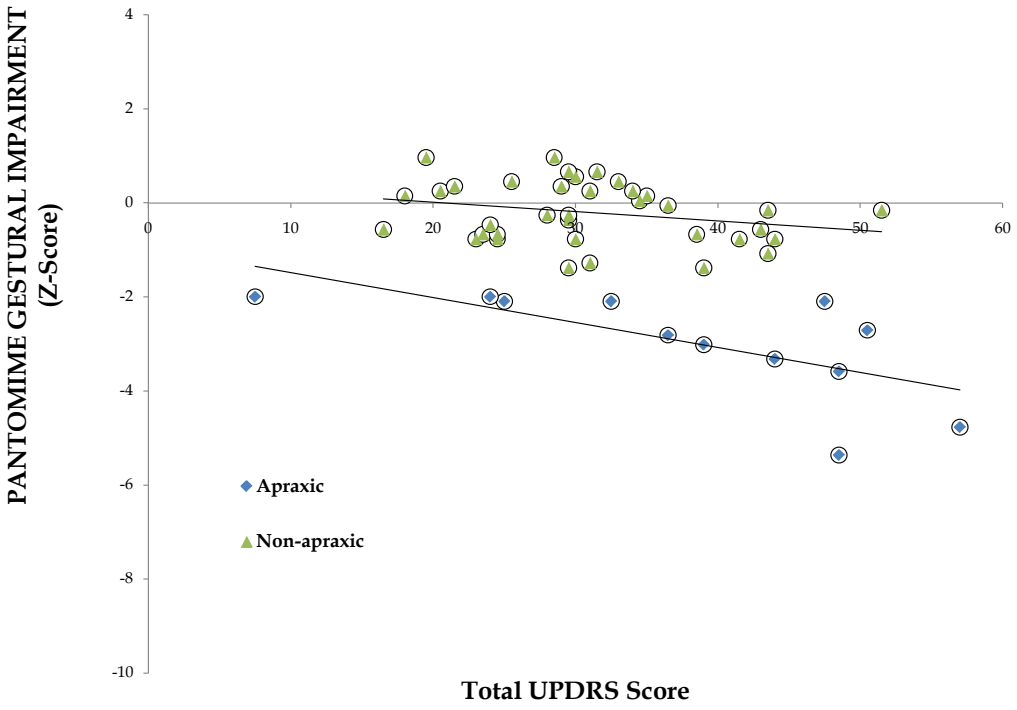

Figure 3.1 Relationship between overall motor severity and impairment in pantomime

There was a stronger significant correlation between imitation and total UPDRS score within both the apraxic and non-apraxic groups. An independent samples t-test was conducted between UPDRS scores of apraxics and non-apraxics yielding a significantly higher average UPDRS(greater severity) amongst the apraxic group ($t_{(46)} = 4.55$, $p < .0001$) compared to the non-apraxic group. Details of the correlation analyses for pantomime and imitation are presented in Figure 3.1 and Table 3.2.

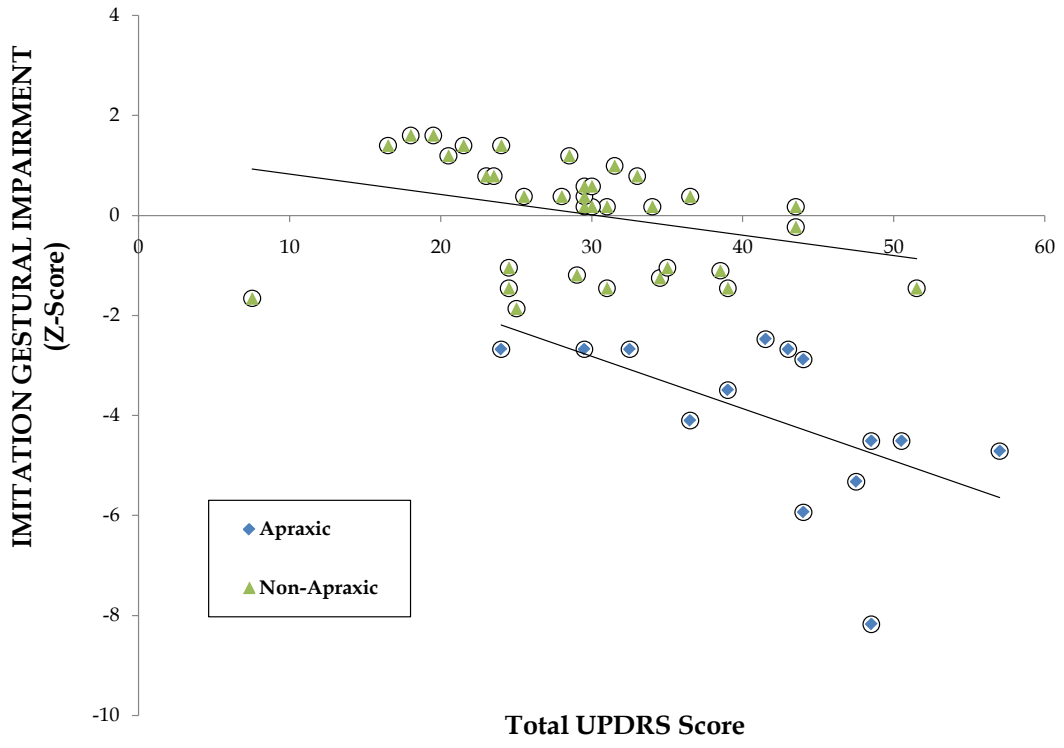

Figure 3.2 Relationship between overall motor severity and impairment in imitation

Table 3.2 – Relationship between total UPDRS and gestural impairment			
TASK	**Group**	**r**	**p – value**
Pantomime	Apraxic	-0.669	.017*
	Non-Apraxic	-0.252	.137
Imitation	Apraxic	-0.570	.033*
	Non-Apraxic	-0.534	.001*

*denotes significance at an alpha level of $p \leq 0.05$

The relationship between cardinal motor symptoms and gestural impairment

Correlations were performed for apraxic and non-apraxic groups separately between primary motor scores (namely tremor, rigidity, and bradykinesia as derived from voluntary movement scores) and gestural performance for pantomime and imitation. The only correlation analysis to reach a level of significance is within the non-apraxic group for rigidity. All other correlations failed to reach significance at an alpha level of .05. Table 3.3 summarizes these findings for pantomime.

Table 3.3 – Relationship between motor symptoms and gestural impairment in pantomime			
PD Symptoms	Group	R	p – value
Tremor	Non-Apraxic	+0.022	.901
	Apraxic	-0.415	.180
Rigidity	Non-Apraxic	-0.331	.050*
	Apraxic	-0.313	.320
Voluntary Movements	Non-Apraxic	+0.028	.871
	Apraxic	-0.329	.296

*denotes significance at an alpha level of $p \leq 0.05$

Table 3.4 – Relationship between motor symptoms and gestural impairment in imitation			
PD Symptoms	**Group**	**r**	**p – value**
Tremor	Non-Apraxic	-0.136	.939
	Apraxic	+0.019	.948
Rigidity	Non-Apraxic	-0.185	.295
	Apraxic	-0.267	.356
Voluntary Movements	Non-Apraxic	-0.234	.183
	Apraxic	-0.441	.107

Figure 3.3 shows the composite gestural scores pitted against each of the aforementioned UPDRS sub-scores.

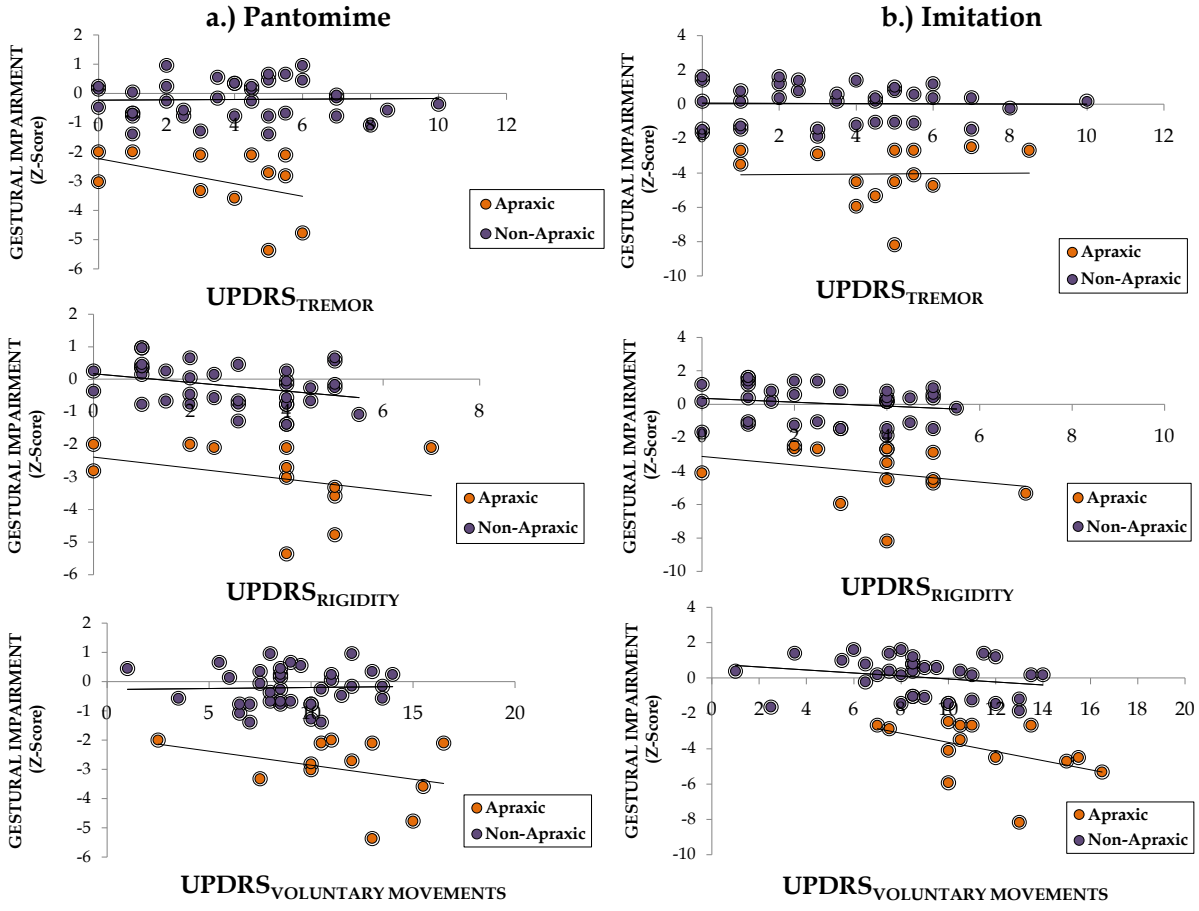

Figure 3.3 Correlations for cardinal motor symptoms and gestural performance.

The relationship between laterality of primary motor symptoms and laterality of apraxia

Correlation analyses were conducted between right side PD symptoms (as a proportion of total severity) and right side apraxia composite scores for both pantomime and imitation, and there were no significant relationships or trends identified. This was also the case for left side PD symptoms and left side apraxia. Figure 3.4 depicts these results and table 3.5 summarizes this information.

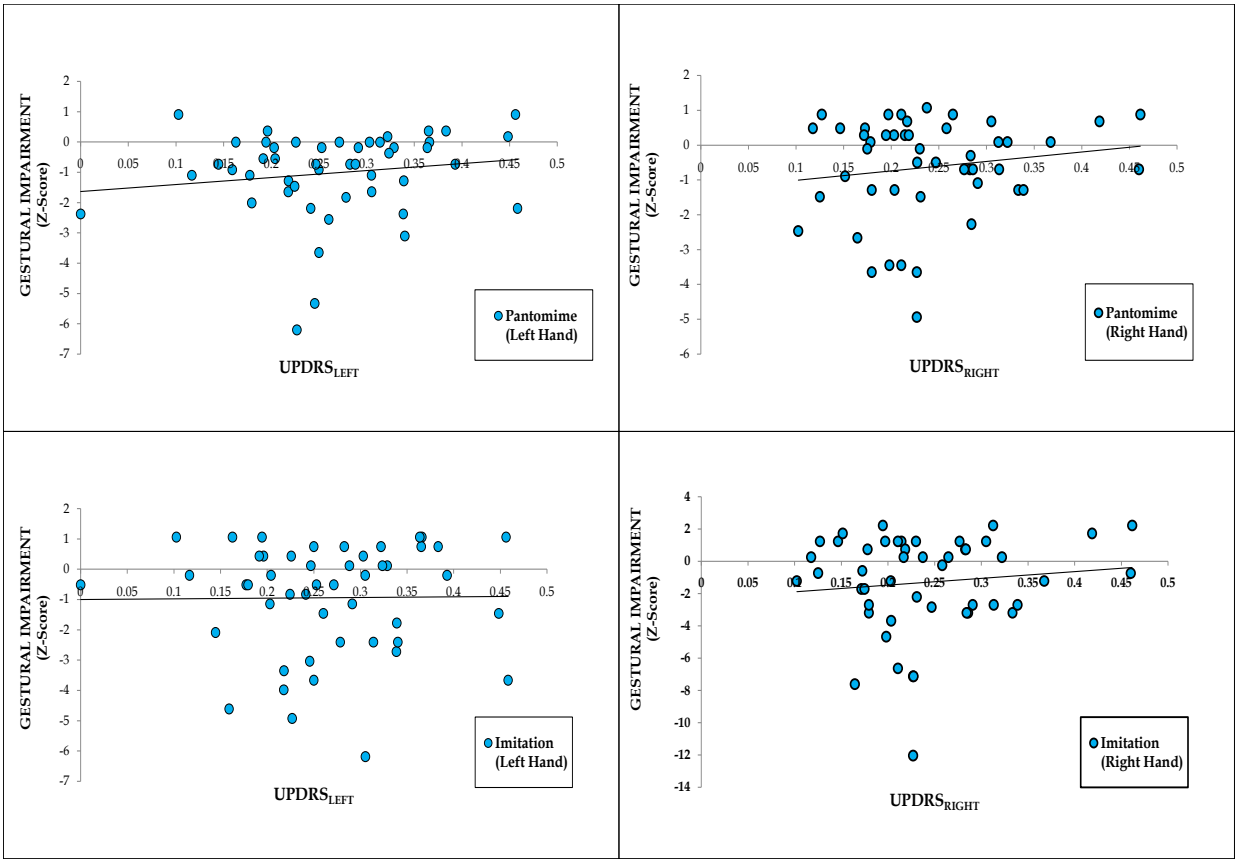

Figure 3.4 Degree to which unilateral symptoms contribute to overall PD Symptoms versus limb specific apraxia symptoms

Table 3.5 – Relationship between laterality of motor symptoms and of gestural impairment			
PD Symptoms	**Task**	**r**	**p – value**
LEFT	Pantomime	0.149	.311
	Imitation	0.011	.939
RIGHT	Pantomime	0.154	.294
	Imitation	0.113	.444

3.4 DISCUSSION

The overall objective of the study was to examine the relationship between apraxia and total motor symptom severity, including the relationship between apraxia and specific cardinal symptoms. The most important goal of the current study was to verify that apraxia can be evaluated independently from primary motor symptoms in the evaluation of gestural performance.

The Relationship between Apraxia and Total Primary Motor Severity

The current study yielded a strong correlation between total motor severity and gestural impairment for both pantomime and imitation. This is a unique result that suggests a link between dysfunction of the basal ganglia and apraxia. This is an important point because it has been previously argued that basal ganglia dysfunction must be accompanied by pathological cortical involvement to manifest apraxia(R. Leiguarda, Merello, Balej et al., 2000). While flawed cortical components cannot be ruled out, it seems that there is a direct relationship between the amount of basal ganglia damage (quantified by total UPDRS) and severity of apraxia. This could be evidence that restricted damage to the basal ganglia could cause apraxia. That said, it is important to consider the maladaptive plasticity changes that could occur with respect to motor cortex(Bagetta, Ghiglieri, Sgobio, Calabresi, & Picconi, 2010; Cenci, Ohlin, & Rylander, 2009).

Interestingly, there is a higher correlation for imitation than pantomime, and notably both the apraxic and non-apraxic groups have a stronger correlation for imitation and total UPDRS. For total UPDRS and pantomime a correlation is found only in the apraxic group. As such, imitation may be the more relevant task for praxis deficits specific to PD (issues with visuomotor transformation), and even at lower severities a relationship can still be detected.

The relationship between Apraxia and Cardinal Motor Symptoms

The correlation analysis demonstrated that cardinal motor symptoms and apraxia were mutually exclusive since there were no significant correlations with gestural impairment in the apraxic group. The UPDRS scores used for this part of the study were chosen because of the likelihood they would interfere with upper limb hand or arm movements. This is why tremor of the hands was chosen as opposed to a total tremor score, omitting such scores as face, lips, chin, and lower extremities. As well, it seemed relevant to use only the upper limb rigidity scores, omitting any lower limb or neck rigidity ratings. The voluntary movement scores are of interest because they tend to incorporate slowness, decreased amplitude, and any arrests of movement, all items that could in theory, contribute to a poor gestural performance. Until now the most thorough examination of the relationship between motor symptoms and apraxia in PD was conducted by Leiguarda et al(R. C. Leiguarda et al., 1997). This study did not comment on the relationship of total UPDRS score and gestural impairment, however a regression analysis was conducted with no significant correlations for rigidity scores, finger taps, opening and closing of the fist, hand movements and alternating movements. The present study showed the same result revealing no correlations for apraxia with the UPDRS subsets, however the current evaluation chose subsets that are much more applicable to gesture production of the upper limbs. It is noteworthy that no correlations were revealed in the non-apraxic group with one exception. For the non-apraxic group there was a correlation for rigidity and gestural scores for pantomime only (not imitation). Perhaps those who are rigid-dominant put less effort into producing a gesture from memory (due to the discomfort), however when imitating, the effort level is matching that of the performer. Nonetheless these results are consistent with the notion that apraxia can be evaluated without being misconstrued by the presence of cardinal motor symptoms.

In summary of these results, it appears that the correlation with the overall UPDRS motor score likely reflects the overall integrity of the basal ganglia and suggests an integral role of the basal ganglia on praxis. However, the specific motor symptoms that are most likely to influence upper limb gesture performance showed no correlation with apraxia which strongly speaks against an influence of PD motor symptoms on praxis.

The Relationship between Apraxia and Laterality of PD Symptoms

The final objective of the study was to verify that the outward manifestation of primary motor symptoms and apraxia are distinct. This was accomplished using the asymmetrical onset of Parkinson's disease motor symptoms as a framework. It was hypothesized that the more affected limb in PD was not consistently the more apraxic limb, which would argue against the idea that there is a direct influence of primary motor symptoms on the manifestation of apraxia. Therefore while apraxia and primary motor deficits can co-occur, they may not directly influence the outward expression of each other. The laterality analysis in the current study essentially showed that bilateral apraxia is not necessarily accompanied by bilateral PD, and unilateral apraxia is not necessarily accompanied by unilateral PD. This is consistent with results by Doan et al, in which PD demonstrated bilateral qualitative reaching impairments despite clinically determined asymmetries(Doan, Melvin, Whishaw, & Suchowersky, 2008).

General Discussion, Limitations and Future Direction.

Up until this point primary motor deficits have been viewed as an obstacle or a hindrance in apraxia assessment and researchers have attempted to minimize the presence of symptoms by examining participants at the optimal dosage of their Parkinsonian medication(Roy, 2000). Leiguarda et al. noted that apraxia impairment did not change significantly between OFF and ON

medication states(R. C. Leiguarda et al., 1997).While this finding is interesting, it does not rule out the value of evaluating PD off their medication, nor does it allow for inferences regarding the role of the basal ganglia in praxis. This finding merely hints that apraxia may not respond to Parkinson's medication. An important limitation about these previous findings (and other studies to date in general) is that the range of disease severities is quite narrow and on the low end of the spectrum when taken from a scale for which the maximum is 108 (average UPDRS motor score in the Leiguarda study was 7.9 ± 5.1 'ON' state, 17.4 ± 8.6 'OFF' state). Thus it is possible to dissociate and evaluate apraxia even in the most severe cases of primary motor symptoms.

It is also important to note that even when testing PD in an 'ON' state, there will still be motor symptoms present and they can be highly variable at times. After five years of treatment, 40-75% of patients develop motor fluctuations, and several experience a "wearing off" phenomenon such that the duration of benefits from dopamine becomes increasingly shorter(Almeida & Hyson, 2008; Rao, Hofmann, & Shakil, 2006). This "ON-OFF" effect is often unpredictable and abrupt, varies not only within but between participants, and is difficult to control particularly during the lengthy test sessions that are characteristic of apraxia batteries.

Further, while it is apparent that medication can dramatically improve some aspects of movement and balance in many (Rao et al., 2006), this is accompanied by several long term and short term side effects. Medication can also produce its own type of motor deficit in the form of dyskinesias which can cause as much disruption and discomfort as other PD symptoms. While being "OFF" medication is a source of temporary discomfort, the rationale for depleting the PD group of their dopamine replacement is twofold: i) fluctuations of motor symptoms and the presence of dyskinesias will be minimal for the entire testing period, and ii) the basal ganglia is in its "least-contributing state", which better represents the consequences of its dysfunction in

healthy motor control. Therefore, the current study challenges the assumption that individuals with PD should be studied on their medication to properly examine praxis, and in fact argues that testing in an 'OFF' state is a clearer depiction of the basal ganglia's role in praxis.

This brings us to the limitations of the study. It is important to point out that both the UPDRS and apraxia battery are rated subjectively. However, the UPDRS is always completed first upon a participant's arrival, therefore there should not be any bias in the rating of PD symptoms as the rater is unaware of the participant's gestural performance. Moreover, because gestural performance is videotaped and rated at a later time, the rater is always unaware of an exact UPDRS score. There is no way to be completely blinded during the evaluation of the gestural impairment as the PD symptoms of each participant are outward and obvious, therefore one could speculate at the approximate severity of motor symptoms. Nonetheless the criteria for both the apraxia battery and UPDRS are very-well defined and leave little room for personal interpretation. Despite being qualitative in nature, items within both assessment tools leave little room for personal interpretation and both bear a high inter-rater reliability. Test–retest reliability has not been yet established for the apraxia battery however the inter-rater reliability has been demonstrated at 0.80(Roy et al., 1998). The test-retest reliability of the UPDRS motor section (III) has been measured at 0.90, while the inter-rater reliability has been measured as satisfactory by a number of studies(Martinez-Martin et al., 1994; Rao et al., 2006; Richards, Marder, Cote, & Mayeux, 1994).

On that note, it is necessary to be skeptical regarding the amount of inference that can be extracted from testing between participants of various disease severities. While this provides insight into the differences between low severity and high severity cases of PD, to truly

understand the course of apraxia in this disease, longitudinal studies should be conducted with those who were determined to have apraxia.

As a future direction it would be valuable to explore the frequency to which bilateral apraxia occurs with bilateral PD symptoms (those who are also more clinically advanced), and the frequency to which unilateral apraxia occurs with unilateral PD. This was beyond the scope of the current study as it is difficult to distinguish between unilateral and bilateral Parkinson's disease, and there are no standard criteria for creating these distinctions. Thus at this time it was more reasonable to define asymmetries in PD symptoms on a continuum. Defining criteria for classifying unilateral and bilateral apraxia would also be an important step.

Overall Conclusions

While it is possible that the apraxia and primary motor impairment seen in PD may share some of the same underlying neuropathology, there is no direct influence of motor symptoms on apraxia in PD. This was supported by the correlation analysis between the cardinal motor symptoms and gestural impairment that failed to reach significance, as well as the lack of correspondence between the limb specific manifestation of PD symptoms and apraxia. In summary, in the evaluation of apraxia in individuals with PD, it is the cases of greater severity that experience the most apraxia as demonstrated by the correlation between total UPDRS and gestural impairment scores. However, there is no significant relationship between specific primary motor deficits and gestural performance, which lends credibility to the notion apraxia can be discerned from elementary motor issues.

CHAPTER 4: A NOVEL & SYSTEMATIC APPROACH TO LOWER LIMB APRAXIA

4.1 INTRODUCTION

Despite the considerable attention gait apraxia has garnered, it remains to be one of the most poorly understood symptoms in neurology. Gait apraxia, is defined as abnormal walking patterns that, alike with other apraxias, are not the product of a primary motor disturbance. However gait apraxia has been widely debated as a potential misnomer as per the strictest definitions of apraxia, that is to say apraxia is the inability to "perform skilled or learned motor acts"(Shik & Orlovsky, 1976). Many would argue that locomotion is a repetitive motor program controlled at the spinal level, and modulated by regions of the brainstem, and thus not a consciously learned act(Zadikoff & Lang, 2005). Another reason it has been thought to be a misnomer is gait apraxia rarely associates with upper limb apraxia and the converse is true such that those with upper limb apraxia often display normal walking patterns(Geschwind, 1975). Elble's discussion of higher level gait disorders puts forth that we should "aim beyond the notion of gait apraxia" when discussing gait disorders as there are no straightforward diagnostic criteria for labeling someone with gait apraxia (Elble, 2007). Elble classifies Parkinson's freezing as one of the highest level gait disorders, characterized by damage to the basal ganglia thalamocortical loop (for diagnostic criteria please see (Nutt, Marsden, & Thompson, 1993). Although not present in everyone, freezing is one of the most debilitating symptoms of Parkinson's disease (PD) as it is characterized by a sudden inability to initiate or continue walking. Nearly one third of individuals with PD experience freezing episodes which lead to falls and decreases in autonomy and quality of life(Bloem, Hausdorff, Visser, & Giladi, 2004). Currently the relationship between apraxia and freezing of gait in Parkinson's disease is not known.

Gait apraxia is also often linked with gesture impairment in the lower limbs, which is in contrast, very infrequently mentioned in the literature. Upper limb apraxia is studied using a multimodal gesture approach(Heath, Roy, Westwood, & Black, 2001; R. C. Leiguarda et al., 1997; Roy et al., 2000), and while the lower limbs have the potential to be studied using a similar framework, there has been a nearly exclusive focus on the upper limbs. This is primarily due to the fact that the lower limbs have fewer degrees of freedom resulting in a limited repertoire for complex movements. It is quite the arduous task to generate a list of both object related and symbolic gestures for the lower limbs that are universally familiar, can be done with each leg/foot independently, and can be done sitting down to avoid the confounds of maintaining balance.

Recently, the first study that systematically evaluated lower limb apraxia showed that of seventeen participants with unilateral stroke presenting with upper limb apraxia, severe lower limb apraxia emerged in six of these participants(Ambrosoni, Della Sala, Motto, Oddo, & Spinnler, 2006). Results of this study showed that lower limb apraxia occurred with upper limb apraxia particularly in cases with larger lesions than those with upper limb apraxia only. Lower limb apraxia has never been examined in a basal ganglia disorder such as Parkinson's disease. Moreover there is a need to assess lower limb gestural impairment more systematically than the previous study. Firstly, the lower limb gestures need to be brought to a level of complexity more comparable to the upper limbs as they have been very simple in nature and strictly intransitive. Furthermore, pantomime and imitation conditions should be created to make the same comparisons as shown in the upper limbs. Previous work has only examined imitation. Thus the objective of the current study was to create a novel assessment tool as an addition to the upper limb methods to observe the association between upper limb apraxia and lower limb apraxia.

Study Objectives & Predictions

The current study had multiple objectives. The first was to use the same dimensional approach for assessing pantomime and imitation in the lower limbs as used for the upper limbs to examine if the nature of the errors was similar. If this is the case, it would be expected that errors in the action dimension will be the most prominent in both tasks, while the plane dimension is also particularly impaired for the apraxic participants in the imitation condition. Furthermore, if the lower limbs follow the same pattern as the upper limbs, it is predicted that participants will be more impaired on imitation than pantomime, and the most impaired form of imitation will be the meaningless gestures.

Subsequently, if pantomime and imitation of the lower limbs function by a similar mechanism to the upper limbs, the frequency for each grouping of apraxic, borderline, and non-apraxic should be relatively equivalent. That said, it is predicted that performance on upper limb tasks should strongly predict performance on lower limb tasks as examined in a correlation analysis.

The final objective of the current study is to compare the frequency of upper limb and lower limb apraxia in freezers versus non-freezers. If freezing and apraxia are related to a similar underlying deficit, it would be predicted that a higher proportion of freezers compared to non-freezers would exhibit apraxia.

4.2 METHODS

Participants

The experimental group for this study consisted of forty-five participants meeting strict clinical criteria of idiopathic Parkinson's disease, details of which can be found in Table 4.1 and Appendix A. All PD participants were assessed after an overnight withdrawal (Mean Duration = 13.7±4.3 hours) from their anti-Parkinsonian medication. Only those with a minimum score of ≥80 on the Modified Mini Mental State Examination were included. All participants were right handed. There were also 16 age-matched (as verified by an independent sample t-test, [$t_{(59)}$= 1.234, p<.8375]) healthy control community volunteers, who had no history of neurological diseases, and were also right handed. More detailed information can be found in Table 4.1 and Appendix A.

Table 4.1 Study Participant Demographics

Group	**Age (Mean ± SD)**	**UPDRS-III (Mean ± SD)**	**Disease Duration (Mean ± SD)**
PD (n=48)	69.2 ± 9.15 years	32.8 ± 10.5	7.7 ± 4.3 years
Healthy (n=16)	68.3 ± 6.7 years	n/a	n/a

Gestural Tasks and Performance Scoring

Participants were required to pantomime and imitate eight meaningful gestures and imitate eight meaningless gestures with each upper limb, then pantomime and imitate eight meaningful gestures with the lower limb and imitate four meaningless gestures. All gestures were performed while seated. A complete list of the gestures can be found in Appendix B. In the pantomime condition participants were asked to pretend how to use or act on an object to perform a certain action. For example "Show me how you would use a knife to slice a piece of bread" or "Show me how you would stub out a cigarette with your toe". The imitation condition

had participants copy the examiner's performance of each gesture. Pantomime was always performed first to avoid cueing the participants as to how each gesture was properly performed. All gestures for both pantomime and imitation were performed by first the right hand or foot, then the left. Each participant was videotaped for later analysis.

Scoring

A composite score was formed by the average percentage accuracy within five dimensions of movement including location, posture, plane, and orientation. Each gesture was given a score of 0, 1,or 2 as clearly defined by separate criteria yielding a total for each dimension (please see appendix A for scoring). Scores for the right hand and left hand, and for right and left feet were pooled together within the PD and the healthy control groups.

Analysis

The first analyses pertained to the control group in which three one-way ANOVAs were performed including i) a comparison of pantomime and imitation. ii) a comparison of each of the five dimensions in pantomime iii) a comparison of each of the five dimensions in imitation.

Percentage accuracy of gesture performance for each PD participant was converted to a Z-score with reference to the mean and standard deviation of the healthy control group. Cutoff scores were developed based on the average composite scores of the healthy control participants such that participants with PD could be classified as apraxic, borderline apraxic, or non apraxic with reference to the mean of the healthy controls as follows. PD participants who scored less than one standard deviation below the mean of the healthy controls were considered to be the non-apraxic group. Those who scored between one and two standard deviations below the mean

of the healthy controls were classified as borderline apraxic, while those scoring below two standard deviations from the mean of the healthy group were classified as apraxic.

The first task was to look at the frequency of PD categorized into apraxic, borderline, and non-apraxic groupings, for both tasks of lower limb pantomime and imitation. Two separate 2X5 ANOVAs of group (apraxic, non-apraxic) by dimension (location, posture, action, plane, orientation) were performed for pantomime and imitation to reveal the distribution of errors. Participants were then classified into four patterns of performance based on whether they were impaired on lower limb pantomime (P_AI_N), imitation (P_NI_A), both (P_AI_A), or neither(P_NI_N). Those who were classified as P_AI_A and P_NI_N were then placed in a repeated measures ANOVA comparing the two groups across the lower limb tasks of pantomime, meaningful imitation, and meaningless imitation. As well, a one-way ANOVA was conducted for performance across pantomime, meaningful imitation, and meaningless imitation with gestural accuracy composite scores used as the dependent measure rather than z-scores. Identical analyses regarding the upper limbs can be found in chapter 2.

The subsequent analyses involved the comparison of upper and lower limb data, the first of which identifies the frequency of co-occurrence of apraxia in upper and lower limb pantomime and imitation. Correlation analyses were then conducted for pantomime and imitation separately to examine the relationship between upper and lower limb performance. The final analysis pertains to the frequency of apraxia in PD participants who are also freezers. Participants were grouped into freezers and non-freezers based on self-report by item 14 of the UPDRS-II. Frequency analyses were conducted for freezers (n=8) and non-freezers (n=37), for the proportion of those who would fall into the range of apraxic, borderline apraxic, and non-apraxic. This was carried out for upper limb pantomime and imitation, and lower limb

pantomime and imitation separately. A chi square analysis was conducted for the proportion of freezers exhibiting apraxia with respect to the proportion of non-freezers exhibiting apraxia.

4.3 RESULTS

Performance of Healthy Control Participants

Healthy control participants exhibited no difference in overall accuracy of pantomime compared to imitation, as reflected in the relatively equal composite scores [$t_{(15)}$= -0.4783; p > .6393]. There were no significant differences revealed in pantomime performance across all dimensions [F(4,75)=0.7558, p > .5573], or imitation performance across all dimensions [F(4,75)= 2. 2483 p > .0718]. Table 4.2 presents the performance accuracy by task and dimension.

Table 4.2 Lower Limb Gestural Performance Accuracy of Healthy Control Participants

DIMENSION	Pantomime		Imitation	
	%	SD	%	SD
Location	93.16	5.50	92.77	7.10
Posture	92.77	7.37	90.63	5.59
Action	93.95	5.41	93.95	5.87
Plane	93.75	5.82	94.73	4.94
Orientation	90.43	7.94	89.45	5.92
Composite	92.81	3.93	92.30	3.66

Apraxia Frequency in PD

Frequency of apraxia category by task is shown in Table 4.3, as determined by z-score (apraxic = $x \leq -2$, borderline = $-2 < x < -1$, non-apraxic = $x \geq -1$). Imitation was found to have a higher frequency of apraxia than pantomime (see Table 4.3).

Table 4.3 Frequency of Lower Limb Apraxia by Task		
	Pantomime	**Imitation**
Apraxic	28.9% (n=13)	33.3% (n=15)
Borderline	20.0% (n=9)	15.6% (n=7)
Non-Apraxic	51.1% (n=23)	51.1% (n=23)

Comparing Apraxic PD Groups Across Task and Dimension

Table 4.4 displays the percentage accuracy of the PD group, but also their z-score in reference to the performance on pantomime of the healthy controls. Those that would have been categorized as "borderline" in the latter analysis are excluded from this point on.

Table 4.4. Pantomime Performance Accuracy of PD						
DIMENSION	**APRAXIC**			**NON-APRAXIC**		
	%	**SD**	**Z**	**%**	**SD**	**Z**
Location	83.41	11.15	-1.77	95.54	4.92	0.43
Posture	72.60	11.06	-2.62	92.75	4.96	0.10
Action	75.92	15.13	-3.81	89.29	6.27	-0.86
Plane	83.41	8.97	-1.78	94.08	4.28	0.06
Orientation	68.99	8.21	-2.70	90.51	6.04	0.01
Composite	76.35	5.64	-3.71	92.43	3.52	-0.09

With PD grouped as apraxic or non-apraxic, a 2X5 ANOVA was performed on the Z scores, with performance on each dimension as the dependent variable. There was a main effect for group in that the apraxic group performed worse than the non-apraxic group [$F(1,34) = 124.54$, $p < .0001$]. There was also a main effect for dimension [$F(4,136) = 1.48$, $p < .0001$] in that all PD participants were more significantly impaired in the action dimension as revealed in Tukey's HSD post hoc analysis. Figure 4.1 depicts these results.

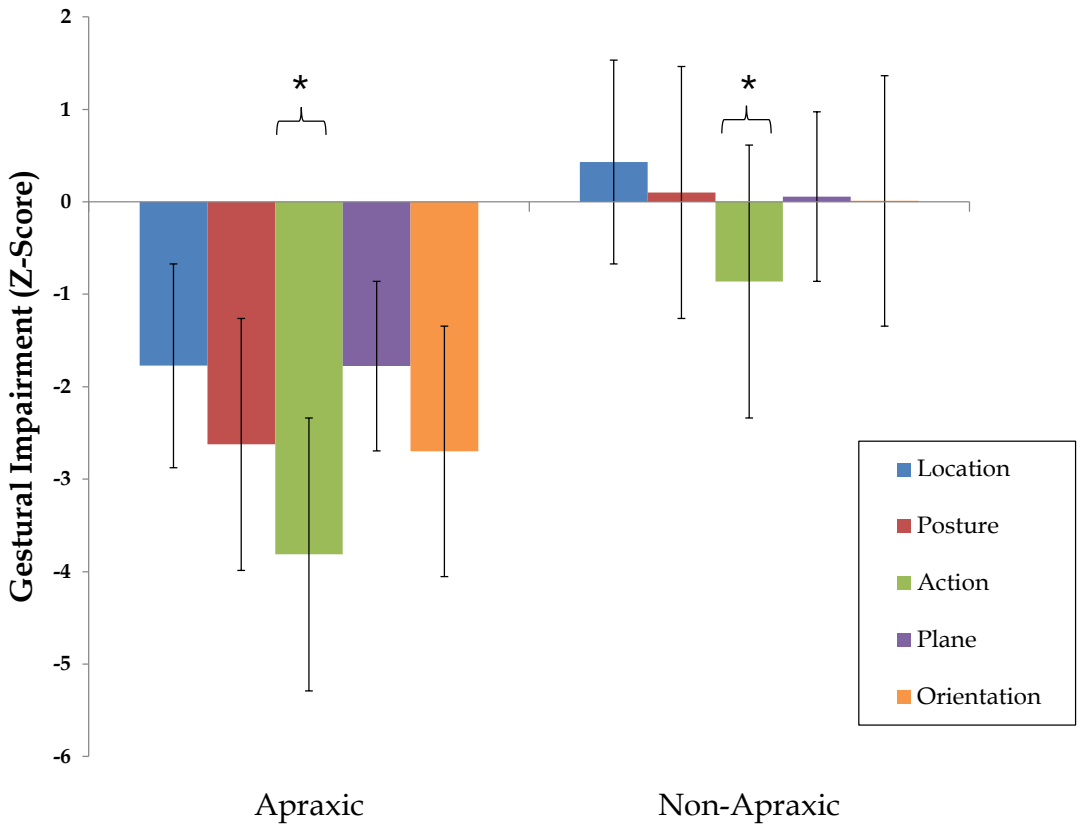

Figure 4.1 – Results for pantomime show a more impaired action dimension across both apraxic and non-apraxic groups.

Table 4.5 displays the percentage accuracy of the PD group, but also their Z score in reference to the performance on imitation of the healthy controls. There was a significant interaction of group by dimension ($F[4,136]=9.17$; $p<.0001$). Tukey's HSD post hoc analyses revealed that in the apraxic group, the location dimension was shown to be less impaired than any other dimension, while the action dimension was more impaired than all other dimensions except plane. In the non-apraxic group the action dimension was once again implicated as the most impaired dimension, however it was only significantly different from location and posture dimensions in this group.

Table 4.5. Imitation Performance Accuracy of PD						
DIMENSION	APRAXIC			NON-APRAXIC		
	%	SD	Z	%	SD	Z
Location	86.25	9.58	-1.27	94.79	4.29	0.47
Posture	76.88	7.91	-2.46	91.98	6.75	0.37
Action	70.01	12.09	-4.08	86.35	6.99	-1.23
Plane	80.42	13.59	-2.89	94.48	4.24	-0.02
Orientation	73.75	8.66	-2.64	88.75	6.60	-0.08
Composite	82.03	5.22	-4.05	93.89	4.48	-0.18

Figure 4.2 depicts these results below.

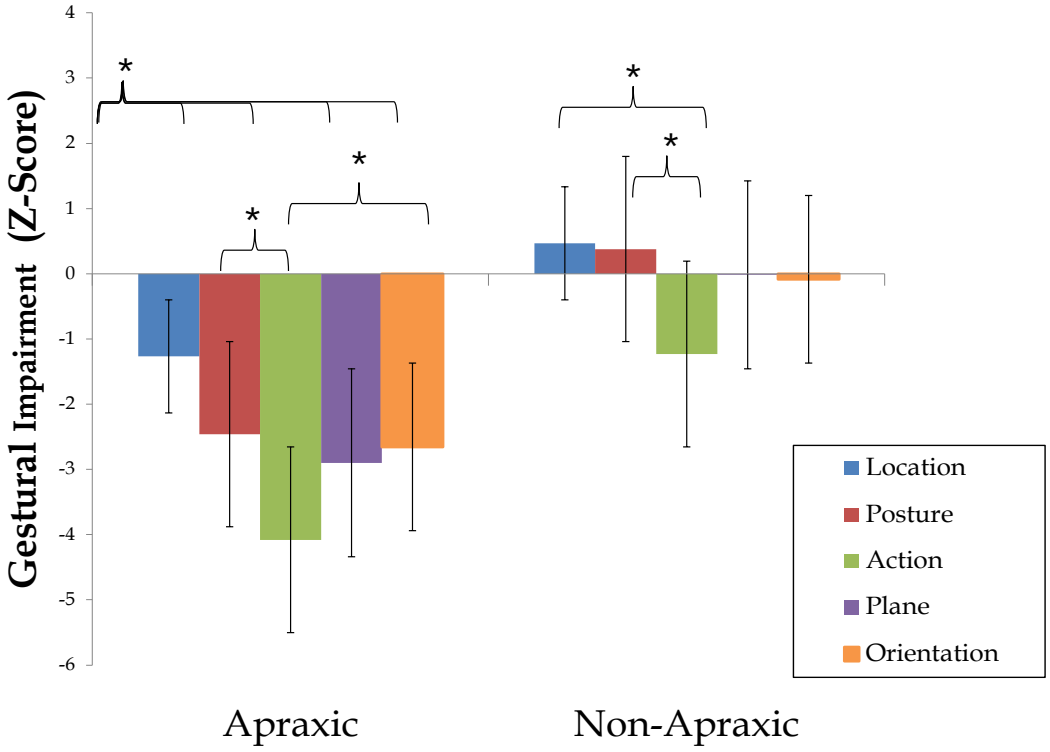

Figure 4.2 – Imitation results show a significant and complex interaction of dimension and group.

Patterns of Apraxia

The following final analyses pertain to how the PD group performed on pantomime relative to imitation. Table 4.6 displays the frequency of PD participants that fall into each pattern of apraxia namely i) P_NI_N: non-apraxic at both pantomime and imitation, ii) P_AI_N: apraxic at pantomime only, iii) P_NI_A: apraxic at imitation only, iv)P_AI_A apraxic at both pantomime and imitation.

Table 4.6. Gestural Performance Accuracy of PD Grouped by Pattern of Apraxia

Pattern	Frequency	Pantomime Accuracy			Imitation Accuracy		
		%	SD	Z	%	SD	Z
P_NI_N	57.8 % (n=26)	92.0%	4.1	-0.16	91.8%	2.8	-0.14
P_AI_N	6.7% (n=3)	82.1%	2.2	-2.66	86.7%	1.3	-1.54
P_NI_A	13.3% (n=6)	88.3%	2.4	-1.10	79.0%	3.7	-3.64
P_AI_A	22.2% (n=10)	74.6%	5.2	-4.54	76.2%	7.9	-4.40

Further, when comparing the average composite scores for pantomime and imitation in each pattern of apraxia, it can be noted that the most severe composite scores are found for both tasks, within the group who is impaired at both the tasks. Figure 4 displays this relationship below, however results must be considered carefully given the statistical power of the selective impairment groups (P_NI_A, P_AI_N) have very small n values.

A Model-based Approach to Lower Limb Apraxia

For the control group, the one-way ANOVA conducted for pantomime, imitation of meaningful gestures and imitation of meaningless gestures revealed a significant main effect [$F(2,30) = 5.20$; $p < .0015$]. Post hoc analysis revealed significantly more impairment for meaningless gestures compared to pantomime ($p<.0169$) and meaningful imitation ($p<.0355$),

while pantomime and imitation did not differ ($p > .9459$). In a group by task ANOVA comparing the apraxic and non-apraxic group on performance of pantomime, imitation of meaningful gestures, and imitation of meaningless gestures, no differences were yielded between these tasks [$F(2,82)= 0.249$, $p > .7805$]. Only a significant main effect of group revealed a less accurate performance by the apraxic group [$F(1,43)=73.1$, $p < .0001$]. A one-way ANOVA was conducted for the three tasks, however instead of Z-scores, composite percentage accuracies were the outcome measure. A main effect of task [$F(2,84)=44.75$, $p < .0001$] revealed a similar performance on meaningful imitation and pantomime, however meaningless imitation was drastically worse.

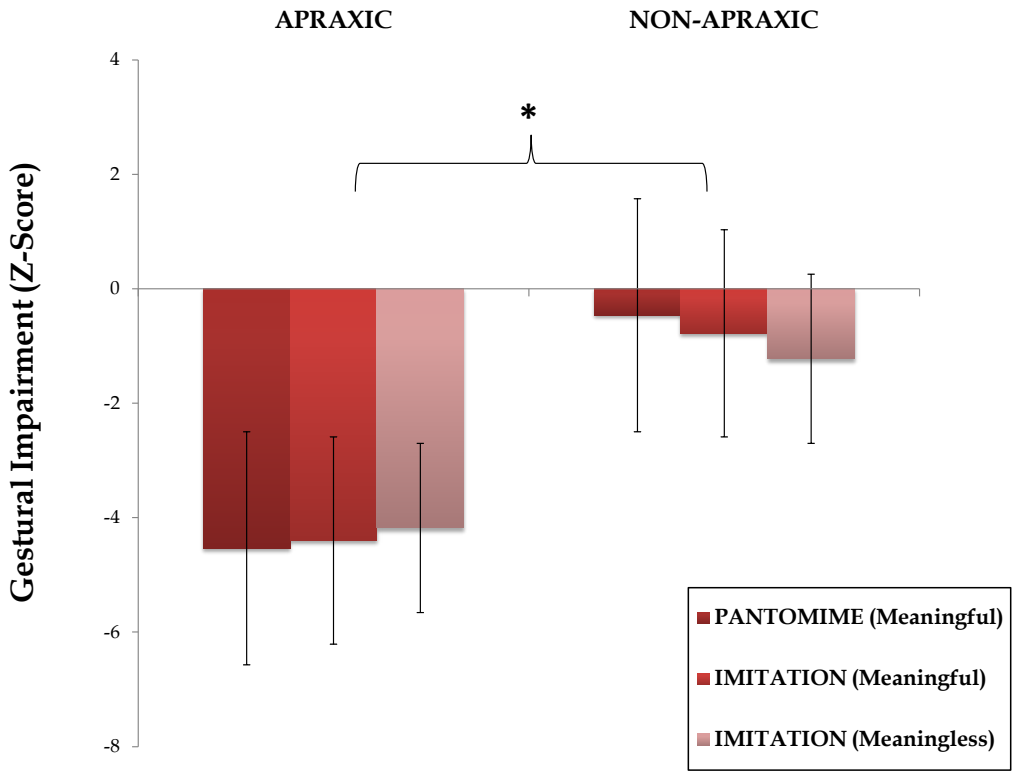

Figure 4.3. Comparison of lower limb task demands across apraxic and non-apraxic groups.

The Relationship between Upper Limb and Lower Limb Apraxia

Table 4.7 displays the frequency to which upper limb and lower limb apraxia co-occur within the PD group. Furthermore the strong correlation between upper limb pantomime and lower limb pantomime as well as upper and lower imitation is shown in Figure 4.4.

Table 4.7 Frequency of Upper Limb and Lower Limb Co-occurrence

Pattern of Apraxia in the Upper Limbs (U_A)	**Pattern of Apraxia in the Lower Limbs (L_A)**	**Frequency of Co-occurrence (U_AL_A)**
Pantomime (n=12)	Pantomime (n=13)	58.3% (n=7)
Imitation (n=14)	Imitation (n=16)	78.6% (n=11)

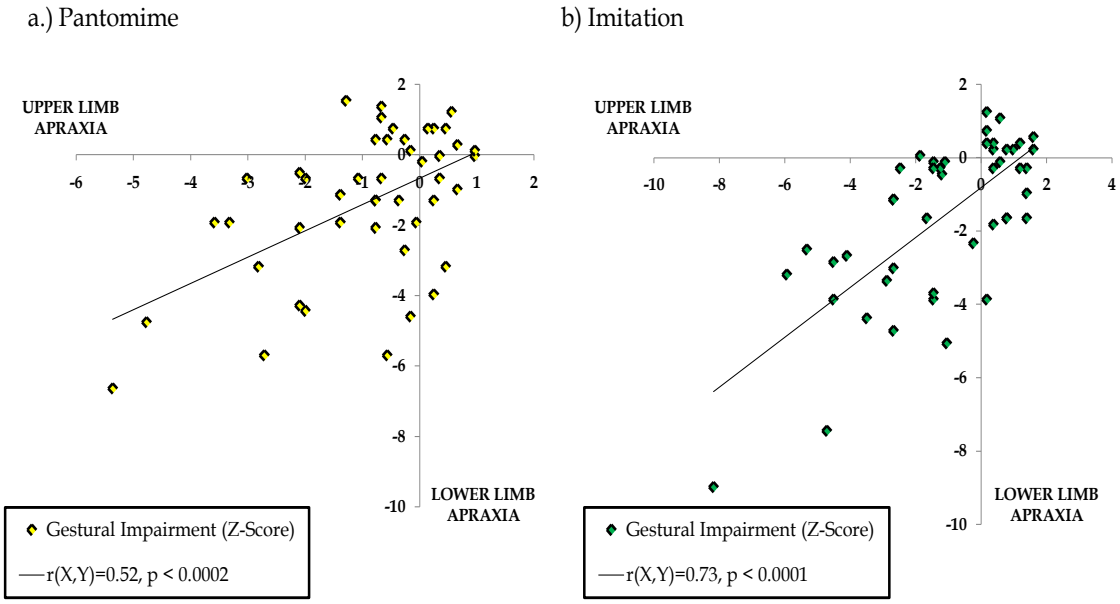

Figure 4.4 Correlation of upper limb and lower limb apraxia for a) pantomime and b) imitation

Performance of Freezers versus Non-Freezers

The final analysis pertains to the frequency of apraxia within the group of PD participants who experience freezing of gait (n=8), as compared to the frequency of apraxia within the group

of PD participants who do not experience freezing of gait(n=37). Figure 4.5 displays these findings with the frequency expressed as a percentage.

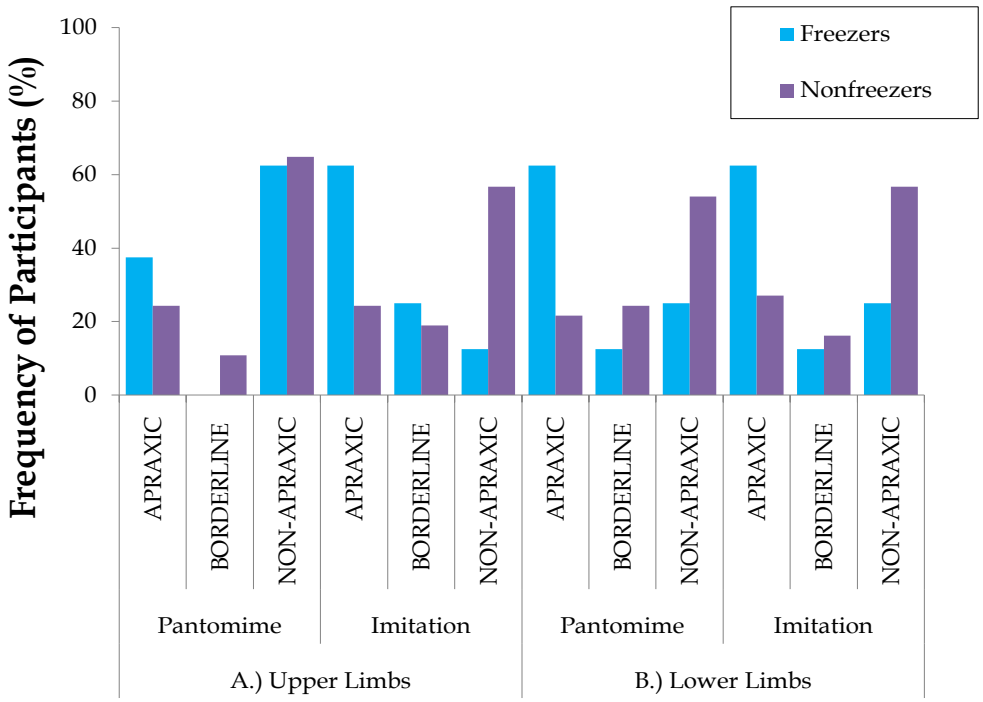

Figure 4.5 Proportion of PD freezers versus PD non-freezers who manifest apraxia in the upper or lower limbs across task.

All chi-square analyses were significant for upper limb and lower limb pantomime and imitation. The observed proportions of the freezers who exhibited apraxia was significantly greater than the proportion of non-freezers who exhibited apraxia. Please see Table 4.8 for these results.

Table 4.8 Chi Square Analysis for proportion of freezers exhibiting apraxia compared to proportion of non-freezers exhibiting apraxia	
Upper Limb Pantomime	$\chi 2 = 18.03$, $p<0.0001$
Upper Limb Imitation	$\chi 2 = 96.38$, $p<0.0001$
Lower Limb Pantomime	$\chi 2 = 98.65$, $p<0.0001$
Lower Limb Imitation	$\chi 2 = 65.18$, $p<0.0001$

4.4 DISCUSSION

This is the first study to evaluate lower limb apraxia in Parkinson's disease which revealed that the frequency of lower limb apraxia was at 28.8% (n=13/45) with respect to pantomime and at 33.3% for imitation (n=15/45). These findings are consistent with what was found in the upper limbs with respect to pantomime (n=12 or 25%) and imitation (n=14, or 29%).

What is also similar to upper limb performance is the nature of errors committed within both pantomime and imitation. For both tasks the action component stood out as the most impaired dimension which is also the case with upper limb evaluation. What was also consistent was there was no difference between impairment on the action and plane dimensions in the imitation task specifically. The lower limb assessment also showed the location dimension in imitation was less impaired than all other dimensions even in the apraxic group. Since impairment in this dimension is thought to be related to spatial errors, the limited degrees of freedom afforded by the lower limbs may have not allowed as many opportunities for errors in lower limbs in this dimension compared to the upper limbs. The frequency of the global impairment (P_AI_A) and selective impairments (P_AI_N, P_NI_A) were relatively similar for the upper limb versus the lower limb. These findings, in concert with the similarity in gestural error types, suggest that the lower limb battery is drawing on a similar mechanism of gesture production as the upper limbs.

In contrast to performance on the upper limbs, lower limb pantomime of meaningful gestures, imitation of meaningful gestures, and imitation of meaningless gestures did not differ in their degree of impairment in terms of Z-Scores. This is important to note because while

imitation and pantomime performance were similar in their degree of impairment in the upper limbs, the performance of meaningless imitation was drastically impaired. This was not the case in the lower limbs in terms of Z-Scores, however this was consistent in terms of composite scores (percentage accuracies).

From these results alone it can be interpreted that lower limb praxis tasks are sensitive to apraxia impairments of response control and organization of a movement in general. However varying the task demands does not seem sensitive enough to isolate the roles of the direct and indirect routes to action. It is most likely that there is just too limited a range of movements for the lower limbs, resulting in less room for error. In other words, in the participants with lower limb apraxia identified, there could have been a "floor effect" in how poor their performance was. Thus the lower limb assessment lacks the sensitivity for the highly impaired end of the spectrum.

With all of these results taken together, it is not surprising how strong the correlations are between upper and lower limb pantomime, and between upper and lower limb imitation. There are also high frequencies of co-occurrence. In both of these analyses, what stands out is the higher frequency of co-occurrence, and the stronger correlation between upper limb and lower limb apraxia in imitation specifically. As discussed with respect to the upper limbs, impaired performance on imitation was likely due to deficits in converting visual information to movement. Earlier, the role of the direct route in imitation (predominant use of the visual information) was discussed, and the nature of this mechanism would likely not differ between the upper and lower limbs in terms of the neural circuitry of praxis. However, if representations for gestures of the upper limbs versus gestures of the lower limbs are stored in a different area of the brain, or accessed via a different mechanism then it is feasible that upper and lower limb

pantomime may be more dissociable than imitation. In other words, while conceptual information for upper limbs and lower limbs may be stored separately, visuomotor transformations likely occur via the same neural circuitry regardless of the limb being used.

The Relationship between Apraxia and Freezing of Gait

The final analysis for this chapter pertains to whether there is a link between apraxia and freezing in PD. A higher percentage of freezers fall within the apraxic range compared to non-freezers regardless of task category or limb used (as verified in a chi-square analysis). This phenomenon is least pronounced in upper limb pantomime. The inferences one can draw from this analysis are limited particularly because there is only a small pool of freezers (n=8) to draw from, however it poses some interesting questions. While there is little consensus on what exactly characterizes gait apraxia, perhaps there is some overlap between diagnosis of freezing and gait apraxia. Elble would argue the term gait apraxia is outdated and that "gait apraxia" bears no association with other types of apraxia(Elble, 2007). The current study is not only the first to examine freezing in association with upper and lower limb apraxia in Parkinson's disease, but the first to indicate a link between a higher-order gait impairment and apraxia. Is it a possibility that freezing and other gait impairments in Parkinson's disease are more related to the executive system deficits observable in upper and lower limb apraxia? The notion that executive function is impaired in freezers has been supported by a number of researchers(Giladi, Huber-Mahlin, Herman, & Hausdorff, 2007; Hausdorff et al., 2006; Yogev-Seligmann, Hausdorff, & Giladi, 2008). The next step in furthering these questions could be to clinically quantify freezing and examine the correlation between upper and lower limb apraxia, and the amount of freezing. This quantification of freezing should perhaps be examined in not only the lower limbs in the context of walking, but in the upper limbs as well.

This study has enabled a novel and systematic evaluation of the lower limbs that is well-coupled with upper limb assessment. Together these evaluation tools could create a framework for studying freezing and gait apraxia in Parkinson's disease. The lower limb battery created for the purpose of this study presents several improvements over the very sparse literature on this topic. Firstly, the lower limb gestures are a combination of transitive, intransitive, and meaningless gestures, which brings them to a level of complexity that is unmatched by any other lower limb battery of tests. Previously lower limb gestures have been very simple in nature and have been for the most part, imitation of intransitive gestures (tracing circles, lines, crosses, etc). This study applied the foundations of the upper limb battery in order to create both pantomime and imitation conditions for the lower limb (the first study to attempt this), and by doing so made the upper limb and lower limb batteries more comparable.

One limitation to the lower limb tasks was the fact that all participants were seated for all of the gesture performances. While many of these gestures were not as naturalistic as one might hope for, what was perhaps more important was eliminating balance as a competing factor in performance accuracy. This was particularly a concern for the Parkinson's disease group for which postural instability is a prominent cardinal symptom. Giving up a part of the "normal context" for a movement was a necessary restriction placed on the participants.

Alike with the upper limb system for evaluation, it is important to point out the qualitative and subjective nature of these assessments. There is certainly a need to develop new approaches that integrate a qualitative error analysis with a completely objective kinematic analysis, and this may actually be a more feasible idea for the lower limbs than the upper limbs given the more restricted and less complex nature of lower limb movement. The current study showed an inter-rater reliability of 0.89 on the lower limb items, which supports the notion that

lower limb assessment should be included in standardized assessments of apraxia as it is simple, insightful, and reliable.

CHAPTER 5: A GENERAL DISCUSSION

This thesis project set out with the general purpose to better understand the consequences of progressive basal ganglia neurodegeneration to learned skilled movement in Parkinson's disease(PD). To achieve this objective, chapter two used a model-based approach to characterize apraxia in PD, working with the assumption that varying task demands and modalities can draw on the different mechanisms that give rise to apraxia. As such, apraxia in PD can be compared to the apraxia seen in stroke and other disorders that have been more extensively investigated. What already sets PD apart from stroke and other disorders is the predominance of a very specific group of primary motor symptoms, many of which could act as a hindrance to upper limb gesturing. Therefore, chapter 3 examined the relationship between apraxia and motor symptoms in PD, to ensure that apraxia detected in the current study was not the result of primary motor deficits. Finally, chapter 4 used the same multimodal gestural tasks to examine apraxia of the lower limbs. This was to see if the impairments observed in the upper limbs would also manifest themselves in the lower limbs, or if there were different patterns of deficits found altogether.

5.1 CONVERGING EVIDENCE OF UPPER AND LOWER LIMB APRAXIA

The 'conceptual-production model' was the approach utilized for examining apraxia in both the upper and lower limbs. Central to understanding this model is the dissociation of the direct and indirect routes to action, and these are most easily teased apart with a detailed comparison of pantomime and imitation. In the past there has been a tendency to overlook the value of the imitation task and focus primarily on pantomime by tool(Hermsdorfer, Terlinden, Muhlau, Goldenberg, & Wohlschlager, 2007; Laimgruber, Goldenberg, & Hermsdorfer, 2005; R. C. Leiguarda et al., 1997). While this is the first systematic comparison of pantomime and imitation in PD, the dissociation of the two tasks has been widely shown in stroke (Alexander,

Baker, Naeser, Kaplan, & Palumbo, 1992; Barbieri & De Renzi, 1988; De Renzi et al., 1980; Poeck, 1982; Roy et al., 2000), as well as CBD(V. Stamenova, Roy, & Black, 2009). This is not to say that imitation has been entirely excluded in past research with PD, however as discussed in chapter two, the gesture types for imitation typically have not resembled the complexity of those performed in pantomime. The current study showed that the frequency of apraxia in both pantomime and imitation was the most common pattern for impairment for PD, which hints at a predominantly executive disorder. However this was also the first study to identify selective impairments in imitation only. With higher frequencies of PD showing impairment in imitation, it may be that imitation is more specific to the deficits caused by basal ganglia damage. There is evidence of this in many other findings from the current study.

When comparing upper limb and lower limb apraxia, there were higher rates of co-occurrence for imitation compared to pantomime, and also a stronger correlation between these task performances. What may be the most compelling finding is that total UPDRS scores had a stronger correlation with impairment on imitation compared to pantomime, despite having a similar relationship with cardinal motor symptom manifestation. The most telling observation may be within the comparison between pantomime, imitation of meaningful gestures, and imitation of meaningless gestures. The worst impairments are associated with imitation of meaningless gestures for both upper and lower limbs. This finding suggests that access to semantics facilitates performance rather than deters it which provides evidence for a deficit in visuomotor transformation.

While these findings are interesting, it is certainly not a seamless explanation since deficits in pantomime are quite common. The most common pattern shown among participants in the current study is impairment at both pantomime and imitation. Furthermore, there were no

differences between pantomime and imitation in terms of Z-scores, and a small number of these participants were actually selectively impaired at pantomime (see chapter 2 for interpretation of selective impairments). Given the results regarding imitation, it is likely that the apraxic participants are suffering from deficits in visuomotor transformation. However since most of these people are also impaired at pantomime, and visuomotor transformation is not required, there is likely a deficit in the general organization and control of movement. This deficit is one of many roles of the executive system. Interestingly impaired executive functioning has been shown to be associated with freezing in PD(Giladi et al., 2007). Thus it may not be surprising that there is a higher proportion of freezers exhibiting apraxia.

5.2 RECOMMENDATIONS FOR THE STUDY OF APRAXIA IN PD

The current study improved the methods for assessment of apraxia in a number of ways, the most significant of which was a novel method for discerning apraxia from primary motor symptoms in a disease for which the latter are quite apparent. While it has become generally well-accepted that apraxia can be observed in disorders in which primary motor symptoms are a prominent feature, it has been an issue that has been somewhat avoided. Rather than meet the challenge of primary motor symptoms head-on, studies often target groups of participants that are lower in severity, and also test participants at their optimal dosage of medication. The current study obtained a wide range of disease severities and tested them after an overnight withdrawal from their medication to observe the basal ganglia in its “least -contributing state”.

In terms of statistical analysis, it is important to examine the relationship between primary motor symptoms (as quantified by subsets of the UPDRS) and performance on gestural tasks. A significant relationship would point to flaws in experimental design as the two must be dissociable. This is something studies need not overlook before any other analyses are

conducted. An analysis was designed for the purpose of this study that examined laterality of motor symptoms on a continuum, such that it is possible to see the degree to which unilateral symptoms contribute to total motor symptoms. It is certainly worthwhile to conduct a limb-to-limb comparison of motor impairment versus praxis impairment given the asymmetrical nature and onset of PD symptoms. While this type of analysis was not conducted for the lower limbs in these participants, with a newly created systematic lower limb apraxia battery, and lower limb specific UPDRS scores, a similar analysis could also be performed in the lower extremities.

The current study showed no relationship between subsets of the UPDRS (that could potentially impede gestural performance) and apraxia impairment. This can be attributed to the detailed scoring criteria used in this study, as it factors in five dimensions of movement. Within these five dimensions of movement (location, posture, action, plane orientation), there are no penalties incurred for slowness and hesitations (bradykinesia), restricted ranges (rigidity), or shaky movements (tremor). It seems unlikely, given the level of detail for each gesture criteria, that apraxia would be confused with motor symptoms.

Another important recommendation for evaluating limb apraxia in not only PD, but all populations, is the use of conceptual tasks that are specific to the gesture production tasks themselves. In the current study, individuals with PD were found to have similar performance on conceptual tasks compared to healthy. This allowed for more inference regarding the impaired aspects of pantomime and imitation, particularly in those who are impaired at both pantomime and imitation. In this study, PD seemed rely heavily on their conceptual knowledge as indicated by their poor performance on meaningless gestures, and this knowledge does seem to be intact, which gives way to other explanations (ie. production system). For example, impairment in terms of the conceptual tasks can rule out a functioning indirect route to action immediately. In

general, the study also proposed that gesture production evaluation should not be limited to the upper limbs. The novel lower limb assessment in this study was consistent with the majority of the results for upper limbs, was relatively easy to administer, and preliminary analyses have shown a higher inter-rater reliability compared to the upper limb assessment.

5.3 LIMITATIONS

This brings us to the limitations of the project. It is important to point out the fact that the apraxia battery is scored through a visual rating, and the scoring of errors could be relatively insensitive to features of a movement that may not be visible to the eye, such as deviations from the "normal" kinematic features of a movement. In addition, this method is very subjective in nature and some scores may have been influenced by rater judgment. However, a high inter-rater reliability (upper limb IRR=0.80, lower limb IRR = 0.89) has been established for the upper limb method across many data-sets, while the lower limb battery employed at least two raters for each task in the current study. Test-retest reliability has not been conducted at this time. Please see Appendix B for more detail regarding the administration of the apraxia battery.

An important component to the conceptual-production system model is the dissociation between delayed imitation and concurrent imitation. For an accurate performance in the delayed imitation condition, working memory needs to be intact. Preliminary analyses regarding the concurrent imitation task have shown no statistical differences between delayed and concurrent imitation on a small subset of the participants used in the current study(King et al., 2009). A few other studies also support this notion that working memory is not a large contributing factor in the deficits revealed in imitation(Goldenberg et al., 1986), however to fully rule out this suggestion, concurrent imitation tasks should be analyzed in full and compared to the delayed imitation of the same gestures. Conversely, there is the potential for selective impairment in

concurrent imitation given the nature of the task bears resemblance with dual task paradigms. Therefore, more simplistic tasks of working memory should be used in concert with the apraxia tasks of delayed and concurrent imitation to see if this dissociation is a valid. That said, many other domains of cognitive function including memory, attention, decision-making etc., are worth looking into. One advantage to another study that was conducted with apraxia in PD(R. C. Leiguarda et al., 1997) is the thorough neuropsychological testing battery coupled to the apraxia testing. Several of these tests were a reflection of frontal lobe function, and by correlation of performance on praxis tests, some inferences could be made regarding the interaction between the basal ganglia and the cerebral cortex. A more thorough neuropsychological evaluation of the PD participants would allow for a better understanding of praxis deficits revealed in this study. This was slightly beyond the scope of the project as the main objective of the study was to identify the frequency and severity of apraxia as pertaining to the information processing model, while ensuring the dissociation of primary motor symptoms.

One of the most controversial debates with respect to the apraxia literature is the cortical versus subcortical question, more specifically is it possible that isolated dysfunction to the basal ganglia cause apraxia? While this study cannot provide a definitive answer to this question, it may be a source of insight. Both Leiguarda and Marsden have posited that the basal ganglia would not cause overt apraxia per se unless it is combined with dysfunction of the cortical components involved in sensorimotor transformation, sequencing, and response selection (R. C. Leiguarda & Marsden, 2000; Marsden, 1998). Without imaging data or further neuropsychological testing it is not possible to rule out undiagnosed damage to the cortex in the participants that present with apraxia in the current study. However, what was found was a strong correlation between apraxia and total motor symptom severity (as quantified by the

UPDRS). This analysis could be evidence of a common neural substrate for apraxia and the outward motor symptoms of PD, as the most severe PD seem to also experience the most severe apraxia. This strong association could suggest that isolated damage to the basal ganglia could cause apraxia. Longitudinal studies, neuro-imaging data, and more objective ways of measuring apraxia and quantifying motor symptoms are necessary steps in answering the question of the basal ganglia's true role in apraxia.

5.4 SIGNIFICANCE OF WORK

Through the study of limb apraxia in Parkinson's disease, a common basal ganglia disorder, this thesis provides new insight into how basal ganglia damage contributes to deficits in skilled movement. Despite being described by Leipmann over 100 years ago(Liepmann, 1988), the study of limb apraxia has garnered very little attention until recently, and Geshwind noted that this was likely because patients rarely complain of apraxia(Geschwind, 1975). Since apraxia is typically not recognized by the patients themselves, the functional implications this disorder has on activities of daily living (ADLs) was likely underestimated and overlooked until recent times. This would be particularly true for diseases such as Parkinson's disease, in which the primary motor symptoms are so prominent little concern is reserved for secondary issues pertaining to cognition. A few recent studies have shown the effects of apraxia on functional independence in stroke (Donkervoort, Dekker, van den Ende, Stehmann-Saris, & Deelman, 2000; Roy et al., 2000), and CBD(Roy et al., 2000), and one can only assume the effects are equally detrimental for ADLs performed by individuals with PD (although this has not been studied). Studies that have looked at the impact of apraxia on daily living have used a myriad of functional measures including object use, performance measures of ADLs, self-reports, and caregiver reports (for review see (Barde, Buxbaum, & Moll, 2007).

All participants in the current study were not in their usual medicated state, it may be interesting to investigate whether apraxia can respond to Parkinsonian medication in PD. Instinctively the answer would be no, given the results of Leiguarda's previous work showing no differences between 'ON' and 'OFF' states(R. C. Leiguarda et al., 1997). However it would still be of interest to study perhaps in concert with other non-pharmacological strategies such as exercise rehabilitation or deep brain stimulation.

It is unknown what types of interventions would be most effective for apraxia in PD. Research in the field of treating apraxia reveals a long list of limitations with many studies involving individual cases, inconsistent apraxia criteria, and presence of aphasia as a confound (for review please see (Buxbaum et al., 2008). There is some evidence that increasing the level of affordances in household objects is beneficial(Barde et al., 2007). Developing personal strategies (such as verbalizing actions) in ADL training has also shown to have positive short term outcomes, however there does not seem to be long lasting advantages(Hartmann, Goldenberg, Daumuller, & Hermsdorfer, 2005; van Heugten et al., 1998). Object-related gestural impairments are more likely to be disruptive to ADLs and it is important to remember that object-related actions are complex and tied closely with semantics. Therefore, it is unclear whether the rehabilitative focus should be more on distinctive motor features, or more related to semantic labeling. To rephrase this dilemma in reference to the results of the current study, given the idea that the deficits are more related to the control and organization of an action in PD, are we better off trying to transformation the motor elements for an action, or do we try to strengthen the conceptual system and hope for a better result downstream in the praxis system? Interventions will likely need to be a combination of the two.

Needless to say, there is a great need to continue studying limb apraxia in Parkinson's disease. In order to manage the deficits and to prepare the patient and family for their future, it is important to understand the natural progression of praxis deficits. The model-based approach to studying apraxia in both the upper and lower limbs enables us to determine the frequencies, patterns and severities of apraxia, and better equips us to predict which systems are more susceptible to deterioration. Now that this information is available, the results of this thesis project have hopefully created a framework for determining coping strategies and future interventions.

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APPENDIX A – Participant Demographics

TABLE I. Healthy Control Participant Demographics		
#	GENDER (M/F)	AGE (YRS)
01	F	68
02	M	66
03	F	71
04	F	68
05	F	72
06	M	74
07	F	74
08	M	76
09	M	78
10	M	65
11	F	61
12	F	69
13	M	59
14	M	62
15	M	60
16	F	77

TABLE II. PD Participant Demographics							
#	**SEX (M/F)**	**AGE (YRS)**	**DISEASE DURATION (YRS)**	**DURATION OFF MEDS (HRS)**	**UPDRS I & II (SCORE)**	**UPDRS III (SCORE)**	**3 MS (SCORE)**
1	M	86	2006	14.5	7	31	82
2	M	81	2000	13	32	48.5	83
3	M	76	2008	16	12	24	85
4	F	63	2008	15	11	7.5	89
5	M	74	2005	No meds	20	57	89
6	M	75	2006	13.5	7	24	94
7	M	72	2002	16	5	25.5	96
8	M	83	2006	12	16	48.5	87
9	M	80	2009	17.5	5	39	91
10	M	71	2004	15	5	29.5	94
11	M	79	2006	11	14	33	97
12	M	81	1992	12	21	43	84

TABLE II. PD Participant Demographics Continued…							
#	**SEX (M/F)**	**AGE (YRS)**	**DISEASE DURATION (YRS)**	**DURATION OFF MEDS (HRS)**	**UPDRS I & II (SCORE)**	**UPDRS III (SCORE)**	**3 MS (SCORE)**
13	M	80	1	13	28	32.5	91
14	F	73	7	16	14	36.5	99
15	F	64	5	12.5	18.5	29	97
16	M	78	5	24	0	23	96
17	M	62	4	13	9	28	91
18	M	75	3	24	14	29.5	97
19	M	70	3	17	14	44	89
20	M	74	6	5	9	24.5	97
21	M	60	2	13.5	9	30	95
22	F	66	5	15	14	21.5	99
23	M	75	8	11.5	9	35	99
24	M	72	3	24	16	29.5	97
25	F	67	9	19.5	2	20.5	97
26	M	53	5	16.5	12	31.5	99
27	F	74	12	12	19	36.5	95
28	M	72	11	5	21	51.5	94
29	F	75	21	11	23	50.5	88
30	F	72	6	17	11	25	98
31	M	73	9	11.5	15	34.5	87
32	M	51	1	24.5	5.5	29.5	83
33	F	62	8	12	4	31	97
34	M	84	17	12	14	41.5	83
35	F	61	11	15.5	12	18	97
36	M	69	5	26.5	3	16.5	97
37	M	70	9	12	33.5	44	98
38	M	73	10	15	13	43.5	89
39	M	61	7	15	14	28.5	92
40	M	68	5	11	15	47.5	82
41	F	50	10	12	7	23.5	96
42	F	66	5	16.5	3	19.5	98
43	M	85	9	13.5	18	39	93
44	M	71	18	14.5	10	43.5	97
45	M	55	7	15.5	8	30	99
46	M	63	4	No meds.	6	24.5	99
47	F	54	7	18	12	34	96
48	M	69	2	≈ 2 weeks	5	38.5	90
AVG	--	69.2	6.8	14.9	12.4	32.9	93.0

APPENDIX B – The Apraxia Battery

I. THE MODIFIED WATERLOO-SUNNYBROOK APRAXIA BATTERY
*denotes modification unique to the current study

†denotes practice item

1. TOOL NAME – (PICTURES)

I am going to show you a series of pictures and ask you to name them.

What would you call this? Screwdriver†

Bottle Opener†

Comb

Toothbrush

Fork

Tweezers

Hammer

Knife

Flipper/Spatula

Watering can

2. TOOL NAME BY FUNCTION – (VERBAL)

Now, I am going to give you a verbal description of an action and I'd like you to tell me what tool would be used for the action I am describing.

What would you use to: Brush your teeth? **(Toothbrush)**

Style your hair? **(Comb)**

Pull out a splinter? **(Tweezers)**

Eat your food? **(Fork)**

Slice a piece of bread? **(Knife)**

Pound a nail? **(Hammer)**

Pour some water? **(Watering Can)**

Flip an egg? **(Flipper/Spatula)**

3. ACTION NAME – (ACTION)

Now, I'm going to do some acting and I'd like you to tell me what object you think I have in my hand (examiner pantomimes gestures)

Name the object I would be using to do this?	Flipper/Spatula
	Knife
	Hammer
	Watering can
	Tweezers (eyebrows for females)
	Toothbrush
	Fork
	Comb

4. TOOL IDENTIFICATION – (PICTURES)

I am going to show you some pictures of objects and I would like you to point to the object I name. (test items only)

Point to the	Comb
	Flipper/Spatula
	Toothbrush
	Tweezers
	Hammer
	Watering Can
	Knife
	Fork

5. TOOL IDENTIFICATION BY FUNCTION – (PICTURES)

This time, I'm going to give you a description of an action and I'd like you to point to the tool that is related to this action. (test items only) – (*circle their response)*

5b. Alternate task: Now, if I took away the _____ (tool name) and you'd have to use something to _____ (action), what else would you use? Even if it was silly, what would you use? – (*mark AT beside their response)*

Point to the object you would use to	†Serve a bowl of soup (ladle) (can)

Style your hair? (comb) (shoe brush)

Slice a piece of bread? (knife) (saw)

Brush your teeth? (toothbrush) (foam brush)

Pound a nail? (hammer) (shoe)

Eat your food? (fork) (chopstick)

Pour some water? (watering can) (tin can)

Flip an egg? (flipper/spatula) (scraper)

Take out a splinter? (tweezers) (needle)

6. ACTION IDENTIFICATION – (VIDEO)

I am going to show you a series of gestures and ask you to identify them. I will tell you about one gesture and ask you to identify the gesture from a group of five on the video screen. Do you understand? You may find that there is more than one yes response.

Which of the following gestures shows the subject pretending …

to use a pair of tweezers to pull out a splinter?

to use a flipper/spatula to flip an egg?

to use a watering can to pour some water?

to use a fork to eat some food?

to use a toothbrush to brush his teeth?

to use a knife to slice a piece of bread?

to use a hammer to pound a nail?

to use a comb to style his hair?

7. ACTION IDENTIFICATION BY TOOL – (VIDEO)

I will show you a tool and then ask you to identify the gesture associated with that tool from a group of five on the video screen. You may find that there is more than one yes response.

Tell me when you see him using: Hammer

Watering Can

Tweezers

Comb

Fork

Knife

Flipper/Spatula

Toothbrush

8. GESTURE RECOGNITION – (VIDEO)

I am going to show you a series of gestures and ask you to identify them. I will demonstrate a gesture and ask you to choose the same gesture from a group of five on the video screen. Do you understand? You may find that there is more than one yes response. (Roll video and after each gesture ask): Is this person doing what I am doing? Yes or No

Is this person doing what I am doing?	Watering Can
	Tweezers
	Hammer
	Fork
	Comb
	Flipper/Spatula
	Toothbrush
	Knife

9. GESTURE ERROR RECOGNITION – (VIDEO)[1]

I am going to show you a series of gestures and I will ask you whether the subject is doing the gestures correctly or not. You may find that there is more than one yes response. (After each gesture ask): Is the person doing the gesture right? Yes or No. Remember that the subject is supposed to be pretending to be holding the tool in their hand.

He is going to pretending to use…	A watering can to pour some water
Correctly or not?	Tweezers to remove a splinter
	A hammer to pound a nail
	A fork to eat some food
	A comb to style his hair
	A flipper/spatula to flip an egg

[1] Task 9 was not conducted for the majority of participants due to technical difficulties.

A toothbrush to brush his teeth

A knife to slice a piece of bread

* Note: there are 32 gestures total and the sequence of the gestures is starting from watering can and running through to knife then returning back to watering can and repeats four times.

All subsequent sections need to be video taped

10. PANTOMIME BY TOOL – (EYES CLOSED) *

All gestures performed with the left hand, then all gestures with the right hand.

I am going to give you the name of an object and I would like you to pretend you are holding that object in your hand. I would like you to show me how you would use it if it were really in your hand. Do you understand?

With your eyes closed show me how you would use a…

Hammer to pound a nail

Flipper/Spatula to flip an egg

Toothbrush to brush your teeth

Watering can to pour some water

Pair of tweezers to pull out a splinter

Knife to slice a piece of bread

Fork to eat food

Comb to style your hair

10 b. LOWER LIMB TRANSITIVE PANTOMIME*

All gestures performed with the left foot, then all gestures with the right foot.

I am going to give you the name of an object and I would like you to pretend you are using that object with your foot. Do you understand?

Kick a Soccer Ball

Stub out a Cigarette

Slip on a Slipper (w/o Hands)

Push a Gas/Drum Pedal

10 c. PANTOMIME BY TOOL – (EYES OPEN) Left then Right

All gestures performed with the left hand, then all gestures with the right hand.

I am going to give you the name of an object and I would like you to pretend you are holding that object in your hand. I would like you to show me how you would use it if it were really in your hand. Do you understand?

Show me how you would use a…

Hammer to pound a nail

Flipper/Spatula to flip an egg

Toothbrush to brush your teeth

Watering can to pour some water

Pair of tweezers to pull out a splinter

Knife to slice a piece of bread

Fork to eat food

Comb to style your hair

11. a.) PANTOMIME INTRANSITIVE

I am going to ask you to demonstrate some gestures for me.

All gestures performed with the left hand, then all gestures with the right hand.

Show me how you would…

Scratch your ear

Put cream on your face

Salute

Hold your nose if there is a bad smell in the room

Wave

Beckon someone over

Make the okay sign

Hail a cab

11. b.) LOWER LIMB INTRANSITIVE PANTOMIME*

All gestures performed with the left foot, then all gestures with the right foot.

Show me how you would…

Trace a W on the Floor with your foot

Stomp your foot

Cross Right Ankle over Left Ankle (then vv)

Trace a Circle with your Toe

12. OBJECT USE BY PICTURE – (PICTURES)

Now, I am going to show you a picture instead and I'd like you to pretend that you are holding that object in your hand. I would like you to show me how you would use it if it were really in your hand. Do you understand?

All gestures performed with the left hand, then all gestures with the right hand.

Show me how you would use this: Fork

Comb

Flipper/Spatula

Hammer

Watering can

Toothbrush

Tweezers

Knife

13. OBJECT USE – (OBJECT)

I am going to give you an object and I would like you to show me how you would use that object.

All gestures performed with the left hand, then all gestures with the right hand.

(Present tool without indicating how to hold the tool)

Show me how you would use this Knife

Flipper/Spatula

Toothbrush

Hammer

Watering Can

Comb

Tweezers

Fork

14. PANTOMIME BY FUNCTION – (VERBAL)

I am going to give you a verbal description of an action without a tool name. Pretend you are holding that tool in your hand and show me how you would use that tool if it were really in your hand. Do you understand?

All gestures performed with the left hand, then all gestures with the right hand.

Show me how you would	Brush your teeth (toothbrush)
	Pull out a splinter (tweezers)
	Flip an egg (flipper/spatula)
	Eat your food (fork)
	Pound a nail (hammer)
	Slice a piece of bread (knife)
	Pour some water (watering can)
	Style your hair (comb)

15a. IMITATION-DELAYED FOR TRANSITIVE GESTURES (Eyes Closed)*

All gestures performed with the left hand, then all gestures with the right hand.

I am going to show you a series of gestures. Once I have finished doing the gesture, I then want you to close your eyes and do the exact same thing that I just did. It is important that you do the gesture the same way that I did using the same hand. Do you understand? Remember it is important that you do not do the action until I have completed it. To help you out I will put my hands down on my lap when I have completed the movement and that is when you are to close your eyes and start doing the movement. Okay? Let's continue.

Fork

Tweezers

Watering Can

Comb

Hammer

Flipper/spatula

Toothbrush

Knife

15b. IMITATION-DELAYED - LOWER LIMB TRANSITIVE GESTURES (Eyes Open)*

All gestures performed with the left foot, then all gestures with the right foot.

I am going to show you a series of lower limb gestures. Once I have finished doing the gesture, I then want you to do the exact same thing that I just did. It is important that you do the gesture the same way that I did using the same foot. Do you understand? Remember it is important that you do not do the action until I have completed it.

Kick a Soccer Ball

Stub out a Cigarette

Slip on a Slipper (w/o Hands)

Push a Gas/Drum Pedal

15c. IMITATION-DELAYED FOR TRANSITIVE GESTURES (Eyes Open)

All gestures performed with the left hand, then all gestures with the right hand.

I am going to show you a series of gestures. Once I have finished doing the gesture, I then want you to do the exact same thing that I just did. It is important that you do the gesture the same way that I did using the same hand. Do you understand? Remember it is important that you do not do the action until I have completed it. To help you out I will put my hands down on my lap when I have completed the movement and that is when you are to start doing the movement. Okay? Let's continue.

Fork

Tweezers

Watering Can

Comb

Hammer

Flipper/spatula

Toothbrush

Knife

16a. IMITATION-DELAYED FOR INTRANSITIVE GESTURES

All gestures performed with the left hand, then all gestures with the right hand.

We are going to do the same things again that we just did. This time we are going to some other types of gestures. Remember that I want you to copy exactly what I have done and that you are

not to start doing the action until I have completed the movement and have put my hands on my lap. Do you understand? Good, let's continue.

Scratch your ear

Put cream on your face

Salute

Hold your nose if there is a bad smell in the room

Wave

Beckon someone over

Make the okay sign

Hail a cab

16b. IMITATION-DELAYED FOR LOWER LIMB INTRANSITIVE GESTURES*

I am going to show you a series of lower limb gestures. Once I have finished doing the gesture, I then want you to do the exact same thing that I just did. It is important that you do the gesture the same way that I did using the same foot. Do you understand? Remember it is important that you do not do the action until I have completed it.

All gestures performed with the left foot, then all gestures with the right foot.

Trace a W on the Floor with your foot

Stomp your foot

Cross Right Ankle over Left Ankle (then vv)

Trace a Circle with your Toe

17. IMITATION-DELAYED FOR NONREPRESENTATIONAL GESTURES (eyes closed)*

All gestures performed with the left hand, then all gestures with the right hand.

I am going to show you a series of gestures. Once I have finished doing the gesture, I then want you to close your eyes and do the exact same thing that I just did. It is important that you do the gesture the same way that I did using the same hand. Do you understand? Remember it is important that you do not do the action until I have completed it. To help you out I will put my hands down on my lap when I have completed the movement and that is when you are to close your eyes and start doing the movement. Okay? Let's continue.

Gesture A: Rotate hand in air above head with index finger extended

Gesture C: Index finger and thumb extended with thumb facing floor, arm abducted and extended at shoulder, elbow flexed with hand positioned in front of body at midline

Gesture E: Pat hand on top of head with fingers extended and palm facing forward

Gesture G: Fingers extended hand placed under chin with thumb facing body midline

Gesture D: Little finger extended with arm abducted at shoulder directly away from body at side and flexed at elbow with hand facing the floor

Gesture B: Palm flat, facing floor, fingers extended moving forward and backward in sagittal plane

Gesture F: Thumb and forth finger in opposition with movement of hand toward and away from chin

Gesture H: Hand on top of head with thumb and first two fingers extended palm facing forward.

17b. IMITATION-DELAYED FOR LOWER LIMB NONREPRESENTATIONAL GESTURES (eyes open)*

I am going to show you a series of lower limb gestures. Once I have finished doing the gesture, I then want you to do the exact same thing that I just did. It is important that you do the gesture the same way that I did using the same foot. Do you understand? Remember it is important that you do not do the action until I have completed it.

All gestures performed with the left foot, then all gestures with the right foot.

GESTURE A: Drag foot from bottom of knee to bottom of shin

GESTURE B: Index finger and thumb extended with thumb facing floor, arm abducted and extended at shoulder, elbow flexed with hand positioned in front of body at midline

GESTURE C: Pat hand on top of head with fingers extended and palm facing forward

GESTURE D: Fingers extended hand placed under chin with thumb facing body midline

17c. IMITATION-DELAYED FOR NONREPRESENTATIONAL GESTURES (eyes open)

I am going to show you a series of gestures that do not mean anything. I want you to copy exactly what I do. It is important that you watch where my hand is and what my fingers are doing. Remember I will do the movement first and once I have put my hands on my lap, I then want you to do what I have just done. Do you understand? Good, let's continue.

Gesture A: Rotate hand in air above head with index finger extended

Gesture C: Index finger and thumb extended with thumb facing floor, arm abducted and extended at shoulder, elbow flexed with hand positioned in front of body at midline

Gesture E: Pat hand on top of head with fingers extended and palm facing forward

Gesture G: Fingers extended hand placed under chin with thumb facing body midline

Gesture D: Little finger extended with arm abducted at shoulder directly away from body at side and flexed at elbow with hand facing the floor

Gesture B: Palm flat, facing floor, fingers extended moving forward and backward in sagittal plane

Gesture F: Thumb and forth finger in opposition with movement of hand toward and away from chin

Gesture H: Hand on top of head with thumb and first two fingers extended palm facing forward.

18. IMITATION-CONCURRENT FOR TRANSITIVE GESTURES

I am going to show you a series of gestures and ask you to do the exact same thing I am doing. It is important that you do the gesture the same way I do it using the same hand. Do you understand?

Do this	Fork
	Tweezers
	Watering Can
	Comb
	Hammer
	Flipper/Spatula
	Toothbrush
	Knife

19. IMITATION-CONCURRENT FOR TRANSITIVE GESTURES WITH VERBAL CUE – (ACTION)

I am going to show you a series of gestures and ask you to do the exact same thing I am doing. It is important that you do the gesture the same way I am doing it. As we do the gesture, I will tell you what we are doing. Do you understand?

You can join in any time	Slice a piece of bread
	Pull out a splinter
	Eat your food
	Brush your teeth
	Pound a nail
	Flip an egg

Style your hair

Pour some water

20. IMITATION-CONCURRENT FOR INTRANSITIVE GESTURES

I am going to show you a series of gestures and ask you to do the exact same thing I am doing. It is important that you do the gesture the same way I am doing it using the same hand. Do you understand? Good, let's continue.

Do this Scratch ear

Cream on face

Salute

Hold nose

Wave

Beckon

Okay sign

Hail a cab

21. IMITATION-CONCURRENT FOR NONREPRESENTATIONAL GESTURES

I am going to show you a series of gestures and ask you to do the same thing I am doing. It is important that you do the gesture the same way I am doing it using the same hand. These gestures are meaningless and so you should watch where my hand is and what my fingers are doing. Do you understand?

Gesture A: Rotate hand in air above head with index finger extended

Gesture C: Index finger and thumb extended with thumb facing floor, arm abducted and extended at shoulder, elbow flexed with hand positioned in front of body at midline

Gesture E: Pat hand on top of head with fingers extended and palm facing forward

Gesture G: Fingers extended hand placed under chin with thumb facing body midline

Gesture D: Little finger extended with arm abducted at shoulder directly away from body at side and flexed at elbow with hand facing the floor

Gesture B: Palm flat, facing floor, fingers extended moving forward and backward in sagittal plane

Gesture F: Thumb and forth finger in opposition with movement of hand toward and away from chin

Gesture H: Hand on top of head with thumb and first two fingers extended palm facing forward.

II. GESTURE SCORING CRITERIA

A) Upper Limb Meaningful

****FORK****

LOCATION ERROR		ACTION ERROR	
2	At midline in front of the body up to mouth No farther than 4 inches away	2	Stab/Lift + smooth motion towards the mouth w/ action from the elbow
1	Right against mouth or Out near ear	1	Absence of any one of above criteria Minor distortion of action
0	More than 4 inches away from the mouth or If done in outer space	0	Absence of more than one criterion OR Any major distortion/inappropriate movement
POSTURE OF HAND		**PLANE OF MOVEMENT**	
Criteria – 1. Thumb and index in opposition 2. 2nd Finger supporting fork 3. Others curled, fork grasped at base			NB: If movement started at inappropriate height (too low/high) this will affect plane (increasing or decreasing Z contribution)
2	One of the criteria is missing or wrong	2	"- X" and Z plane
1	Two or all criteria are missing or wrong	1	Plane exaggerated or Z plane only.
0	Two or all criteria are missing or wrong	0	X or Y plane only or other combination of planes
ORIENTATION			
2	Palm of hand is parallel to midline and fingers away from body or palm parallel to ground		
1	Palm faces body		
0	Any variation that is greater than 90 degrees		

**** TWEEZERS****

LOCATION ERROR		ACTION ERROR	
2	In front of the body B) Fingers with tweezers are one inch away from splinter site	2	Pinch and pull action
1	In front of body but tweezers fingers are touching splinter site. Improper location w/ all other correct	1	Pinch alone Pull back alone
0	Both hands are not in alignment. Improper location w/ touching or multiple errors	0	No pinching or pulling back Some nonsensical motion
POSTURE OF HAND (Tweezer hand)		**PLANE OF MOVEMENT**	
Criteria 1. Thumb & index finger extended to hand 2. Slightly apart 3. Other fingers curled			
		2	Z plane primarily (Z-Y Plane)
2	All above correct	1	Y only or is the major plane (motion is to the side)
1	One missing or wrong		
0	Two or more missing or wrong	0	XY Plane (No motion?)
ORIENTATION			
2	Palm facing ground, wrist slightly flexed (tweezer hand)		
1	Palm perpendicular to ground		
0	Palm with fingers pointing upward. Palm facing up to ceiling.		

** WATERING CAN**

LOCATION ERROR		ACTION ERROR	
2	In front of body between waist and nipple line	2	Some degree of elevation; rotation; adduction
1	Too far to ipsilateral side	1	Any one of the above missing or exaggerated
0	Too far to contralateral side. Too high/low.	0	No rotation. Or No movement Or gross/multiple exaggeration of components
POSTURE OF HAND		**PLANE OF MOVEMENT**	
Criteria 1. Thumb over first section of index finger 2. Other fingers curled around handle 3. Finger knuckles in alignment			
		2	Y-Z plane
2	All three criteria are correct	1	Y Plane exaggerated or Z plane exaggerated
1	One of the criteria is wrong		
0	Two or more criteria are wrong	0	Any single plane or rotation only (no plane).
ORIENTATION			
2	Palm perpendicular to ground or parallel to midline, wrist neutral and in line with forearm		
1	Any variation that is equal or less than 45 degrees		
0	Palm parallel to floor or variation greater than 90 degrees		

COMB

LOCATION ERROR		ACTION ERROR	
2	Anywhere on the scalp, no more than 3 inches Away	2	Conforms to the head, top to bottom or front to back. (Primarily at elbow & shoulder)
1	Anywhere on the head or above the head Anything greater than 3 inches away	1	Wrist movement is exaggerated
0	Any other body part Anywhere on the face	0	No movement. Any movement perpendicular to the head
POSTURE OF HAND		**PLANE OF MOVEMENT**	
Criteria 1. Thumb and index finger in opposition 2. Fingers curl to support comb 3. Comb firmly grasped			
		2	Parallel to head
2	All three criteria are showing and correct	1	45 degree variation.
1	One of the criteria is missing or wrong		
0	Two or all criteria are missing or wrong	0	Perpendicular to the head
ORIENTATION			
2	Palm of hand is parallel to head		
1	Slight variation, any angle between 45 and 90 degrees		
0	Any variation that is greater than 90 degrees		

****HAMMER****

LOCATION ERROR		ACTION ERROR	
2	Anywhere midline to ipsilateral side b/t shoulder and hip ("strike zone")	2	Repetitive up and down movement at elbow and wrist
1	Too high or too low	1	Exaggerated up, down, shoulder included Distortion of movement
0	Contralateral side. Anything over midline.	0	No repetition Any other kind of movement, including rotation
POSTURE OF HAND		**PLANE OF MOVEMENT**	
Criteria – 1. Fingers curled and tight around 2. Thumb along hammer base 3. Hammer grasped at base, head facing ground and away from body			
		2	Z in X direction (+ bit of Y?) X in Z direction (+ bit of Y?)
2	All three criteria are showing and correct	1	Off by 45 degrees
1	One of the criteria is missing or wrong	0	Z in Y direction or lateral X-Y movements Y in Z direction
0	Two or more criteria are missing or wrong		
ORIENTATION			
2	Palm facing midline, thumb towards the camera		
1	Any slight variation in hand position		
0	Palm facing the ground		

****FLIPPER/SPATULA****

LOCATION ERROR		ACTION ERROR	
2	In front of the body between waist and the nipple Line	Criteria	1. Forward thrust of arm (X) 2. Elevation (+Z) 3. Medial rotation (+Y)
1	At the right height but too far to ipsilateral side		
0	Too high or too low Too far to the contralateral side	2	All three criteria are showing and correct
POSTURE OF HAND		1	One of the criteria is exaggerated or missing
Criteria 1. Fingers curled and tight around base 2. Thumb along flipper base 3. Flipper grasped at base, with flat face up		0	Two or all criteria are missing or wrong
		PLANE OF MOVEMENT	
2	All three criteria are correct	2	X (Thrust), +Z (Elevation), +Y (Rotation)
1	One of the criteria is wrong	1	If any one plane is exaggerated or missing Movement in only two planes
0	Two or more criteria are wrong	0	Movement in only one plane Improper combination of planes
ORIENTATION			
2	Palm facing the midline, thumb towards the camera		
1	Any slight variation in hand position (nothing greater than 45 degrees)		
0	Palm facing the ground		

****TOOTHBRUSH****

LOCATION ERROR		ACTION ERROR	
2	Midline to length of toothbrush being put in front of mouth	2	Up and down (wrist) AND back and forth (elbow/shoulder) motion. Fluid and repetitive.
1	Too high or too low; sloppy in face region	1	Either of above alone/uncoupled Whole arm moves, exaggerated movement
0	Not near the face, below the chin	0	Non-repetitive motion or motion in outer space No motion
POSTURE OF HAND		**PLANE OF MOVEMENT**	
Criteria 1. Fingers curled around handle 2. Index finger protruding (tool pincer) 3. Thumb along index/grasping brush head		2	Hand along Z AND shoulder along Y Hand along X AND shoulder along Y
2	All three criteria are showing and correct	1	Distribution in either Y or Z planes
1	One of the criteria is missing or wrong	0	X plane only
0	Two or all criteria are missing or wrong		
ORIENTATION			
2	Palm towards ground		
1	Slight variation that is less than 90 degrees (Palm facing camera)		
0	Variation that is equal to or greater than 90 degrees (Palm facing face)		

****KNIFE****

LOCATION ERROR		ACTION ERROR	
2	"Strike zone" Midway between hip and shoulder b and ipsilateral side	2	"Flex'n of shoulder w/ ext'n of elbow" + "ext'n shoulder w/ flex'n of elbow" (coupled, fluid and repetitive)
1	Too high or too low; too far to ipsilateral side.	1	Non-continuous motion. Move from wrist only.
0	Crosses midline of the body	0	No movement. Side to side motion (adduction/abduction)
POSTURE OF HAND		**PLANE OF MOVEMENT**	
Criteria 1. Fingers curled and tight around base 2. Index finger protruding ("tool pincer" grip) 3. Thumb along index finger/knife base		2	In +/- X direction
		1	X to Y range X to "- Z" range
2	All three criteria are showing and correct	0	Y only Z only Or other combination (circular)
1	One of the criteria is missing or wrong		
0	Two or more of the criteria are missing or wrong		
ORIENTATION			
2	Palm of hand parallel to ground, fingers pointing away from the body (0-45° is OK)		
1	Slight variation in position (45 to 90 degrees)		
0	Variation is greater than 90 degrees		

B.) Upper Limb Non-Representational

A. ROTATE HAND IN AIR ABOVE HEAD

LOCATION ERROR		ACTION ERROR	
2	In front of the body at the midline	2	[redacted]
1	Anywhere in front of the body either below or above the midline	1	
0	Movement is not done in front of the body Movement done at the side	0	
POSTURE OF HAND		**PLANE OF MOVEMENT**	
Criteria 1. Thumb and index finger extended 2. Arm fully abducted & wrist straight 3. Other fingers curled			
		2	[redacted]
2	All three criteria are showing and correct	1	
1	One of the criteria is missing or wrong		
0	Two or all criteria are missing or wrong	0	
ORIENTATION			
2	Hand is at midline with lateral side of arm facing forward		
1	Any slight variation in the wrist		
0	If back of hand or palm is showing forward		

C. INDEX & THUMB EXTENDED W/ HAND IN FRONT AT MIDLINE

LOCATION ERROR		ACTION ERROR	
2	Movement correctly above head	2	Movement is rotation finger using whole hand and wrist
1	Too high but directly above head	1	Distortion of movement, using arm instead of wrist, using finger only
0	Hand is put on side of the head Hand is put in front of the head Hand is put at back of the head	0	Any other movement No rotation of hand OR back and forth movement
POSTURE OF HAND		**PLANE OF MOVEMENT**	
Criteria 1. Extended index finger 2. Other fingers curled 3. Thumb wrapped around other fingers			
		2	Finger traces circle in the XY plane
2	All three criteria are showing and correct	1	Moderate variation in plane (45 degrees)
1	One of the criteria is missing or wrong	0	Major variation in plane (ZX or ZY plane)
0	Two or all criteria are missing or wrong		
ORIENTATION			
2	Palm of the hand is facing forward and fingers pointing towards ceiling		
1	If palm of hand or fingers are rotated off by 45 degrees		
0	If palm or fingers are turned greater than 90 degrees (pointing sideways, back of hand facing forward)		

E. PAT HAND ON TOP OF HEAD

LOCATION ERROR		ACTION ERROR	
2	Hand is directly on top of head and centred	2	Movement done mostly w/ elbow
1	Hand is slightly off either more to front or back but still touching crown of head	1	Movement w/ elbow AND wrist Movement w/ elbow AND shoulder
0	Hand not touching crown of head (too far to front, back or side)	0	Sideways movement instead of Up/Down Wrist or shoulder only
POSTURE OF HAND		**PLANE OF MOVEMENT**	
Criteria 1. Fingers extended 2. Thumb extended 3. Fingers and thumb are tight		2	Movement in the coronal (YZ) plane only Primarily in the Z plane
			Coronal movement primarily in Y plane Coming forward (some X)
2	Are three criteria are showing and correct	1	
1	One of the above criteria is missing or incorrect	0	Only X or Only Y (forward/backwards on head or side to side)
0	Two or all criteria missing or incorrect		
ORIENTATION			
2	Palm of hand is facing forward		
1	Any variation that is equal or less than 45 degrees		
0	Any position that is greater than 90 degrees (palm of hand facing backwards, etc)		

G. HAND UNDER CHIN AT MIDLINE

LOCATION ERROR		ACTION ERROR	
2	Hand in midline and touching under chin	2	[redacted]
1	Hand not touching chin but in midline	1	
0	Not on the midline; anywhere beside the body	0	
POSTURE OF HAND		**PLANE OF MOVEMENT**	
Criteria 1. Fingers extended 2. Thumb straight & in line with hand 3. Fingers tightly together			[redacted]
		2	
2	All criteria are showing and correct	1	
1	One of the above criteria is missing or incorrect		
0	Two or all criteria missing or incorrect	0	
ORIENTATION			
2	Hand is facing sideways w/ thumb facing midline		
1	Hand is at an angle of 45 degrees or less		
0	Hand at an angle greater than 45 degrees or hand w/ thumb not facing body		

D. LITTLE FINGER EXTENDED

LOCATION ERROR		ACTION ERROR	
2	Hand is at the side of the body Arm abducted and elbow flexed	2	[redacted]
1	Arm too high or too low No abduction/no flexion	1	
0	If arm is in front of body	0	
POSTURE OF HAND		**PLANE OF MOVEMENT**	
Criteria 1. Little finger extended 2. Other fingers curled 3. Thumb wrapped around fingers			[redacted]
2	All criteria are showing and correct	2	
1	One of above criteria is missing or incorrect	1	
0	Two or all criteria missing or incorrect	0	
ORIENTATION			
2	Palm facing down towards the ground (zero degrees); finger points parallel to midline (sagittal plane)		
1	Palm or finger closer to 45 degrees from target position		
0	Palm or finger closer to or greater than 90 degrees from target		

B. OPEN HAND MOVING IN SAGGITAL PLANE

LOCATION ERROR		ACTION ERROR	
2	At side midway between hips and shoulder	2	All movement is at the elbow and shoulder
1	If movement is too high or too low	1	Distortion of action Swing motion instead of going straight
0	If gesture is done anywhere else but beside body	0	Movement in hand only w/ no arm Bent wrist not in line with arm Towards and away from the side
POSTURE OF HAND		**PLANE OF MOVEMENT**	
Criteria 1. Fingers extended 2. Thumb extended 3. Hand is tight not opened		2	Arm at side in the sagittal plane moving forwards and backwards
2	If all three criteria are showing	1	Bent wrist action in same plane Distortion of action
1	If one of the criteria is missing or wrong	0	Abduction and Adduction instead of forwards and backwards Action across the body
0	If two or more criteria are missing or wrong		
ORIENTATION			
2	Palm of hand must be facing the floor		
1	Slight variation in hand position, to the side, anything less than 45 degrees		
0	Palm of hand facing the ceiling, anything greater than 90 degrees		

F. THUMB AND FOURTH FINGER TO/FROM CHIN

LOCATION ERROR		ACTION ERROR	
2	Movement is done to front of chin	2	Movement is in the elbow only
1	Movement is done to any other part of chin	1	Elbow plus shoulder movement Elbow plus wrist movement
0	Movement is far away from chin	0	Shoulder only Wrist only
POSTURE OF HAND		**PLANE OF MOVEMENT**	
Criteria 1. Fingers extended 2. Thumb extended 3. Thumb and fourth finger tips touching		2	Movement in sagittal plane even if action is distorted
2	All three criteria are showing and correct	1	If in sagittal plane and some other plane also
1	One of the above criteria is missing or incorrect	0	If completely in some other plane
0	Two or all criteria are missing or incorrect		
ORIENTATION			
2	Palm of hand is facing towards the face AND fingers pointing up		
1	Palm of hand is sideways to the face OR Fingers point to side		
0	Palm of hand is facing away from face (back of hand towards chin) OR Fingers point forward		

H. HAND ON HEAD WITH TWO FINGERS EXTENDED

LOCATION ERROR		ACTION ERROR	
2	Hand on top of head	2	[redacted]
1	Hand above head but not touching	1	
0	Hand at front/back of head or to the side	0	
POSTURE OF HAND		**PLANE OF MOVEMENT**	
Criteria 1. Index and middle finger extended 2. Thumb extended 3. Other fingers curled		2	[redacted]
		1	
2	All three criteria are showing and correct	0	
1	One of the criteria is missing or incorrect		
0	Two or all criteria are missing or incorrect		
ORIENTATION			
2	Palm is facing forward (i.e. towards camera) AND fingers point up		
1	Slight variation in position of palm or fingers (equal to or less than 45 degrees)		
0	Variation greater than 90 degrees (palm backwards or perpendicular)		

C) Lower Limb Meaningful

SOCCER BALL

LOCATION ERROR		ACTION ERROR	
2	At midline in front of the body	2	Slow drawing of foot backwards and abrupt fwd movement (some sideways movement okay)
1	Crosses Midline	1	All at one speed, only kicks forwards
0	Too Far Ipsilateral (chair boundaries)	0	Circular motion or up and down stomp. Kicks backwards
POSTURE		**PLANE OF MOVEMENT**	
2	Bent knee, extends with movement Foot 90 degrees with leg	2	Primarily X Plane, some +z and slight Ydeviations
1	Remains Bent for whole movement Slight lateral or medial rotation of ankle	1	Primarily Y Plane with some X.
0	Leg stays straight for entire movement	0	Y or Z plane only or other combo of planes
ORIENTATION			
2	Sole Faces the ground, with end of gesture facing forwards		
1	Sole faces ground whole time		
0	Any variation that is greater than 90 degrees		

CIGARETTE STUB

LOCATION ERROR		ACTION ERROR	
2	At midline in front of the body, ankle aligns with hip and knee	2	Toes contacting the floor, pivots heel back and forth
1	Crosses Midline	1	Stomps Cigarette out
0	Too Far Ipsilateral (chair boundaries)	0	Other action
POSTURE		**PLANE OF MOVEMENT**	
2	Plantar Flexion of the ankle	2	Heel moves in the Y Plane
1	Flatfooted, no flexion of the ankle	1	Movement is in the Z plane (up and down stomp)
0	Dorsiflexion of the ankle	0	Movement in the X Place
ORIENTATION			
2	Sole Faces Ground and Backwards (45 Degree angle)		
1	Sole Faces Ground only		
0	Any variation that is greater than 90 degrees		

SLIPPER

LOCATION ERROR		ACTION ERROR	
2	At midline in front of the body, ankle aligns with hip and knee	2	Downwards then Forwards Motion
1	Crosses Midline	1	Forwards Only
0	Too Far Ipsilateral (chair boundaries)	0	Circular motion or other action
POSTURE		**PLANE OF MOVEMENT**	
2	Plantar Flexion of Ankle, then straighten out	2	X and –Z
1	No flexion for any part of the gesture	1	Missing Z
0	Other combination of postures	0	Any Other Combination of Planes
ORIENTATION			
2	Sole Faces Ground and Backwards (45 Degree angle), then flattens facing ground		
1	Sole Faces Ground only		
0	Any variation that is greater than 90 degrees		

GAS PEDAL

LOCATION ERROR		ACTION ERROR	
2	At midline in front of the body, within An Inch of or Contacting the ground	2	Heel contacts floor, goes up and down with front h foot
1	Crosses Midline, ankle aligns with knee, 1-3 inches off the ground	1	Uses whole foot to control pedal rather than using Heel as leverage.
0	Too Far Contralateral, >3 off the ground	0	Circular motion or other action
POSTURE		**PLANE OF MOVEMENT**	
2	Dorsi Flexion of Ankle, then straighten out	2	Z with some +X
1	Straight the whole time	1	Z only
0	Other combination of postures	0	Any Other Combination of Planes
ORIENTATION			
2	Sole Faces Ground and Forwards (45 Degree angle), then flattens facing ground		
1	Sole Faces Ground only		
0	Any variation that is greater than 90 degrees		

****W****

LOCATION ERROR		ACTION ERROR	
2	In Front of Body, on Floor	2	Back, forth, back forth – left to right
1	Traces Letter in the air	1	Down Up, Down, up from Left to Right OR Traces it backwards
0	Too far ipsilateral (right foot) Too far Contralateral (left foot)	0	Other
POSTURE		**PLANE OF MOVEMENT**	
2	Plantar Flexion of the ankle. Toes pointed	2	x and y
1	No Flexion	1	Y and z
0	Dorsiflexion	0	Other
ORIENTATION			
2	Sole of the foot faces floor and backwards, 45 degree lift from toes		
1	Sole of feet faces the floor, no lift		
0	Faces Sideways		

****STOMP FOOT ONCE****

LOCATION ERROR		ACTION ERROR	
2	In Front of Body, on Floor (ankle aligned with knee straight up and down)	2	Lifts whole foot, stomps once
1	Too Far Contralateral or Ipsilateral	1	Stomps more than once
0	Too far forward or backwards.	0	Does not lift whole foot
POSTURE		**PLANE OF MOVEMENT**	
2	Knee and ankle aligned (foot 90 degrees)	2	Z+, Z-
1	Knee extended	1	Some X or Y
0	Plantar or Dorsiflexion	0	Circular movement
ORIENTATION			
2	Sole of the foot faces floor, toes forward		
1	< 45 degrees variation		
0	> 45 degrees		

CROSS RIGHT ANKLE OVER LEFT ANKLE (Vice Versa for Left)

LOCATION ERROR		ACTION ERROR	
2	Correct ankle on top of other ankle, contralateral Placement	2	Crosses ankle over top of other Top foot does most the moving
1	Incorrect ankle on top of other ankle	1	Achieves correct configuration by keeping top foot stationary and slips bottom foot under
0	Ankle on knee, or other place	0	Other action
POSTURE		**PLANE OF MOVEMENT**	
2	Foot at 90 degree angle to leg, relaxation of Ankle permitted, knees bent	2	Y; slight +x, and slight +Z is fine
1	Legs Straight	1	Exaggerated X or Z
0	Other posture	0	Other Combination of Planes
ORIENTATION			
2	Sole of foot facing contralateral side		
1	< 45 degrees of variation		
0	>45 degrees of varation		

TRACE CIRCLE WITH TOE

LOCATION ERROR		ACTION ERROR	
2	Heel does not contact with the floor, in front of Body	2	Traces Circle with toe
1	Foot does not contact Floor or whole foot used	1	Traces multiple circles (1+) or other enclosed Figures
0	Too far contralateral or Ipsilateral	0	Traces line or nothing
POSTURE		**PLANE OF MOVEMENT**	
2	Toes pointed, Plantar Flexion of Ankle	2	Equal amounts of X and Y
1	One of the above missing	1	Unequal amounts of X and Y
0	Both of the above missing	0	Z
ORIENTATION			
2	Sole should be facing down and backwards (45 degrees)		
1	Sole Faces Floor		
0	Other		

D) Lower Limb Non-Representational

KNEE DRAG

LOCATION ERROR		ACTION ERROR	
2	Heel contacts slightly below knee, drags down Front of shin	2	Raises heel up and drags down
1	Drags down side of leg, or initial contact is 6-8inches away from knee but still drags down the front, or does not make contact with leg but still in correct area	1	Repetitive dragging movement up and down Leg
0	Nowhere near front of leg	0	Does not resemble action
POSTURE		**PLANE OF MOVEMENT**	
2	Ankle dorsiflexed, Flexion of the knee	2	Z only (+Z and then –Z), some –X
1	Foot relaxed	1	Some Y variation if stable leg is slouched (<45 degrees)
0	Leg is straight	0	Any other plane combination
ORIENTATION			
2	Sole of foot facing midline		
1	<45 degrees of variation, foot faces floor		
0	>45 degress of varation,		

IPSI DRAG

LOCATION ERROR		ACTION ERROR	
2	Foot begins inline/infront of other foot, Slides Ipsilaterally in front of body	2	Brings foot in front of other Drags foot Laterally
1	Foot is too far contralateral/ipsilateral to start (relative to other foot),	1	Lateral Drag only
0	Movement begins behind or beside foot. Minimum ¾ length of foot should be ahead of other foot.	0	Other action
POSTURE		**PLANE OF MOVEMENT**	
2	Flat foot, 90 degree to shin, flexed knee	2	XZ to align feet, then Y for lateral drag
1	Ankle flexed (heel/toes contact floor only)	1	Some XY in the drag
0	Fully Straight ened Leg	0	Z or X for the Drag
ORIENTATION			
2	Sole facing floor		
1	45 degree variation for plantar or dorsi flexion (backwards/forwards)		
0	>45 degree varation		

PLANT AND DRAG

LOCATION ERROR		ACTION ERROR	
2	Forward Stomp infront of body, Drags foot back inline with other foot	2	Forward Stomp, Drag Backwards
1	Feet are not aligned at the end point	1	Stomp or Drag Alone
0	Movement does not occur in front of body	0	Both Actions missing or distorted
POSTURE		**PLANE OF MOVEMENT**	
2	Knee almost fully extended for Stomp, Returns to a flexed position. Ankle not flexed	2	ZX for Stomp, -X for Drag
1	Correct Knee position, but some ankle flexing In either direction	1	Missing one of the above
0	Knee joint Remains at same angle for all of Movement	0	Y
ORIENTATION			
2	Sole facing floor		
1	45 degree variation for plantar or dorsi flexion (backwards/forwards)		
0	>45 degree varation		

CIRCLE + ANKLE CLICK

LOCATION ERROR		ACTION ERROR	
2	1. Begins with Heel contacting top of toes (other fo 2. Moves in outside personal space in a circle 3. ends with ankles contacting together	2	CW circle (RF), CounterCW (LF), Click Ankles Together
1	One criteria missing	1	Circle only OR Incorrect Circle Direction
0	Two or more criteria missing	0	Other action
POSTURE		**PLANE OF MOVEMENT**	
2	Knee Flexed, Ankle straight Rotation Comes from Knee	2	XY only
1	Rotation comes from the ankle	1	XY still, but with a little Z
0	Extended leg	0	Missing X or Y
ORIENTATION			
2	Sole Facing Floor		
1	<45 degrees		
0	>45 degrees		

APPENDIX C – The Unified Parkinson's Disease Rating Scale (UPDRS)

I. MENTATION, BEHAVIOR, MOOD

(Self-Report, Questionnaire Style)

1. Intellectual Impairment

0-none
1-mild (consistent forgetfulness with partial recollection of events with no other difficulties)
2-moderate memory loss with disorientation and moderate difficulty handling complex problems
3-severe memory loss with disorientation to time and often place, severe impairment with problems
4-severe memory loss with orientation only to person, unable to make judgments or solve problems

2. Thought Disorder

0-none
1-vivid dreaming
2-"benign" hallucination with insight retained
3-occasional to frequent hallucination or delusions without insight, could interfere with daily activities
4-persistent hallucination, delusions, or florid psychosis.

3. Depression

0-not present
1-periods of sadness or guilt greater than normal, never sustained for more than a few days or a week
2-sustained depression for >1 week
3-vegetative symptoms (insomnia, anorexia, abulia, weight loss)
4-vegetative symptoms with suicidality

4. Motivation/Initiative

0-normal
1-less of assertive, more passive
2-loss of initiative or disinterest in elective activities
3-loss of initiative or disinterest in day to say (routine) activities
4-withdrawn, complete loss of motivation

II. ACTIVITIES OF DAILY LIVING

(Self-Report, Questionnaire Style)

5. Speech

0-normal
1-mildly affected, no difficulty being understood
2-moderately affected, may be asked to repeat
3-severely affected, frequently asked to repeat
4-unintelligible most of time

6. Salivation

0-normal
1-slight but noticeable increase, may have nighttime drooling
2-moderately excessive saliva, hay minimal drooling
3-marked drooling

7. Swallowing

0-normal
1-rare choking
2-occasional choking
3-requires soft food
4-requires NG tube or G-tube

8. Handwriting

0-normal
1-slightly small or slow
2-all words small but legible
3-severely affected, not all words legible
4-majority illegible

9. Cutting Food/Handing Utensils

0-normal
1-somewhat slow and clumsy but no help needed
2-can cut most foods, some help needed
3-food must be cut, but can feed self
4-needs to be fed

10. Dressing

0-normal
1-somewhat slow, no help needed
2-occasional help with buttons or arms in sleeves
3-considerable help required but can do some things alone
4-helpless

11. Hygiene

0-normal
1-somewhat slow but no help needed
2-needs help with shower or bath or very slow in hygienic care
3-requires assistance for washing, brushing teeth, going to bathroom
4-helpless

12. Turning in Bed/ Adjusting Bed Clothes

0-normal
1-somewhat slow no help needed
2-can turn alone or adjust sheets but with great difficulty
3-san initiate but not turn or adjust alone
4-helpless

13. Falling-Unrelated to Freezing

0-none
1-rare falls
2-occasiona, less than one per day
3-average of once per day
4->1 per day

14. Freezing When Walking

0-normal
1-rare, may have start hesitation
2-occasional falls from freezing,
3-frequent freezing, occasional falls
4-frequent falls from freezin

15. Walking

0-normal
1-mild difficulty, day drag legs or decrease
arm swing
2-moderate difficultly requires no assist
3-severe disturbance requires assistance
4-cannot walk at all even with assist

16. Tremor

0-absent
1-slight and infrequent, not bothersome to patient
2-moderate, bothersome to patient
3-severe, interfere with many activities
4-marked, interferes with many activities

17. Sensory Complaints Related to Parkinsonism

0-none
1-occasionally has numbness, tingling, and mild aching

2-frequent, but not distressing
3-frequent painful sensation
4-excruciating pain

III. MOTOR EXAM

(Judged by an experience rater, total out of 108)

18. Speech

0-normal
1-slight loss of expression, diction,volume
2-monotone, slurred but understandable, mod. impaired
3-marked impairment, difficult to understand
4-unintelligible

19. Facial Expression

0-Normal
1-slight hypomymia, could be poker face
2-slight but definite abnormal diminution in expression
3-mod. hypomimia, lips parted some of time
4-masked or fixed face, lips parted 1/4 of inch or more with complete loss of expression

20. Tremor at Rest

+ Face, Right and Left Upper Extremities, Right and Left Lower Extremities
0-absent
1-slight and infrequent
2-mild and present most of time
3-moderate and present most of time
4-marked and present most of time

21. Action or Postural Tremor

+Right and Left Upper Extremities
0-absent
1-slight, present with action
2-moderate, present with action
3-moderate present with action and
posture holding
4-marked, interferes with feeding

22. Rigidity

+ Neck, Right and Left Upper Extremities, Right and Left Lower Extremities
0-absent
1-slight or only with activation
2-mild/moderate
3-marked, full range of motion
4-severe

23. Finger taps

+ Right and Left Upper Extremities

0-normal
1-mild slowing, and/or reduction in amp.
2-moderate impaired. Definite and early fatiguing, may have occasional arrests
3-severely impaired. Frequent hesitations and arrests.
4-can barely perform

24. Hand Movements (open and close hands in rapid succession)

+ Right and Left Upper Extremities

0-normal
1-mild slowing, and/or reduction in amp.
2-moderate impaired. Definite and early fatiguing, may have occasional arrests
3-severely impaired. Frequent hesitations and arrests.
4-can barely perform

25. Rapid Alternating Movements (pronate and supinate hands)

+ Right and Left Upper Extremities

0-normal
1-mild slowing, and/or reduction in amp.
2-moderate impaired. Definite and early fatiguing, may have occasional arrests
3-severely impaired. Frequent hesitations and arrests.
4-can barely perform

26. Leg Agility (tap heel on ground)

+ Right and Left Upper Extremities

0-normal
1-mild slowing, and/or reduction in amp.
2-moderate impaired. Definite and early fatiguing, may have occasional arrests
3-severely impaired. Frequent hesitations and arrests.
4-can barely perform

0-normal
1-mild slowing, and/or reduction in amp.
2-moderate impaired. Definite and early
fatiguing, may have occasional arrests
3-severely impaired. Frequent hesitations
and arrests.
4-can barely perform

27. Arising From Chair (pt. arises with arms folded across chest)

0-normal
1-slow, may need more than one attempt
2-pushes self up from arms or seat
3-tends to fall back, may need multiple tries but can arise without assistance

4-unable to arise without help

28. Posture
0-normal erect
1-slightly stooped, could be normal for older person
2-definitely abnormal, mod. stooped, may lean to one side
3-severely stooped with kyphosis
4-marked flexion with extreme abnormality of posture

29. Gait
0-normal
1-walks slowly, may shuffle with short steps,
no festination or propulsion
2-walks with difficulty, little or no assistance,
some festination, short steps or propulsion
3-severe disturbance, frequent assistance
4-cannot walk

30. Postural Stability (retropulsion test)
0-normal
1-recovers unaided
2-would fall if not caught
3-falls spontaneously
4-unable to stand

31. Body Bradykinesia/ Hypokinesia
0-none
1-minimal slowness, could be normal, deliberate character
2-mild slowness and poverty of movement, definitely abnormal, or dec. amp. Of movement
3-moderate slowness, poverty, or small amplitude
4-marked slowness, poverty, or amplitude

IV. COMPLICATIONS OF THERAPY

A. DYSKINESIAS

32. Duration: What proportion of the waking day are dyskinesias present?
0 = None
1 = 1-25% of day.
2 = 26-50% of day.
3 = 51-75% of day.
4 = 76-100% of day.

33. Disability: How disabling are the dyskinesias?
0 = Not disabling.
1 = Mildly disabling.
2 = Moderately disabling.
3 = Severely disabling.
4 = Completely disabled.

34. Painful Dyskinesias: How painful are the dyskinesias?
0 = No painful dyskinesias.
1 = Slight.
2 = Moderate.
3 = Severe.
4 = Marked.

35. Presence of Early Morning Dystonia
0 = No
1 = Yes

B. CLINICAL FLUCTUATIONS

36. Are "off" periods predictable?
0 = No
1 = Yes

37. Are "off" periods unpredictable?
0 = No
1 = Yes

38. Do "off" periods come on suddenly, within a few seconds?
0 = No
1 = Yes

39. What proportion of the waking day is the patient "off" on average?
0 = None
1 = 1-25% of day.
2 = 26-50% of day.
3 = 51-75% of day.
4 = 76-100% of day.

C. OTHER COMPLICATIONS

40. Does the patient have anorexia, nausea, or vomiting?
0 = No
1 = Yes

41. Any sleep disturbances, such as insomnia or hypersomnolence?
0 = No
1 = Yes

42. Does the patient have symptomatic orthostasis?
(Record the patient's blood pressure, height and weight on the scoring form)
0 = No
1 = Yes