

THE EFFECT OF FRONTAL LOBE FUNCTION ON PROVERB INTERPRETATION

IN PARKINSON'S DISEASE

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ABSTRACT

The cognitive impairment associated with PD involves a broad range of deficits including difficulty with executive functions such as working memory, inhibition, decision-making, and cognitive multitasking, learning, and visuoperceptual skills. Even early in the disease, when motor symptoms tend to predominate, there is evidence that cognitive functions can be compromised. Owing to the presence of executive-type dysfunction in PD, some researchers likened the cognitive deficit of PD to that seen with frontal lobe damage. The anatomical basis of PD, however, suggests otherwise. Dopamine depletion in the basal ganglia, and the downstream depletion of dopamine in the frontostriatal circuitry is often thought to be the foundation of the cognitive deficits associated with PD.

In addition to cognitive impairments, a language deficit attends Parkinson's disease (PD) alongside the other motor and non-motor aspects of the disease. This language deficit is characterized by difficulty processing various types of figurative language, and has been associated with various PD-related cognitive deficits, such as deficits in working memory (WM). Varied assessment tools have been used to characterize the neuropsychological functions associated with this language deficit, most of which involve some measure of frontally-based cognitive skills.

The purpose of this study was to examine the influence of frontal lobe function on higher-level language function in the non-demented PD (NDPD) population. To investigate this influence, the performance of two groups of participants (i.e., one NDPD

group and one control group) was compared on both a proverb interpretation task and on a statistically derived measure of frontal lobe function.

Results indicated a relation between performance on the measure of frontal lobe function and performance on the proverb interpretation task in the PD group only. Significant findings are discussed in relation to the neuropsychological underpinnings of the figurative language deficit in PD.

INTRODUCTION

First described by Dr. James Parkinson in 1817, this eponymous disease has traditionally been identified as a movement disorder, characterized by a classic triad of motor symptoms (i.e., bradykinesia, tremor, and rigidity) with the recent addition of postural instability to this list. A preponderance of evidence, however, indicates that this multifaceted and heterogeneous neurodegenerative disorder extends beyond the margins of motor symptomatology to include both cognitive and behavioral components.

Because Parkinson's disease (PD) has traditionally been viewed as a movement disorder, much is known about its concomitant motor speech disorder. Whereas the motoric aspects of PD have a deleterious effect on speech production, they do not impinge on language function. Owing in part to the dichotomy between speech and language, the extent to which language ability is affected in PD remains controversial.

Only in the last two decades has there been a trend towards investigating language function in PD (e.g., Bayles, Tomoeda, Wood, Cruz et al., 1997; Berg, Bjornram, Hartelius, Laakso et al., 2003; Grossman, 1999; Pell & Monetta, 2008). In many of these studies, language function has been associated with various neuropsychological tests and/or functions, resulting in a number of hypotheses regarding the interface of cognition and language. This is most evident in research regarding the understanding of figurative or nonliteral language by persons with PD.

To situate this research in its proper context, a brief overview of the neuropathology of PD will be followed by a description of the known cognitive deficits

associated with PD. Cognitive dysfunction in PD will then serve as a backdrop for discussion of the figurative language impairment associated with PD. From this perspective, the rationale for the present study will be developed.

1.1 Brief overview of the neuropathology of PD

Historically, the neuropathology of PD involves the degeneration of dopaminergic (DA) output neurons in the basal ganglia, primarily in the pars compacta of the substantia nigra (SNpc). The presence of both Lewy bodies (LBs) (neuronal intracytoplasmic inclusions) in the substantia nigra as well as other brain regions, and Lewy neurites in the axons and dendrites are also histopathological hallmarks of PD (Cardoso, Moreira, Agostinho, Pereira & Oliveira, 2005). The most pronounced biochemical deficit in PD is reduced dopamine content in the striatum, periaqueductal ventral tegmentum, neocortex, hippocampus, and cingulate gyrus secondary to the loss of dopamine output from the SN. The degeneration of the basal ganglia, traditionally pathognomic of PD, may, in fact, be caused by a spectrum of genetic, toxin-induced (Gorell, Johnson, Rybicki, Peterson et al., 1997; 1998) age-related idiopathic, and even viral factors (Cornford, Chang, & Miller, 1995).

1.2 Role of Dopamine in PD

Given the known dopamine depletion in basal ganglia structures in PD, it is important to consider dopamine supplementation in the context of PD.

Levodopa (L-dopa), a precursor affecting primarily levels of dopamine (DA) (Cardoso *et al.*, 2005), ameliorates the motor symptoms in PD. Levodopa (L-dopa) is a widely used and effective treatment for PD. The effects of L-dopa on cognitive functioning, as opposed to its effect on motor function, are more varied and complex. Deleterious as well as beneficial effects of L-dopa have been reported (Gotham, Brown, & Marsden, 1988; Kulisevsky *et al.*, 1996; Kulisevsky, 2000; Swainson *et al.*, 2000). For example, Gotham *et al.* observed beneficial effects of L-dopa on alternating fluency, but detrimental effects on conditional associative learning. Cools (2006) and Cools *et al.* (2001) reported that the effect of L-dopa on cognitive function depends critically on task demands as well as on basal levels of dopamine in certain areas of the striatum. In early PD, L-dopa may improve certain cognitive functions that are associated with severe dopamine depletion in the dorsal striatum, while simultaneously impairing other cognitive functions. Impairment occurs via “over-dosing” of L-dopa to regions that remain relatively intact (e.g., ventral striatum).

Although neither dosage nor medication status are variables in this study, because L-dopa figures so prominently in the treatment of PD, it is important to bear in mind that the standard medication preparations combine levodopa with carbidopa. Carbidopa improves the action of levodopa and reduces some of its side effects. Dosages vary across patients and across stages of the disease, although most people with PD take some form of L-dopa in three or four divided doses per day (<http://neurology.health-cares.net/parkinsons-disease-l-dopa.php>). Optimal time for testing is reported to be approximately two to three hours after taking medication. This provides a window of

time in which people are able to participate in testing without the negative effects associated with being near the end of a medication cycle.

1.3 Cognition in PD

Even in the early stages of PD, when motor symptoms typically predominate, researchers have reported evidence of cognitive impairment (Cooper, Sagar, Jordan, Harvey & Sullivan, 1991; Dubois & Pillon, 1997; Levin, Labre & Weiner, 1989; Taylor, Saint-Cyr, & Lang, 1990; Williams-Gray, Foltynie, Brayne, Robbins & Barker, 2007). As the disease progresses, the cognitive sequelae of PD tend to worsen although not always in tandem with the increasing severity of motor symptoms (Burn, Rowan, Allan, Molloy et al., 2006).

Examining the evolution of cognitive dysfunction in a cohort of newly-diagnosed patients with idiopathic PD, researchers reported that upon follow-up at a mean time of 3.5 years post-diagnosis, more than half of the 126 person cohort showed evidence of further cognitive impairment, with frontostriatal deficits predominating amongst the nondemented group (Williams-Gray, Foltynie, Brayne, Robbins & Barker, 2007).

Cognitive function in PD may deteriorate to the point where the diagnostic entity becomes PD with dementia (PDD). Dementia occurs in approximately 30% to 50% of people with PD, although prevalence estimates range from a low of 9% to a high of 93% depending on the diagnostic criteria used (Jacobs, Stern, & Mayeux, 2000). Annual incidence rates for dementia in PD are reported to be approximately 15% (according to Mayeux et al., 1990). Risk factors for PDD include increasing age, older age at PD onset, longer duration of disease, family history of dementia, greater severity of motor

symptoms, depression, hypertension, limited educational attainment, and poor tolerance of medication (e.g., Burn et al., 2006; Glatt, Hubble, Lyons, Paolo et al., 1996; Hughes et al., 2000; Jacobs et al., 2000; Marder, Tang, Cote, Stern & Mayeux, 1995). Additional risk factors for PDD include specific cognitive changes such as the presence of certain types of MCI (Janvin, Larsen, Salmon, Galasko et al., 2006), as well as changes in executive type neuropsychological functions (Woods & Troster, 2003).

Aside from PDD, the primary cognitive sequela of PD in the nondemented population is marked impairment of frontal/executive functions (Barbosa, Limongi & Cummings, 1997; Dalrymple-Alford, Kalders, Jones, & Watson, 1994; Dubois & Pillon, 1997; Levin, Tomer & Rey, 1992; Zgaljardic, Borod, Foldi & Mattis, 2003). Despite the best efforts of researchers, controversy still surrounds the construct of executive function. It has been suggested that executive functions are supervisory in nature because they involve higher-level organization and execution of complex thoughts and behavior. According to Stuss and Levine (2002), “executive functions are high-level cognitive functions that are involved in the control and direction of lower-level functions” (p. 407). D’Esposito and Grossman (1996) suggest that executive function is a broad category of cognition associated with the frontal lobes. Accordingly, executive function encompasses cognitive abilities such as: inhibition, abstraction, attention, problem-solving, reasoning, modulation of ongoing activity, working memory, and simultaneous operation of multiple cognitive processes (i.e., multitasking) (Owen, Sahakian, & Robbins, 1998; Smith & Jonides, 1999).

Many researchers in neuropsychology posit that the construct of executive function is “fractionable” (e.g., Baddeley, 1996; Duke & Kaszniak, 2000; Miyake et al., 2000). This further suggests that greater coordination of brain activity should be necessary to accomplish higher level cognitive processes. As such, tasks designed to tap executive function are likely to be sensitive to frontal lobe function precisely because these higher level cognitive processes require the coordinated activity of multiple and diffuse brain regions. Subsequently, it may appear that the frontal lobes participate to a greater extent than other areas of the brain in executive functions. These “executive” functions, in turn, depend on the integrity of other “lower level” cognitive processes such as visual and auditory attention, and visuospatial perception (Miyake et al., 2000). Should problems arise in any of the lower level processes on which the “executive functions” depend, performance on a measure of executive function could be misinterpreted as frontal lobe dysfunction.

1.3.1 Frontostriatal circuitry and cognition in PD

The anatomical relation between the frontal lobes and the basal ganglia opens the door for discussion of what is perhaps the most widely researched phenomenon in PD – the role of frontostriatal circuitry in the cognitive dysfunction in PD.

Several lines of evidence indicate that the basal ganglia are involved in motor, nonmotor, and cognitive operations. In a seminal paper by Alexander, DeLong, and Strick (1986), it was proposed that the basal ganglia participated in five parallel loops with the cerebral cortex. One of the five cortico-basal ganglionic circuits involved

skeletomotor areas of the cortex while another was with oculomotor areas. The remaining three loops formed circuits with nonmotor areas of the frontal lobe. These nonmotor regions included 1) the dorsolateral prefrontal cortex (DLPFC), 2) the lateral orbitofrontal cortex (OFC), and 3) the anterior cingulate/ medial orbitofrontal cortices. These frontal regions are known to be involved in a multitude of cognitive functions among them working memory, rule-based learning, attention, and strategic planning. Thus, based on the five circuit anatomical model, it is clear that at least three of the corticobasal circuits may be involved in cognitive processes or functions.

Clinical and pathological studies of the cognitive disturbances produced by basal ganglia pathology provide further support for the proposed corticobasal circuitry. Damage to the caudate and putamen (i.e., the input channels of BG circuitry) produces both cognitive and motor symptoms, with PD as a case in point. With the advent of ventral pallidotomy surgery as a treatment for PD, at least one study has found that this surgical procedure may alleviate motor symptoms while causing cognitive impairments (Trepanier, Saint-Cyr, Lozano & Lang, 1998). This is so because the surgery involves interruption of the abnormal signals sent by the basal ganglia to the motor circuits via output channels in the internal segment of the globus pallidus (GPi). Basal ganglia outflow from these circuits innervates motor areas of the cortex. To be effective, the pallidal lesions tend to be large, and likely extend into pallidal output channels that innervate prefrontal cortex.

Dubois and Pillon (1997) suggested that given the modulatory role of the basal ganglia, neuropsychological deficits such as those common in PD (e.g., disorders of

behavioral regulation, deficits in memory, and impaired visuospatial abilities) might be the consequence of more fundamental deficits involving the allocation of attentional resources, the temporal organization of behavior, the workings of working memory, and the invocation of strategies necessary for task completion, all of which are functions commonly ascribed to the frontal lobes. This suggests a “functional continuity or complementarity between the basal ganglia and associated areas of the prefrontal cortex.” (Dubois & Pillon, 1997, p. 2).

Additional evidence for the role of the basal ganglia in cognition can be drawn from the seminal work of Taylor, Saint-Cyr and Lang (1986) who examined frontal lobe dysfunction in PD. The working hypothesis for this experiment was that as a consequence of PD, disturbed caudate outflow would result in cognitive deficits reflecting a dependence on the integrity of the prefrontal cortex. Using a battery of neuropsychological tests including measures that tapped general intelligence, psychomotor skills, memory, visuospatial and executive functions, these researchers tested both patient and control groups. While no global cognitive decline was found in the PD group, a small but notable cluster of deficits emerged in terms of their ability to generate efficient strategies when tasks required self-directed planning. Results of the administration of several tests selected for their sensitivity to frontal lobe functions (i.e., *Wisconsin Card Sorting Test (WCST)*, *FAS test*, *Design Fluency*, *Trail Making Test parts A and B*, and the *Delayed Recognition Test*) distinguished patients with strongly right lateralized symptoms from those with left lateralized symptoms. Further analysis of the strategic planning deficit was found to be related to disease severity as well as

intelligence (as measured by an intelligence quotient, IQ) and age. Taylor et al. concluded that owing to the role of the prefrontal cortex in self-directed behavioral planning, the validity of the posited caudate outflow model in predicting the consequences of caudate dysfunction was upheld.

Clarification of the role of basal ganglia circuitry in the cognitive sequelae of PD can be drawn from the work of Zgaljardic, Borod, Foldi and Mattis (2003) and Zgaljardic et al. (2006). In examining how frontostriatal circuitry might provide the substrate for the pattern of neuropsychological deficits common in PD, Zgaljardic et al. (2003) outlined associations among three frontal cortical regions and cognitive and behavioral functions: the anterior cingulate cortex (ACC) is hypothesized to play a role in response initiation, intention, inhibition, and conflict monitoring; the dorsolateral prefrontal cortex (DLPFC) mediates what are typically thought of executive functions – set shifting, complex problem solving, organizational strategies, working memory, and retrieval of remote memories; and the orbitofrontal cortex (OFC) which has been associated with monitoring functions such as disinhibition, decision-making based on reward contingencies, impulse control, perseveration, mood, and personality. These three circuits, which connect the frontal cortical regions to the basal ganglia, are particularly relevant to the cognitive deficits in PD since the DLPFC acts as a moderator and directs the entire system.

Subsequently, Zgaljardic et al. (2006) reported a study in which neuropsychological measures of executive function and self-report behavioral inventories, categorized by frontostriatal circuit function, were administered to both nondemented PD patients and controls. Because the DLPFC is a focus of interest in the

realm of cognition in PD, and the other two circuits tend to have a more behavioral focus, only the tests administered for the DLPFC circuit will be outlined. Based on the results of previous research, the following test measures were used: category fluency, phonemic fluency, backward digit span (WMS), Spatial span test (WMS), Odd Man Out Test, Verbal Fluency Test, modified version of the Conditional Associate Learning Test, and the Frontal Systems Behavior Scale (FrSBe).

Results of this study revealed significant group differences for each of the three circuits (i.e., ACC, DLPFC, and OFC), with the PD group performing worse than the control group in all cases. Importantly, for the PD group alone, indices of impairment were greater for tasks associated with DLPFC than with OFC function. Regression analysis also revealed that *an index of DLPFC circuit performance was the only significant factor that optimally discriminated between individuals with or without PD.*

Zgaljardic et al. (2006) concluded that "...the DLPFC lends greater influence to the overall executive impairment found in NDPD patients, whereas cognitive and behavioral sequelae associated with ACC and OFC functions appear to be less prevalent" (p. 1140).

The Zgaljardic et al. (2006) study provides corroborative evidence for the findings of Bondi et al. (1993) in which nondemented PD participants and controls were tested on three categories of tests: tests sensitive to frontal system dysfunction, tests of learning and memory, and tests of visuoperceptual and visuoconstructive tasks. The tests sensitive to frontal system dysfunction used in this experiment included the *modified Wisconsin Card Sorting Test*, the *California Sorting Test*, a generative naming task (including phonemic and semantic tasks), and a verbal temporal ordering task. Results of this study indicated

that nondemented PD participants demonstrated selective deficits on frontal system tasks. Importantly, it was performance on these frontal system tasks that accounted for much of the variability in performance on tests in the other two domains (i.e., learning and memory, visuoception). Once performance on the frontal system tasks was statistically covaried against performance on the tests of learning and memory and the tests of visuo-perceptual and visuoconstructive ability, previously demonstrated significant impairment in these domains no longer remained. Thus, both the Bondi et al. (1993) and the Zgaljardic et al. (2006) studies provide compelling evidence that it is the frontal system dysfunction that optimally discriminates between individuals with and without PD, and that frontal system dysfunction accounts for a majority of the reported variability in performance across other cognitive domains.

Further evidence for the role of frontostriatal circuitry in cognitive impairments in early PD are reported by Lewis et al. (2003) who conducted an event-related fMRI study investigating the neural correlates of neuropsychological deficits in executively impaired and executively unimpaired PD patients. On a working memory task, fMRI revealed significant intensity reductions in bilateral caudate during both retrieval and manipulation phases of the WM task, and in frontal cortical regions during the manipulation, but not retrieval, of information for the executively impaired cohort.

Additional characterization of the impact of frontostriatal circuitry on cognitive deficits in PD is provided by Owen, James, Leigh, Summers and colleagues (1992) who outlined frontostriatal cognitive deficits at different stages of PD. This study revealed that non-medicated patients with mild clinical symptoms, presumably early in the course of

the disease, were impaired only on attentional set-shifting and not on tasks of spatial working memory and planning. Medicated patients with mild clinical symptoms exhibited impairments on all three tests sensitive to frontal lobe function – spatial working memory, attentional set-shifting and initial thinking/planning time in the Tower of London task, suggesting that more extensive regions of frontostriatal circuitry had become involved as the disease progressed. Later still, when clinical symptoms were severe, patients were impaired on all tests sensitive to frontal functioning including those from the previous stage as well as measures of span and the ability to invoke minimum move solutions for the Tower of London. Owen et al. (1992) concluded that certain deficits (e.g., attentional set-shifting) appear to precede others (e.g., planning deficits) in PD, and that these deficits differ from the pattern found in patients with frontal lobe damage. That these differences exist suggests that accuracy and efficiency of planning may be mediated by mechanisms within the frontal lobes, while the speed of processing may be modulated by neurotransmitter systems that innervate the prefrontal cortex and/or the caudate nucleus. When PD alters the balance of either or the neurotransmitter systems or the cortical projections, disruptions in any or all of speed, accuracy, and efficiency of planning may occur. Indeed, evidence for slowed response speed in frontally-impaired PD patients exists (Berry, Nicolson, Foster, Behrmann & Sagar, 1999), while non-frontally impaired PD counterparts performed on par with control counterparts.

In a recent article, Owen (2004) provided a comprehensive overview of the role of frontostriatal circuitry in the cognitive dysfunction in PD. Detailing the role of different regions of the lateral frontal cortex in executive processing, Owen highlighted two

distinct systems within lateral frontal cortex that mediate different aspects of executive processing via reciprocal connections to modality-specific posterior cortical association areas. The ventrolateral frontal cortex is vital for low level control processes and is posited to be the first level of interface between posterior cortical regions and the lateral frontal cortex. The mid-dorsolateral frontal cortex, in contrast, is posited to embody a higher level of executive control and is recruited when tasks involve active manipulation and monitoring of information within memory. This two-stage model of lateral frontal cortical function provides a framework for how "...two anatomically and cytoarchitecturally distinct regions of the frontal lobe are linked with different aspects of executive processing..." (p.528).

On the basis of this and other research, Owen (2004) reviewed a model of frontostriatal cognitive degeneration in PD in which higher-level executive processes such as manipulation of information, planning, and strategizing, assumed to depend critically on the integrity of the dorsolateral frontal cortex, may be more vulnerable to the effects of PD than more basic mnemonic functions such as maintenance and recall, which are hypothesized to depend on more ventral frontal regions. Owen (2004) further outlined how the pattern of executive deficits in PD may result from depletion of striatal dopamine rather than from frontal lobe pathology. Dopamine depletion in frontostriatal circuitry is thought to interrupt the flow of information through the circuits. The nature of dopamine depletion in PD is such that the putamen is more severely depleted than the caudate nucleus, and the caudal putamen is more affected than the more rostral portions. The putamen has generally been associated with motor deficits in PD while the caudate

nucleus has been associated with the cognitive sequelae of PD. The head of the caudate experiences the greatest dopamine depletion, and it is this anatomical location that is most heavily connected to the dorsolateral frontal cortex. By this account, the head of the caudate may succumb to earlier and more devastating effects of dopamine depletion in PD, yielding the pattern of cognitive impairment noted above. Ventral aspects of the caudate which are more richly connected to ventral regions of the frontal lobe tend to be spared in the early stages of PD and, consequently, functions dependent on this region may also be spared early on.

Taken together, there is compelling evidence to support the claim of frontostriatal involvement in the cognitive impairment associated with PD. From an anatomical standpoint, there are three distinct nonmotor loops – the ACC, the OFC and the DLPFC. The latter of these three has been shown to be most sensitive to the overall executive impairment found in NDPD patients. Evidence from neuropsychological and neuroimaging studies, as well as theoretical models, supports the contention that the reciprocal nature of the frontostriatal circuits and their unique functions accounts for some of the cognitive impairment seen in PD. Interestingly, from both a dopamine depletion perspective and a neuroanatomical perspective, there is a continuum of cognitive deficit in PD such that the early stages of the disease tend to be associated with less severe cognitive symptoms whereas later in the disease process more diffuse cognitive processes tend to be vulnerable to the effects of PD. Despite different formulations for the description of deficits, it is certain that frontostriatal circuitry plays a pivotal role in the evolution and expression of the cognitive deficits in PD.

1.3.2 Working memory in PD

In conjunction with the role of frontostriatal circuits in executive function, significant evidence exists regarding a working memory deficit in PD. In a recent meta-analysis of performance on simple span and more complex working memory (WM) tasks in PD, Siegert, Weatherall, Taylor, and Abernethy (2008) reported that people with PD demonstrated a more pronounced deficit in visuospatial, as compared to verbal, WM. Other research in this regard indicates a veritable WM deficit with respect to the ability to update or manipulate contents of WM rather than a verbal span deficit in PD (Altgassen et al., 2007; Gilbert et al., 2005). Monchi, Taylor and Dagher (2000) conducted a simulation experiment to model the WM deficit in normal subjects, PD, and in persons with schizophrenia. Results of their study indicated that the WM deficits in PD arise from a problem in the disinhibitory process arising from the basal ganglia.

Working memory capacity is decreased in PD (e.g., Gabrieli, Singh, Stebbins & Goetz, 1996). By way of example, a study of verbal memory in nondemented PD patients revealed that PD patients were impaired in their ability to learn verbal material under incidental, but not intentional, conditions (Ivory, Knight, Longmore & Caradoc-Davies, 1999). Results of another study on working memory indicated that when nondemented PD patients were grouped according to their performance on a measure of executive function (i.e., the Tower of London task) and tested on a novel working memory task, the “Tower of London defined executive deficit” group were impaired at manipulation of information within verbal working memory. By contrast, both controls and the not executively impaired PD group did not demonstrate this same pattern. The three groups

did not differ in their ability to either maintain or retrieve information within verbal working memory (Lewis, Cools, Robbins, Anja et al., 2003).

In summary, the cognitive deficits associated with PD have been the topic of much study. The research indicates that the basal ganglia and the fronto-striatal circuits provide the anatomical basis for many of the cognitive deficits seen in PD, and these often are manifested as executive dysfunction. By its very nature, executive function has been associated with the frontal lobes. As research techniques become more refined, the intricate and intimate nature of this relation will be further delineated.

1.3.3 Assessment of frontal lobe function in PD

In the case of PD, many researchers have concluded that the cognitive deficits in PD resemble those of people with frontal lobe damage based on subjects' performance on various neuropsychological measures (Brown & Marsden, 1990). When researchers report that a cognitive deficit is associated with performance on a given measure of neuropsychological function, it is not always possible to ascertain exactly which cognitive processes have been tapped by that test.

In a meta-analytic review of executive function and the frontal lobes, Alvarez and Emory (2006) reviewed lesion and neuroimaging studies in which three of the most widely used executive function assessment instruments had been used to examine the validity of the executive function construct viz a vis activation and damage to the frontal lobes. These tests were– the *Wisconsin Card Sorting Test* (WCST), phonemic verbal fluency (FAS test or some variant), and the *Stroop Color Word Interference Test*.

Results of the meta-analysis (qualitative analysis of lesion studies; quantitative analysis of imaging studies) revealed that the three major indices examined are sensitive indicators of frontal lobe damage. The WCST has the strongest and most consistent relation to the frontal lobe, with phonemic verbal fluency (i.e., FAS test) demonstrating the second strongest.

Although many of the same tests are used across studies in the NDPD population, no single study has incorporated all of the tests that tap a given construct in a systematized way. This methodological limitation constrains the generalizability of results. Table 1 summarizes some of the neuropsychological tests used across representative studies of cognitive impairment in PD, along with some of the most salient findings in each study. Visual inspection of the table reveals that three tests tend to recur across studies – the *Wisconsin Card Sorting Test* (WCST), the most widely used test of frontal lobe function, measures of verbal fluency measures (e.g., phonemic, semantic, alternating), and digit span testing as a measure of working memory.

Table 1: Neuropsychological measures used in representative studies of cognition in PD

| Author(s)/ Year | Study Population | Frontal Lobe Tests Administered | Most Salient Results |
|----------------------------------|-----------------------------|---|---|
| Taylor, Saint-Cyr, & Lang (1986) | 40 PD 40 NC | WCST FAS (word fluency) Design fluency Trail Making Test Delayed Recognition Test | 1) Tests thought to be sensitive to frontal lobe function distinguished patients with right lateralized symptoms 2) Deficits in strategic planning in PD |
| Gotham, Brown, & Marsden (1988) | 16 PD 16 NC | WCST Verbal Fluency – category, alternating categories Subject-ordered pointing tasks | 1) WCST – patients impaired ON & OFF L-dopa 2) Verbal fluency – patients impaired OFF L-dopa |

Table 1: Neuropsychological measures used in representative studies of cognition in PD

| Author(s)/ Year | Study Population | Frontal Lobe Tests Administered | Most Salient Results |
|--|-----------------------------|--|--|
| Levin, Llabre & Weiner (1989) | 41 PD 41 NC | Verbal fluency – category Vocabulary subtest of WAIS-R WCST Digit Span 10-item multiple choice version of Gorham’s Proverbs Test Auditory Trails Corsi Cubes | 1) significant cognitive changes occurring early in disease process (i.e., < 2 years) 2) performance on Proverbs Test, as a measure of abstraction, was impaired |
| Owen, James, Leigh et al. (1992) | 44 PD 44 NC | Tower of London Attentional set-shifting task | 1) all PD subjects impaired in set-shifting ability 2) medicated PD subjects impaired in planning for Tower of London task |
| Bondi, Kaszniak, Bayles & Vance (1993) | 19 PD 19 NC | Verbal Fluency – letters, names, semantic categories Modified WCST California Sorting Test Verbal Temporal Ordering | 1) NDPD subjects demonstrated selective deficits on frontal system tasks 2) Once performance on frontal related tasks was statistically covaried out of performance of skills in other domains, those domains were no longer impaired |
| Higginson, King et al. (2003) | 32 PD | Digit span FAS test WAIS-III executive measures CVLT executive measures WCST Stroop test | 1) memory problems associated with PD are related to executive dysfunction, in general, and to working memory impairment, in particular. |

Table 1: Neuropsychological measures used in representative studies of cognition in PD

| Author(s)/ Year | Study Population | Frontal Lobe Tests Administered | Most Salient Results |
|--|-----------------------------|---|--|
| Zgaljardic et al. (2006) | 29 PD 32 NC | Testing related to DLPFC Odd Man Out Spatial Span Digit Span Verbal Fluency Petrides Conditional Associate Learning Frontal Systems Behavior Scale | 1) Indices of impairment greatest for DLPFC-related tasks (v. ACC or OFC) 2) Only an index of DLPFC test performance discriminated between individuals with and without PD |
| de Frias, Dixon, Fisher, & Camicioli (2007) | 50 PD 48 NC | Stroop interference index Trail Making Test (part B) Digit Ordering Test | 1) Individuals with advanced disease had slower neurocognitive speed and more inconsistency than patients with earlier stage PD 2) Greater inconsistency in neurocognitive speed was related to poorer executive functioning in late stage PD |

To develop a more reliable measure of frontal lobe (FL) function minus the effects of age, the modified Wisconsin Card Sorting Test (mWCST), the FAS test, backward Digit Span and Mental Arithmetic from the Wechsler Adult Intelligence Scale-Revised (WAIS-R) and Mental Control from the Wechsler Memory Scale-Revised (WMS-R) were used in a factor analysis, along with four other neuropsychological tests (see footnote) purported to measure medial temporal lobe function, to obtain two independent factors (Glisky, Polster, & Rothieux, 1995)¹. The aim of the factor analysis

¹ Tests assessing medial temporal lobe function from Glisky et al., (1995) - Logical Memory I, Verbal Paired Associates I, and Visual Paired Associates II (all from the Wechsler Memory Scale- Revised), and the Long-Delay Cued Recall measure from the California Verbal Learning Test (CVLT; Delis, Kramer, Kaplan & Ober, 1987).

was to identify two independent factors "...that reflected the operation of different cognitive processes and different brain structures but were independent of age" (Glisky et al., 1995, p. 231).

The frontal lobe measures included in the factor analysis included (a) number of categories achieved on the modified WCST (Hart, Kwentus, Wade, & Taylor, 1988), (b) the total number of words generated on the Controlled Oral Word Association Test (Benton & Hamsher, 1976; otherwise known as the FAS test), (c) score on Mental Arithmetic from the Wechsler Adult Intelligence Scale- Revised (WAIS-R; Wechsler, 1981), (d) score on Mental Control from the Wechsler Memory Scale – Revised (WMS-R; Wechsler, 1987), and (e) Backward Digit Span from the WMS-R.

According to Glisky and Kong (2008), these frontal lobe tests are thought to sample executive control processes associated with higher level working memory tasks. Previous studies with older adults have demonstrated that individuals with high FL scores outperform individuals with low FL scores on source memory tasks (Glisky et al., 1995; 2001). In these studies, it has been suggested that the cognitive processes sampled by the FL factor may reflect those involved in the integration of information, particularly at the time of encoding.

Although the present study does not address source or item memory, use of the FL function factor is justified in that it provides a statistically derived method for sampling frontal lobe function. Its application to the PD population is appropriate not only to sample FL function which is known to be vulnerable in this population, but also because the composite z-score reflects the common variance among its constituent tests

which increases reliability. This FL function factor will figure prominently in the testing conducted for the present study. Further information regarding the FL function factor will be presented in the section on method.

1.4 *Language skills in PD*

The cognitive deficits associated with PD are manifest not only on neuropsychological tests but on tests of language function as well. The language deficits of people with PD have not been linked to a discrete anatomical locus; rather, they have been associated with frontal lobe dysfunction.

Research indicates that language skills such as comprehension of complex syntax (Grossman, 1999; Grossman, Carvell, Gollomp, Stern et al., 1993; Kemmerer, 1999), aspects of verbal fluency (Auriacombe et al., 1993; Azuma et al., 1997; Bayles, Trosset, Tomoeda, Montgomery & Wilson, 1993; Gurd & Ward, 1989; Henry & Crawford, 2004; Piatt et al., 1999; Randolph, Braun, Goldberg & Chase, 1993) and facility with various aspects of figurative language (Berg et al., 2003; Cohen, Bouchard, Scherzer & Whitaker, 1994; Levin, Llabre, & Weiner, 1989; Monetta & Pell, 2007) are all vulnerable to the effects of PD.

Research into the syntactic comprehension deficit in PD can inform the study of the figurative language deficit associated with PD. Using functional magnetic resonance imaging (fMRI) to examine the brain loci involved in syntactic comprehension in both controls and PD participants, Grossman et al. (2003) reported that the left posterolateral temporal cortex (PLTC), left dorsolateral IFC extending into premotor cortex, right

PLTC and bilateral occipital cortex (due to visual presentation of stimuli) were involved in syntactic processing. In PD participants, as in healthy seniors, activation in left PLTC, left dorsolateral IFC extending into premotor cortex, right PLTC and bilateral occipital cortex was found for all sentence types, although activation was less for PD patients. For sentences that taxed working memory, right parietal cortex was recruited as well. Notably, PD participants did not demonstrate as much activation in the striatum as did healthy seniors. For PD participants to achieve sentence comprehension equal to that of their control counterparts, they must engage several additional brain regions associated with working memory.

Kemmerer (1999) attributed the sentence processing deficit in PD to limitations in working memory capacity, and implicated the neuropathology of PD in operationalizing this deficit. Progressive depletion of dopamine influences the two main dopaminergic projection systems in the brain; the nigrostriatal and the mesocortical systems. These dopaminergic projection systems modulate both prefrontal cortical function and striatal function. Both prefrontal cortex and the striatum are involved in working memory. Thus, it is possible that the working memory capacity that subserves sentence processing depends on these two dopaminergic projection systems and is deleteriously affected by dopamine depletion.

1.4.1 Higher-level language function in PD: relation to neuropsychological function

A growing body of literature suggests that deficits in higher level language function in PD may impede both social and pragmatic functioning. For instance, NDPD

study participants have been found to have difficulty with the following: comprehension of figurative language (Levin, Llabre, & Weiner, 1989; Lewis, LaPointe, Murdoch, & Chenery, 1998; Pell & Monetta, 2008), metaphor (Monetta & Pell, 2007), inferential-type tasks (e.g., drawing inferences from paragraph-level text) (Berg et al., 2003; Monetta, Grindrod, & Pell, 2006), higher-level verbal reasoning (Cohen, Bouchard, Scherzer & Whitaker, 1994), discourse comprehension (Copland, Chenery, & Murdoch, 2001; Murray & Stout, 1999), and pragmatic function (McNamara & Durso, 2003).

Across the aforementioned studies, performance of PD participants was inferior to that of controls. More strikingly, performance on many of the measure(s) in question was often related to performance on neuropsychological tests that are purported to tap into measures of frontal lobe functions. For instance, results of a study of in which a measure of proverb comprehension was administered to PD patients early in their disease process (i.e., disease duration of less than 3 years from report of first symptom) indicated that PD participants, in contrast to controls, performed significantly worse on embedded figures, facial recognition, proverbs, and verbal and figural memory (Levin, Llabre, & Weiner, 1989). In this study, a 10-item multiple choice version of Gorham's proverbs test was used (Gorham, 1956*a*). Levin et al. suggested that the deficits demonstrated by the PD participants reflected frontal lobe disturbance. In the Monetta and Pell (2007) study of metaphor comprehension, PD participants who performed more poorly on a measure of verbal working memory were also impaired in the processing of metaphorical language. Monetta and Pell suggested that certain higher-level forms of language manipulation, such as that required in metaphor comprehension, may be dependent on the intact

functioning of the fronto-striatal systems involved in working memory. The fact that these systems may be compromised early on in the course of PD may underlie some of the deficits in higher-level language function in this population. This line of reasoning echoes that posited by Levin et al. (1989) where it was suggested that the cognitive changes evidenced in early PD may underlie some of the neuropsychological changes observed on testing.

In a study of discourse priming of homophones, Copland, Chenery and Murdoch (2001) found that PD participants demonstrated priming for appropriate and inappropriate lexical associates of the target at short inter-stimulus intervals (ISIs), but did not demonstrate this pattern of performance at the long ISIs. Copland et al. interpreted these results as supporting the conclusion that PD patients are capable of automatic lexical processing at very short post-presentation intervals, but that they experience breakdown in discourse-based meaning selection and inferencing at longer ISIs when attentional and strategic mechanisms must be used to keep stimuli in mind. These results may reflect a disruption in function attributed to fronto-striatal circuitry such as attentional/strategic information processing, working memory operations, and attention-based selection and suppression of competing responses.

Corroborating evidence for the aforementioned conclusion can be drawn from the work of Monetta, Grindrod, and Pell (2008) in which working memory capacity was related to inference generation during story comprehension in adults with PD. Findings from this study indicated that only a subgroup of PD patients with verbal WM deficits

were significantly impaired in their ability to draw inferences from aurally presented short stories.

These studies suggest that the deficits in higher-level language functions in the NDPD population may be attributed to disruptions in fronto-striatal circuitry that relates to working memory and/or depletion of attentional resources. It is unclear from the studies above whether the identified deficits hold for all types of higher-level language processing. A closer look at higher-level language processing is warranted in this regard.

1.5 Neuropsychological correlates of figurative language comprehension

Results of early behavioral and lesion studies accorded the right hemisphere a prominent role in figurative language processing. In summary, deficits following right hemisphere damage have involved nonliteral language (Van Lancker & Kempler, 1987; Van Lancker, 1990; Winner & Gardner, 1977), theme and topic maintenance, apprehension of humor, context relevance, and inference (e.g., Brownell, Carroll, Rehak, & Wingfield, 1992; Brownell, Potter, Bihrlé, & Gardner, 1986).

More recently, Burgess and Chiarello (1996) suggested a figurative language processing model that incorporated both top-down and bottom-up cognitive processes. According to this model, the left hemisphere was involved in rapid semantic and syntactic processing while the right hemisphere was engaged with more pragmatic functions (e.g. inferencing). Because both these processes are integral to comprehension of figurative language, an important role for the right hemisphere posited. A similar position, referred to as the dual process model (Van Lancker, 2006), suggests that

although the entire brain is required for optimal language performance, there may be two separate modes of processing nonliteral language. One mode supports competence for novel language, utilizing standard semantic, phonological and grammatical rules. The other mode supports competence with familiar expressions that are processed in terms of canonical forms and conventional meanings. A right hemisphere-subcortical circuit has been suggested as one way in which the production and comprehension of many types of nonliteral language is modulated.

Studies that address the neural correlates of comprehension of other forms of figurative language (e.g., idioms and/or metaphors) are relevant here. Recent neuroimaging studies of idiom comprehension in healthy subjects indicate that figurative comprehension of both ambiguous and unambiguous idioms is supported by bilateral inferior gyri and left middle temporal gyrus. Zempleni and colleagues (2007) suggest that figurative comprehension depends critically on a bilateral neural network and is not the sole province of either hemisphere. Lauro, Tettamanti, Cappa and Papagno (2008) used a sentence-to-picture matching task in which participants were asked to judge whether literal or idiomatic sentences matched a picture. In processing both the literal and idiomatic sentences, a common neural network was engaged, with the idiomatic processing eliciting greater activation overall in terms of both magnitude and spatial extent. The network activated for the nonliteral processing involved the left temporal cortex, left superior medial frontal gyrus, left inferior frontal gyrus (IFG). Activations were also present in the right IFG and right superior and middle temporal gyri and temporal pole. Connectivity analysis indicated that during idiom processing, the medial

prefrontal area significantly increased the connection between frontotemporal areas bilaterally. The researchers concluded that the prefrontal cortex plays a pivotal role in idiom comprehension, perhaps owing to the need to select between alternative sentence meanings.

In a study addressing the time course of idiom processing, Fogliata et al. (2007) used repetitive transcranial magnetic stimulation (rTMS) to disrupt function in left prefrontal and temporal cortex, regions identified as important for idiom processing. Results indicated a selective impairment in accuracy for idiom processing when rTMS was applied to the prefrontal and temporal cortex after picture presentation. rTMS to the prefrontal cortex continued to affect performance with idiomatic processing even later following picture presentation. These findings were taken as evidence that the prefrontal region is involved in both retrieval of relevant information from semantic memory and in monitoring the response, possibly by inhibiting alternative or literal interpretations.

The neural correlates of metaphor processing have been widely studied in normal adults using neuroimaging techniques. In a study of metaphorical versus literal word meanings, Lee & Dapretto (2006) reported activity in the left prefrontal and temporo-parietal regions for nonliteral (i.e., metaphoric) word processing. Eviatar & Just (2006) reported higher levels of activation in left IFG and in bilateral inferior temporal cortex for metaphoric utterances, findings echoed in the work of Rapp, Leube, Erb, Grodd & Kircher (2004; 2007). Rapp et al. (2004) further noted that activation in the left IFG may reflect semantic inferencing that occurs during metaphor comprehension.

In a set of three divided visual field experiments in which metaphorical and literal sentence familiarity were varied, Schmidt, DeBuse, and Seger (2007) reported a right hemisphere advantage for unfamiliar sentences containing distant semantic relationships, regardless of whether the sentences were metaphorical or literal.

Results of these studies suggest that previous accounts of greater right hemisphere involvement in the processing of figurative language in general, and of metaphor processing in particular, may have been overstated. Rather, the data suggest that the right hemisphere may play an active role in the comprehension of figurative language because of its increased complexity. The right hemisphere might also play an important part in processing distant semantic relationships, whereas the left hemisphere is postulated to play a role in the processing of close semantic relationships.

The literature reviewed above suggests overlapping neuroanatomical regions involved forms of figurative language such as metaphor and idiom processing. The left IFG and left temporo-parietal region were activated across studies; task-specific constraints may have influenced the activation of other gyri and regions in individual experiments.

In a recent review, Thoma and Daum (2006) noted that the prefrontal cortex (PFC) has been implicated in figurative language processing. The PFC is intimately interconnected with subcortical structures (e.g., Alexander, DeLong & Strick, 1986 – 3 parallel fronto-subcortical circuits thought to subservise cognition). These fronto-subcortical circuits have been shown to contribute to cognitive functions, most notably executive control functions (ECF) (Heyder, Suchan & Daum, 2004). Because of the

known anatomical connections between PFC and subcortical structures, it is at least speculatively plausible that subcortical structures might participate in the processing of figurative language.

Support for the involvement of subcortical structures in figurative language processing obtains from a limited number of studies. Chenery, Copland, & Murdoch (2002) reported deficits in word fluency and in the interpretation of ambiguous and figurative language in a population of participants with Huntington's disease and a group of patients with stroke-induced focal lesions of non-thalamic subcortical structures.

Whereas the processing of figurative language in both general and clinical populations has been the topic of much research, and the processing of certain types of figurative language has been the subject of study in the NDPD population, one area that remains largely unstudied in the PD population is proverb comprehension.

1.6 Proverbs

Proverbs are simple and concrete statements that capture shared values, beliefs and the wisdom of a society (Meider, 1993). They are "...familiar, fixed, sentential expressions that express well-known truths, social norms, or moral concerns..." (Gibbs & Beitel, 1995, p. 134). Some proverbs (e.g., "lightning doesn't strike twice") have meanings that are true both literally and figuratively (Ferretti, Schwint, & Katz, 2007).

Certain fundamental proverb structures exist that form the basis for many common proverbs. Gibbs and Beitel (1995) outline the following proverbial structures: "where there's X there's Y" (e.g., where there's smoke, there's fire), "no X without Y"

(e.g., no pain, no gain), “like X, like Y” (e.g., like father, like son), and “one X does not make a Y” (e.g., one flower does not a dozen make). Proverbs also have a certain meter (e.g., *you can lead a horse to water but you can’t make him drink*), rhyme (e.g., *haste makes waste*), slant rhyme (e.g., *a stitch in time saves nine*), alliteration (e.g., *live and let live*), assonance (e.g., *a rolling stone gathers no moss*), personification (e.g., *necessity is the mother of invention*), paradox (e.g., *no news is good news*) and parallelism (e.g., *a penny saved is a penny earned*). These markers help listeners identify proverbs. The more proverbial markers a statement has, the greater the likelihood that it will be judged as a proverb. Importantly, it is the combination of concrete vocabulary and definite syntax make a proverb’s relatively fixed form more memorable.

1.6.1 Comprehension of figurative language: the special case of proverbs

Proverbs enjoy a privileged status among other forms of figurative language because “...their figurative and literal senses are distinct but related in a principled way” (Temple & Honeck, 1999, p. 44). Specifically, although a proverb’s literal and figurative meaning are qualitatively different, its figurative meaning can be constructed by accessing the literal meaning of the component lexical items, invoking contextual support and using additional comprehension strategies (Temple & Honeck, 1999).

Factors such as familiarity, context, syntactic complexity, abstractness, and salience influence proverb comprehension. Familiarity facilitates comprehension such that familiar proverbs are easier to understand than unfamiliar proverbs (Cunningham, Ridley, & Campbell, 1987; Katz & Ferretti, 2001; Penn, Jacob & Brown, 1988; Temple

& Honeck, 1999; Turner & Katz, 1997). Context also biases proverb comprehension. Honeck, Welge, & Temple (1998) reported a study in which subjects were asked to render a judgment about the appropriateness of a proverb as restatement of the theme of a written paragraph. When the proverb was literally related to the context, reaction time decreased; when the proverb was figuratively related to the context, reaction time increased. In a study of online reading of proverbs, Katz & Ferretti (2001) reported that for both familiar and unfamiliar proverbs, context influenced resolution of ambiguous meanings during reading. Familiar proverbs were read more rapidly than unfamiliar proverbs, and this effect emerged by the second word for familiar proverbs. Using electrophysiological data (i.e., event-related brain potential; ERP), Ferretti, Schwint, & Katz (2007) demonstrated that the nonliteral use of a word produces a spike of greater amplitude (N400) than when that same word is used literally, and with respect to proverbs, that this effect is evident by the third word in the trope. This finding is incompatible with theories or models of nonliteral language comprehension that posit that the entire sentence must be processed before a nonliteral meaning can be determined.

The ability to understand and explain proverbs develops across the lifespan (Nippold, Uhden, & Schwarz, 1997) with marked improvement during adolescence and early adulthood. During later adulthood, age-related changes in proverb interpretation have been reported in both older adults (age 60-79 years; Uekermann, Thoma, & Daum, 2008) and the old-elderly (age 80-92; Ulatowska, Chapman, & Johnson, 1995). In the Uekermann et al. study, older adults demonstrated impairment in selecting correct interpretations from among presented alternatives as well as executive function deficits -

reduced working memory as measured by the backward digit span test (WAIS), difficulty with set-shifting as measured by the *Wisconsin Card Sorting Test*, and inhibition of habitual responses as measured by the Stroop interference test. This association between select neuropsychological functions and performance on various proverb comprehension tasks is reminiscent of similar associations reported in the realm of syntax and other higher level language functions.

Attempting to relate any type of receptive language phenomenon to neuropsychological function is difficult because both are somewhat opaque. With respect to proverbs, Honeck (1997) suggested that proverb comprehension is an unobservable and hypothetical construct. Owing to the illusive nature of proverbs and how they are understood, a number of theories have been proposed to try to account for various aspects of proverb comprehension. These are outlined below.

1.6.2 Theories of proverb comprehension: an overview

Paremiology, the study of proverbs, of necessity involves the study of proverb comprehension. Research on measures of proverb comprehension has led to much speculation, but no consensus, about how proverbs are processed. For example, the conceptual metaphor hypothesis (CMH) posits that proverbs

“...have complex, specific interpretations because of people’s metaphorical mappings of information from various, familiar source domains onto less familiar and usually vaguer target domains. These mappings are unidirectional or metaphorical...because one domain of knowledge is used to structure another, but not the reverse.” (Gibbs & Beitel, 1995, p. 136)

A conceptual metaphor is a simple statement that encapsulates metaphorical understanding. For example, Gibbs (1994) cites the following expressions frequently used to talk about love and human relationships (e.g., “*Look how far we’ve come*”, “*It’s been a long, bumpy ride*”, “*We’re at a crossroads*”). All of these familiar expressions can be captured by one metaphorical system of understanding and reflected in the conceptual metaphor “Love is a journey”. This metaphor involves understanding the domain of love in terms of the more concrete domain of experience represented by journey. Gibbs & Beitel (1995) continued to highlight the tight and invariant mapping of exemplars from one domain (e.g., the lovers in relationship) to entities in the domain of a journey (e.g., a traveler, a vehicle, a destination, etc.). This invariant mapping occurs when a familiar and substantive body of knowledge is mapped onto a less familiar and often more abstract domain of knowledge. According to this hypothesis, proverb comprehension proceeds from understanding different conceptual metaphors common in quotidian thought. Accordingly, a conceptual metaphor might serve as the link between a proverb’s literal (i.e., source domain) and figurative (i.e., target domain) meanings.

An opposing view was articulated in Kemper’s seminal paper (1981) in which she concluded, on the basis of four experiments, that figurative meaning can be directly accessed without prior computation of a literal meaning (Gibbs, 1979; Gibbs & Doolittle, 1994; Kemper, 1981). This theory predicts that figuratively biased proverbs should be processed more quickly than literally biased proverbs.

A more traditional theory of proverb comprehension, the standard pragmatic model, suggests that a proverb is understood in stages (Honeck, Welge, & Temple, 1998;

Temple & Honeck, 1999). Based on early work by Grice (1975) and Searle (1979) regarding the cooperative principle and communicative intent, this theory subsumes the multistage assumption according to which accessing the literal meaning of a figurative utterance is obligatory and must occur prior to determining the figurative meaning. This model predicts that figurative understanding should take longer than literal understanding. In a series of elegant experiments, Temple and Honeck (1999) demonstrated that when asked to read short paragraphs and then judge whether the proverb presented appropriately restated the theme of the paragraph, reaction time was faster when the proverb was literally, rather than figuratively, related to the context. The researchers concluded that their data supported the multistage assumption. Further elucidation of this assumption suggests that proverb comprehension entails five phases – construction of literal meaning, recognition that the literal meaning is inadequate and should be rejected, transformation of the literal meaning, construction of a figurative meaning, and instantiation of this meaning. These five stages are encompassed in the conceptual base theory of proverb comprehension (Honeck, 1997; Honeck & Temple, 1994; Honeck, Voegtle, Dorfmueller, & Hoffman, 1980) according to which comprehension of a proverb results from an orderly series of processes that assist in the transformation of the literal meaning of proverb to its nonliteral meaning.

Another explanatory mechanism posited with respect to the comprehension of figurative language is that of suppression. According to Gernsbacher and Robertson (1999), much of figurative language comprehension proceeds by suppression of literal meanings, where suppression refers to "...a general, cognitive mechanism, the purpose of

which is to attenuate the interference caused by the activation of extraneous, unnecessary or inappropriate information.” (p. 1619). In this manner, the nonliteral meaning of expressions such as metaphor and idioms are reached by first suppressing the literal meaning of constituent lexical parts (Gernsbacher & Roberston, 1999). This line of reasoning would predict that proverb comprehension might be compromised if there were a failure to attenuate interference from associations between words and personal experience (Gibbs & Beitel, 1995) or between an expression’s literal and figurative meanings.

Additional support for the notion of suppression can be found in the work of Keysar (1994) who posited that literal and figurative interpretations can be activated in parallel, that context can constrain the selection of either the literal or nonliteral interpretation of a metaphor, and context does so by two opposing forces: plausibility (a positive force) and elimination (a negative force). Elimination works via suppression.

Giora (1999) and Giora and Fein (1999) also suggested that suppression plays a role in figurative language comprehension. Like Keysar, they proposed that literal and figurative interpretations of metaphorical, as well as idiomatic, expressions can be activated in parallel, but they proposed some asymmetries in what gets activated and what gets suppressed. Their proposals about activation are based on a 'graded salience' account of figurative language comprehension, according to which salient interpretations are more activated than less salient interpretations. By 'salient' the authors mean interpretations that are independent of context. In this way, the graded salience hypothesis predicts which interpretations should be more versus

less activated, but not which interpretations should remain activated or be suppressed.

Regardless of which theory of proverb comprehension is best supported by a preponderance of the data, it is important to remember that proverb comprehension is assessed by various means of having study participants match, make judgments about, interpret or instantiate selected proverbs. The real task of how figurative meaning is assigned to a proverb remains unobserved; it is a hypothetical construct whose nature can only be inferred (Honeck, 1997).

1.6.3 Neural correlates of proverb comprehension

Although no studies have addressed the neural substrates of proverb comprehension per se, evidence from populations with neurodegenerative diseases affecting fronto-subcortical structures, as well as other subcortical structures, suggests that fronto-striatal circuits play a role in the comprehension of figurative language. What is known has been inferred from behavioral and lesion studies. For example, a role for the cerebellum in higher-level language function can be inferred from a report about patients with olivo-ponto-cerebellar atrophy who performed poorly on a proverb interpretation task (Arroyo-Anllo & Botez-Marquard, 1998), and from a study of patients with left cerebellar lesions (Cook, Murdoch, Cahill, & Whelan, 2004). In patients with agenesis of the corpus callosum, performance on Gorham's Proverbs test was deficient relative to controls (Paul, Van Lancker, Schieffer, Dietrich, & Brown, 2003). Despite having intact right hemispheres and basal ganglia, these patients lacked the normal interhemispheric communication that seems to be important for the successful integration of information.

Other research suggests that frontally-based cognitive processes such as working memory and mentally sifting through a variety of competing responses are involved in proverb comprehension. Deficits in working memory have been shown to exert a negative impact on proverb comprehension (e.g., Moran, Nippold, & Gillon, 2006; Qualls & Harris, 2003) as well on the comprehension of metaphoric sentences (Monetta & Pell, 2007).

In a more recent single case study of a 63-year-old man with PD who received subthalamic nucleus (STN) deep brain stimulation (DBS), a decrement in performance on a proverb explanation task was noted at both three and eight months post-surgery (Moretti, Torre, Antonello, Capus et al., 2001). Although it is unclear what proverb explanation task was used in this study (the study was conducted in Italy and likely used an Italian proverb explanation task not detailed in the paper), the authors suggested that DBS might affect abstract reasoning via its frontal influence.

Although none of the aforementioned studies provide direct evidence regarding the impact of PD on proverb comprehension, it is at least of speculative interest that subcortical structures play a role in both cognition and in figurative language processing in general, and have been identified as important in this regard in the PD population.

1.7 Purpose of current study

The confluence of cognitive, neuropsychological, and linguistic phenomena in the NDPD population provide the basis for the study of previously unexamined types of figurative language.

Proverbs were chosen as a vehicle to examine the influence of frontal lobe function on higher-level language function in the NDPD population because proverbs have concrete vocabulary and finite syntax which help them to be memorable (Higbee & Millard, 1983). Proverbs have both literal and figurative meanings which make them a suitable subject for the study of higher-level language processing. Finally, proverbs constitute an important component of one's cultural literacy (Hirsch, 1988) and occur frequently across communication contexts.

The purpose of the current study is to investigate the nature of proverb interpretation and its relation to frontal lobe function in the non-demented PD (NDPD) population, a population with known frontal lobe dysfunction. Because proverb interpretation draws on frontally-related cognitive skills and because even non-demented individuals with PD may have deficits in frontal lobe function, it was hypothesized that performance on a test of proverb comprehension would be related to performance on a measure of frontal lobe function. When measures of frontal lobe function are included in assessment protocols used in experiments involving the PD population, they may offer discriminant ability between individuals with and without PD, as well as between subgroups of individuals with PD. This type of discriminant ability is not conferred by other neuropsychological tests (e.g., Bondi et al., 1993; Zgaljardic et al., 2006), and thus provides a rationale for inclusion of assessment of putative frontal lobe functions in PD using a Frontal Lobe Function Factor (FLFF; Glisky et al., 1995).

Variation in performance on the frontal lobe function factor in both PD participants and healthy controls is anticipated, as is between-group variability with respect to performance on the Proverbs Test.

Research Questions

1. Do individuals with PD perform differently than healthy controls participants on the Proverbs Test?
2. Is performance on the Proverbs Test related to performance on the Frontal Lobe function factor?

METHOD

2.1 Participants

Thirty participants with idiopathic Parkinson's disease (PD) were recruited (17 male, 13 female). An additional 30 age- (within 3 years) and education- (within 2 years) matched individuals without a history of neurological impairment were recruited to serve as controls (CTL) (11 male, 19 female). All participants were native speakers of English between 65 and 85 years old, had normal or corrected vision and hearing, had completed high school, and had no self-reported history of learning disabilities or other neurological problems.

Additional inclusionary criteria for the PD group included a diagnosis of idiopathic PD by a board-certified neurologist. Exclusionary criteria for this group were: a diagnosis of early-onset PD (operationally defined as onset prior to the age of 40), a history of Parkinson plus syndromes, and having undergone deep brain stimulation surgery.

Permission for research and recruitment was obtained from the Institutional Review Board (IRB) at the University of Arizona. Subjects were recruited from the Tucson, AZ area. Participants with PD were recruited via distribution of an IRB-approved flyer by a neurologist at a local movement disorders clinic.

Descriptive statistics including the mean, standard deviation, and range for both the PD and CTL groups are shown in Table 2. The table includes descriptive statistics for the demographic variables age and education, and for three PD-specific variables – time

since diagnosis, UPDRS² motor score, and a calculated L-dopa equivalency value expressed in milligrams.

Total L-dopa equivalent is a measure used in PD research that provides a mechanism for expressing the sum of a person's PD medications in Levodopa units. Given that there are a variety of medications used in the treatment of PD with brand names such as Mirapex, Requip, Neupro, Parlodel, and Lisuride (downloaded 12/29/2008, <http://www.webmd.com/parkinsons-disease>), being able to consider them using a common denominator can be helpful. 'Total L-dopa equivalent' serves this function by calibrating dosages of the common medications prescribed for PD in terms of their L-dopa equivalent. This is accomplished using a conversion formula, and results in a total L-dopa equivalent expressed in milligrams. In this study, the following conversion formula was used:

$$\text{Equivalent levodopa dose (in milligrams)} = [\text{levodopa (x 2 if COMT inhibitor)(x 2 if 10 mg of Selegiline or 1.1. if 5 mg of Selegine)}] + [\text{Prampipexole x 400}] + [\text{Ropinirole x 40}] + [\text{Cabergoline x 160}] + [\text{Pergolide x 200}] + [\text{Bromocriptine x 10}] + [\text{Lisuride x 160}]$$

(Rowe, Hughes, Ghosh, Eckstein, Williams-Gray et al., 2008; Williams-Gray, Hampshire, Robbins, Owen, & Barker, 2007).

Table 2: Characterization of study participants

| | <i>PD</i> | <i>Control</i> |
|-------------------|--------------|----------------|
| Age | | |
| M (SD) | 73.9 (5.967) | 73.2 (5.268) |
| Range | [65-85] | [65-82] |
| Education (years) | | |
| M (SD) | 16.9 (2.734) | 16.47 (2.403) |
| Range | [12-20] | [12-20] |

² UPDRS – Unified Parkinson's Disease Rating Scale (see references).

Table 2: Characterization of study participants

| | <i>PD</i> | Control |
|---------------------------|-----------------|----------------|
| Clinical Variables | | |
| PD duration (# yrs.) | | |
| M (SD) | 6.63 (5.15) | |
| Range | [1-25] | n/a |
| UPDRS motor score | | |
| M (SD) | 18.775 (8.3) | |
| Range | [0-108] | n/a |
| Ldopa equivalent (mg) | | |
| M (SD) | 1338.5 (1043.9) | |
| Range | [50 – 3900] | n/a |

2.2 Procedure

2.2.1 Screening

The *Mini-Mental State Examination* (Folstein, Folstein, & McHugh, 1975) was administered to all participants as a coarse measure of cognitive ability. The MMSE is a widely used mental status test comprised of 11 items designed to broadly assess orientation, attention, and memory. The maximum attainable score on the MMSE is 30. A cut-off score of 24 was used for the PD group, whereas a cut-off score of 26 was used for the control group (Lemsky, Smith, Malec & Ivnik, 1996).

A hearing screening was conducted to determine hearing status. Age- and gender-specific reference ranges (Morrell, Gordon-Salant, Pearson, Brant, & Fozard, 1996) were used as indices of hearing. If a participant failed the screening, they were referred for a full audiologic assessment and were demitted from the study.

2.2.2 Test protocol

A battery of cognitive and linguistic tests was administered to all participants. For the PD participants, all testing was conducted with participants taking their medication as usual. This battery was designed to provide information about putative frontal lobe function, general linguistic function, and proverb comprehension. The battery was comprised of published tests for which normative data were available. A complete description of each test is provided below. Administration of the battery was divided across 1 to 2 sessions, depending on participant stamina. Participants with PD were able to complete the battery in approximately two hours. Control participants were able to complete the battery within approximately one hour.

Order of administration of tests was counterbalanced within group (PD and CTL). Constraints on variations to the order of administration included the need to always administer screening tasks first, and to maintain the order of administration of tasks comprising the Frontal Lobe function factor.

2.2.3 Tests

The *Western Aphasia Battery-Revised* (WAB-R; Kertesz, 2006) was used to test proficiency in basic language skills. It provides a measure of receptive and expressive language function using indices of language fluency, auditory comprehension, repetition, and naming ability. Together these four primary linguistic functions yield a single composite score referred to as the aphasia quotient (AQ). A non-aphasic AQ is greater than or equal to 94 (out of a possible 100).

The *Homophone Meaning Generation Test* (Warrington, 2000) was used to test participants' ability to generate multiple meanings for single words. This 8-item test is comprised of four same-spelling homophones (e.g., tip, slip) and four different-spelling homophones (e.g., right/write/rite). Words were presented one at a time and participants were instructed to "come up with as many meanings as possible" for each word. Responses were transcribed verbatim on the answer form. One point was awarded for each response that had a unique meaning. Raw scores were converted to scaled scores which ranged from one to 20. This test was administered as part of a larger data collection effort, but data were not included in the analysis for this project. The raw data are presented in APPENDIX B.

The *Geriatric Depression Scale – Short Form* (Weintraub, Oehlberg, Katz, & Stern, 2006; Yesavage et al., 1983) was used as a coarse measure to assess the likelihood of the presence of depression. This 15-item self-report measure was administered to each participant. For each of the 15 questions, either a 'yes' or a 'no' response was elicited. If a participant achieved a score of 5 or greater out of 15, he or she was referred on for further psychological assessment. Because depression is a common concomitant of PD, its presence was used as a covariate in the regression analysis.

The *Frontal Lobe Function Factor* (FLFF) is comprised of five tests that, together, have been shown by means of factor analysis, to capture common variance associated with frontal lobe functions (Glisky, Polster, & Rothieux, 1995).

The tests included in the FL factor are: the *Modified Wisconsin Card Sort Test* (Hart, Kwentus, Wade, & Taylor, 1988), the *Controlled Oral Word Association Test* (i.e.,

FAS test; Benton and de Hamsher, 1976), the *Mental Arithmetic* subtest from the *Weschler Adult Intelligence Scale-Revised (WAIS-R; Weschler, 1981)* and both the *Mental Control* subtest and the *Backward Digit Span* subtest from the *Weschler Memory Scale-Third Edition (WMS-III; Weschler, 1997)*. They are administered in the following order:

a) *Mental Arithmetic* subtest from the *Weschler Memory Scale - III (WMS-III)*.

Participants were asked to solve mental arithmetic problems (e.g., “Raffle tickets cost 25 cents each. How much would it cost to buy 6 tickets?”). Each of the 10 problems had a maximum time allocation, ranging from 15 seconds to two minutes. Problems one through nine received a score of either zero or one, whereas for problems ten through 14, a score of zero, one, or two was possible. The maximum attainable score on this test was 19. Testing was discontinued if a participant made four consecutive mistakes.

b) *Modified Wisconsin Card Sorting Test (mWCST)*: This 72-item test is a shorter version of the widely used Wisconsin Card Sorting Test. The participant was instructed to place each consecutive card (from the deck of 72) below the stimulus card he or she thought it best matched. The examiner informed the participant only whether or not the response was correct. After six consecutive correct responses according to the initial correct principle (e.g., color), the matching criterion was changed without warning. The criterion proceeded from color to form to number. Testing was discontinued after successful completion of six categories (color, form, number, color, form, number) or until the deck had been used up; whichever

occurred first. The score used for the Frontal Lobe Function Factor was the number of categories completed. Detailed scoring guidelines are published in the manual.

c) *Controlled Oral Word Association Test* (i.e., FAS test). In this timed test, participants were asked to provide as many words as they could that begin with an assigned letter (first 'F', then 'A', and finally 'S') in a one-minute time frame. The examiner recorded all words provided by the participant. Repetitions and proper nouns were deleted from the final tally. The score is the total number of words produced across all three letters.

d) *Backward Digit Span* subtest - *Weschler Memory Scale-Third Edition (WMS-III)*
This test requires mental tracking and verbal repetition of increasingly long strings of digits starting with three digit strings. Participants were asked to repeat sequences in reverse order (e.g., "6-9-8-7-5-4", "now say the numbers backwards"). Two exemplars were presented at each level, and testing was discontinued when responses to both exemplars within a level were incorrect. The score represents total correct.

e) *Mental Control* subtest - *Weschler Memory Scale-Third Edition (WMS-III)*.

This test required the participant to rapidly retrieve and mentally manipulate overlearned information (e.g., letters of the alphabet, months of the year) in forward and reverse orders. Each response was timed. Additional points were awarded when answers were completely accurate and within pre-determined time frames. There are 10 tasks with a total possible score of 40 points.

According to Glisky et al. (1995), the FLFF scores were derived by first removing the variance attributable to age from each of the tests included in the composite measure by way of regression analysis, converting the residuals to z-scores, and averaging the z-scores across test with equal weighting. A regression formula was subsequently derived based on the data from 227 normally-aging, community-dwelling older adults aged 65 to 90, who were tested as part of an ongoing project (Glisky & Kong, 2008). FLFF scores in the present study were calculated for each individual based on that regression equation.

Gorham's *Proverbs Test* (Gorham, 1956a; 1956b) was used to test ability to interpret common proverbs (e.g., "Strike while the iron is hot" or "All that glitters is not gold"). Each participant was presented with 12 proverbs of equivalent difficulty. Form II of the test was used for all participants, and can be found in APPENDIX A.

Traditional administration of the test requires that the participant write a response for each of the 12 proverbs. Test administration was modified to accommodate for both the micrographia and motor difficulty with writing that often accompanies PD. To standardize administration and to obviate any influence of oral presentation, the proverbs were presented via computer (Sony VAIO FX 215 laptop). Each proverb was typed on a separate slide using black typeface on a white background. Participants advanced from proverb one through twelve at their own pace, using the right arrow key, explaining each one orally. All responses were digitally recorded (Olympus Digital Voice Recorder VN-4100PC) and transcribed verbatim. The original 3-point scoring system was used such that each response was awarded 0, 1, or 2 points depending on the level of abstract thinking reflected in the answer. A sample of the scoring rubric is presented below:

Table 3: Scoring rubric for Gorham's Proverbs Test

| Proverb | 0 point answer | 1 point answer | 2 point answer |
|-----------------------------------|---|-----------------------------|---|
| "Don't judge a book by its cover" | A nice cover doesn't make good reading. | Don't judge a person wrong. | Appearances are deceiving. |
| "Let sleeping dogs lie" | Because it might bite. | Don't make troubles. | Let people alone when they are not bothering you. |

Following administration of the *Proverbs Test*, each participant was asked to complete a familiarity checklist on which each of the 12 proverbs just encountered were listed. Each proverb was clearly typed, and next to each one was a column titled "familiar" followed by a column titled "unfamiliar". To complete the checklist, participants placed a check mark in the appropriate column for each proverb. This information was used to calculate a "familiarity index", as follows: [Total # proverbs - # of unfamiliar proverbs] / Total # of proverbs. This calculation yielded a proportion of proverb familiarity that was used to determine if group differences existed with respect to familiarity.

2.3 Statistical Analysis

To answer the question of whether PD and Controls perform differently on the Proverbs Test, a 2-tailed independent samples t-test was conducted, at alpha (α) level equal to .05. The t-test for independent samples provides a way to compare the mean performance of each group on the dependent variable.

To answer the question about whether performance on the Frontal Lobe Function Factor was related to performance on the Proverbs Test for both the clinical and non-

clinical groups studied, multiple regression was used. The decision to use multiple regression was based on the need to use several independent variables to predict the dependent variable (performance on the Proverbs Test). Stepwise regression was the method of choice for this analysis because it allows for predictor variables to be introduced into the regression equation one at a time, and the change in the multiple correlation (i.e., R-squared) is determined at each step along the way. Predictor variables are entered in order of decreasing ability to account for additional variance in the criterion variable. The p-value for keeping a variable in the equation was .05, and the p-value for excluding a variable was .10.

In the regression analysis, the criterion variable was performance on the Proverbs Test, and the predictor variables varied by group. For the PD group, predictors included performance on the FLFF and on the MMSE, the number of years since diagnosis, performance on the UPDRS, and total levodopa equivalent.

Performance on the GDS-SF and on the WAB-AQ score were not used in the regression analysis due to a lack of significant group differences.

Ad hoc analyses included calculation of partial correlations among variables of interest for the PD group (i.e., performance on Proverbs Test, years since diagnosis, UPDRS score, and L-dopa equivalent). Likewise, similar calculations were conducted for performance on the FL function factor. All statistical analyses were conducted using SPSS v.16.0 software.

2.4 Reliability scoring

A random sample of 12 participant files, or 20% of the complete sample, was selected for reliability scoring. Point-to-point reliability scoring for the MMSE, the GDS-SF, and the five subtests comprising the FL function factor was completed by a certified speech-language pathologist, other than the examiner, who was blind to the purpose of the experiment. Point-to-point reliability for the MMSE was 83%, 100% for the GDS-SF, and 95.2% for the FL function factor. Another certified speech-language pathologist who was blind to the purpose of the experiment performed point-to-point reliability scoring for the Proverbs Test. This was relatively low at 83%, although disagreements with respect to scoring were discussed and resolved. Point-to-point reliability was calculated by comparing the scores assigned by the examiner to those calculated by the external raters. A percentage agreement between them was calculated.

Intra-rater agreement for scores on the WAB-AQ was 85%. Inter-rater agreement for the transcription of the Proverbs Test (original transcription completed by someone other than examiner) was calculated to be 90%.

RESULTS

The primary purpose of this study was to compare the performance of people with and without Parkinson's disease (PD) on a proverb comprehension task. A secondary purpose was to investigate whether performance on the proverb comprehension task was related to frontal lobe function in both the clinical and non-clinical population studied herein.

3.1 Demographic Variables

Performance on the MMSE proved to be the single demographic variable on which the two groups differed. All CTL participants scored at or above 26/30 on the MMSE, the value considered to be the cutoff for normal cognitive functioning (Lemsky et al., 1996). The cut-off score for participation in the study for PD participants was 24, although the lower limit in this sample was 25. This one point difference between groups with respect to the lower limit of the MMSE scores was significant $t(58) = 2.45$, $p = .017$. Otherwise, there was no significant difference between groups with respect to either age $t(58) = .482$, $p > .05$, years of education $t(58) = .652$, $p > .05$, performance on the GDS-SF $t(58) = 1.946$, $p = .056$, or performance on the WAB-R AQ $t(58) = 1.340$, $p > .05$.

Table 4: Summary of demographic information

| <i>Demographic Variable</i> | <i>PD</i> | <i>CTL</i> |
|-----------------------------|---------------|---------------|
| MMSE | | |
| M (SD) | 28.07 (1.596) | 28.97 (1.217) |
| Range | [25-30] | [26-30] |
| GDS- SF | | |
| M (SD) | 3.00 (2.626) | 1.80 (2.124) |
| Range | [0-11] | [0-8] |

Table 4: Summary of demographic information

| <i>Demographic Variable</i> | <i>PD</i> | <i>CTL</i> |
|-----------------------------|----------------|----------------|
| WAB-R AQ | | |
| M (SD) | 98.467 (1.011) | 98.837 (1.125) |
| Range | [95.6-99.6] | [95-100] |

3.2 Proverb Comprehension Task

To compare the performance of the PD and CTL groups on the proverb comprehension test, a 2-tailed independent measures t-test was conducted. Results revealed a statistically significant difference between groups, $t(58) = |4.006|$, $p < .001$, $\eta^2 = 0.216$, with PD participants performing below age- and education-matched controls. Results of Levene's test for equality of variances were significant $F=15.571$, $p=.000$, indicating that group variances differed from one another and that the homogeneity of variance assumption was violated. Calculation of the t statistic using values that took the unequal variances into account resulted in the same t-value reported above, $t(46) = |4.006|$, $p < .001$. Figure 1 displays the boxplots showing the median, overall range, and interquartile range of scores on the Proverbs test for both groups of participants. Visual inspection of this plot indicates that the medians, the overall ranges, and the interquartile ranges differ between groups.

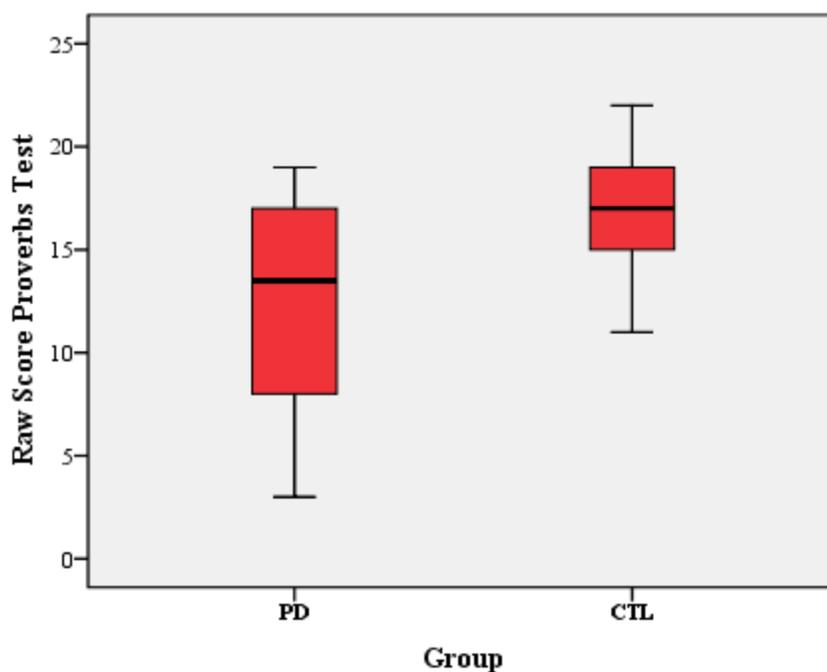


Figure 1: Boxplot of score on Proverbs Test. The range of possible scores on the Proverbs test is zero to 24.

Group differences in the plot above reflect between-group comparisons. Only limited normative data is available for the Proverbs Test, and no normative data is available for persons in the age range used in this study. However, data from 100 Air Force re-enlistees and 100 eleventh and twelfth grade high school students indicates that on Form II, the form of the test administered to participants in this study, the mean score was 13.9 with a standard deviation of 5.6. Although the mean reported in the normative data more closely approximates the mean of the PD group in this study (i.e., 12.77), than that of the control group (i.e., 16.93), it is noteworthy that these data were reported in 1956, and all of the data were collected in Texas on young people. Based on the limited data it is not possible to know whether older adults would have performed similarly, or

whether additional education and/or life experiences would have conferred any additional advantage in proverb interpretation.

Participants in both groups were asked to respond to all 12 proverbs on the test.

Select illustrative responses from the PD group are presented in Table 6, with a representative sampling of the range of scores on the test (i.e., 0, 1, and 2).

Table 5: Sample responses from the PD group

| Subject | Proverb | Response Given | Target Response | Score |
|---------|--|--|---|-------|
| 1303 | Strike while the iron is hot. | Um, strike while the iron is hot – the iron um, the iron uh...I think it has something to do with shoeing horses and um if you're the iron horseshoe is hot that's when you pivot to shoe the horse or something like that. You can't do that task if the iron is cooled off, so do it before the iron cools off or something like that. | Seize an opportunity when it presents itself. | 0 |
| 1303 | All that glitters is not gold. | Panning for gold is uh looking at black sand and seeing if you see gold flecks in the in in in the sand that you're panning and uh you can often see glitter uh that's coming from pyrite and not actually gold. It looks like gold and they call pyrite fool's gold um because it can fool somebody [into] thinking that it's actually gold in the sand that they're panning. So again, all that glitters is not gold - could be iron pyrite. | Appearances can be deceiving; don't be taken in too easily. | 0 |
| 1304 | The proof of the pudding is in the eating. | How true. We many times will get pudding and I'm discouraged from even trying it. Lots of times it's chocolate pudding and you want vanilla or vice versa. Chocolate used to be my favorite. | Experience is the best teacher; you can tell how good a thing is by how it works. | 0 |
| 1312 | Better be happy than wise. | Never heard that one. Better be happy than wise. [examiner prompt – What does the proverb mean?] | Better be satisfied than smart and dissatisfied. | 1 |

Table 5: Sample responses from the PD group

| Subject | Proverb | Response Given | Target Response | Score |
|-------------|--------------------------------|---|---|-------|
| | | That's a complex question. Better be happy than wise. I never heard that before. Better be happy than wise. Depending on the situation I guess. If you're looking for monetary gain, could land up on the grass. Happiness is great, wisdom is great. I sound like a grandfather. | | |
| 1305 | All that glitters is not gold. | If something is beautiful it is not necessarily worth a lot. | Appearances can be deceiving; don't be taken in too easily. | 2 |

Select illustrative responses from the Control group are presented in Table 7, with a representative sampling of the range of scores on the test (i.e., 0, 1, and 2).

Table 6: Sample responses from the Control group.

| Subject | Proverb | Response Given | Target Response | Score |
|-------------|--|--|---|-------|
| 2304 | Strike while the iron is hot. | Take advantage of the situation while it's current. | Seize an opportunity when it presents itself. | 2 |
| 2309 | A rolling stone gathers no moss. | This rolling stone gathers no moss. That means if you keep moving you're not as likely to uh gather moss. Um, it's harder to hit a target when it's moving than when we stand still. | One who doesn't settle down doesn't accomplish much. | 1 |
| 2313 | The proof of the pudding is in the eating. | It may not look good but it may taste really good. | Experience is the best teacher; you can tell how good a thing is by how it works. | 0 |

Although participants were asked to attempt to explain each proverb, some proverbs more than others elicited comments regarding its familiarity, regardless of any attempt at a response. Familiarity ratings provided by 59 of 60 subjects were captured in a “familiarity index” that was calculated for each participant. For the PD group, the mean and standard deviation on the familiarity index were $.6062 \pm .2512$. For the CTL group, the mean and standard deviation on the familiarity index were $.6927 \pm .0671$. A t-test comparing the two groups familiarity indices resulted in a significant Levene’s test for equality of variances, $F = 13.931, p = .000$, and a non-significant t-statistic, $t(57) = |1.820|, p = .078$.

The familiarity index was positively correlated with overall performance on the Proverbs Test, $r(59) = .334, p = .010$, suggesting that performance on the Proverbs Test improved as more proverbs were reported as being familiar. Despite this positive correlation, proverb number four, “One may ride a free horse to death”, was one proverb often cited by participants as being unfamiliar. In the PD group, 22 out of 30 participants or 73.3 percent of respondents reported that it was unfamiliar. In contrast, in the healthy control group, where data was available for 29 of the 30 participants, 26 out of those 29 or 89.6 percent of respondents indicated that proverb number four was unfamiliar. Overall, 81.2 percent of the participants in the study rated proverb number four as unfamiliar. Data for the remaining eleven proverbs are presented in Figure 2. The figure shows that proverbs 1, 4, 11, and 12 were least familiar across groups. For the CTL group, proverbs number 4 and 11 were least familiar. For the PD group, proverb number

11 was least familiar (6/30), proverbs number 1 and 4 were tied for the next least familiar (8/30) position, and proverb number 12 was slightly more familiar (9/30).

Despite these differences in familiarity, the CTL group still outperformed their PD counterparts. This suggests that although familiarity may contribute to performance on the proverb interpretation task, it is not a determinant of performance. To realize this group difference in performance, the CTL group must be able to interpret proverbs even when they are unfamiliar.

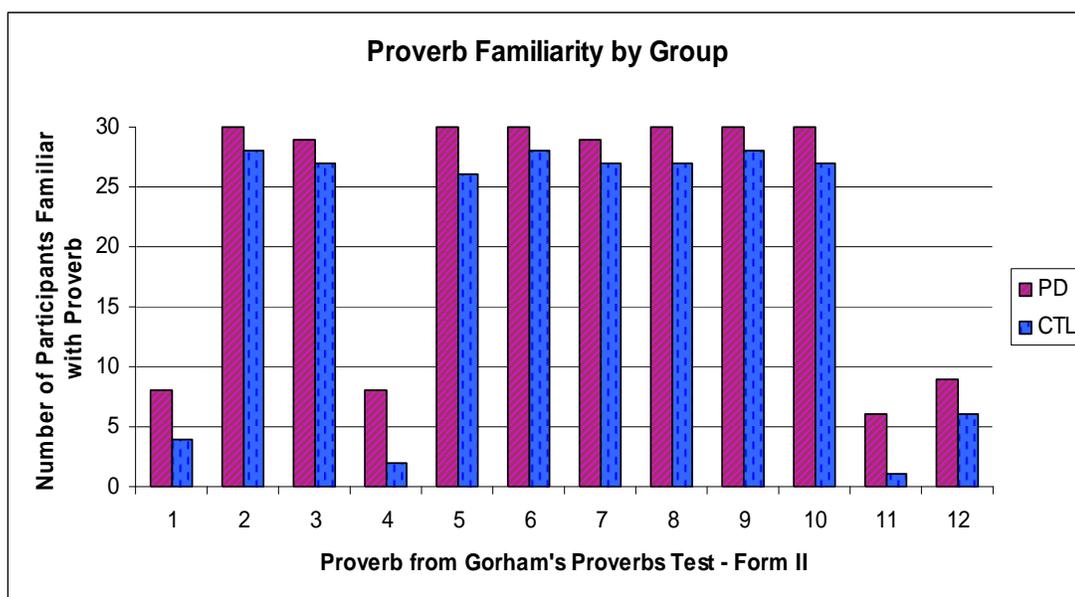


Figure 2: Proverb familiarity by group.

To determine the effect size, Cohen's 'd' was calculated to be 1.069, suggestive of a large effect size.

3.3 Proverb comprehension and frontal lobe function

Given the between-groups difference in performance on the Proverbs Test, exploratory data analysis was used to examine group performance on the FL function factor. This between group difference was statistically significant, $t(58) = |2.603|$, $p = .012$. Levene's test for homogeneity of variances was not significant, $F=3.585$, $p=.063$, indicating that the homogeneity of variances assumption was not violated. Figure 3 displays the box plots showing the median, overall range, and interquartile range of the FL scores for the two groups. Visual inspection of this plot indicates that relative to the PD group, the control group demonstrated less variability in their scores as well as a smaller interquartile range. The PD group had larger overall range as well as larger interquartile range. The boxplot below illustrates that the groups differed in their performance on the FL function factor.

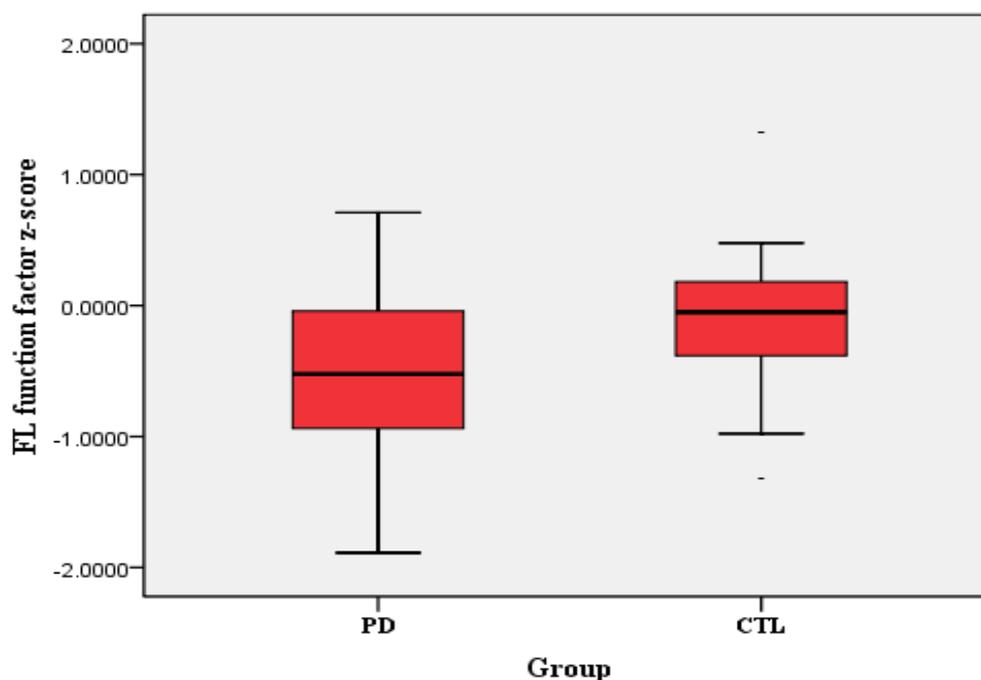


Figure 3: Group performance on the FL function factor.

3.3.1 Regression analysis for the entire cohort

To explore the relation between proverb comprehension and executive function, regression analysis for the entire experimental cohort (i.e., $N=60$) was conducted followed by a separate regression analysis for the PD group.

Scatter plots of the data for each group separately are shown in Figure 4 and for the two groups together in Figure 5. Visual inspection of Figure 4 indicates that for the PD group, a straight line with a positive slope could be visualized through the points $r = .669, p < .001$, whereas for the Control group, the data points form a cloud through which a straight line could not be drawn, $r = .078, p = .680$.

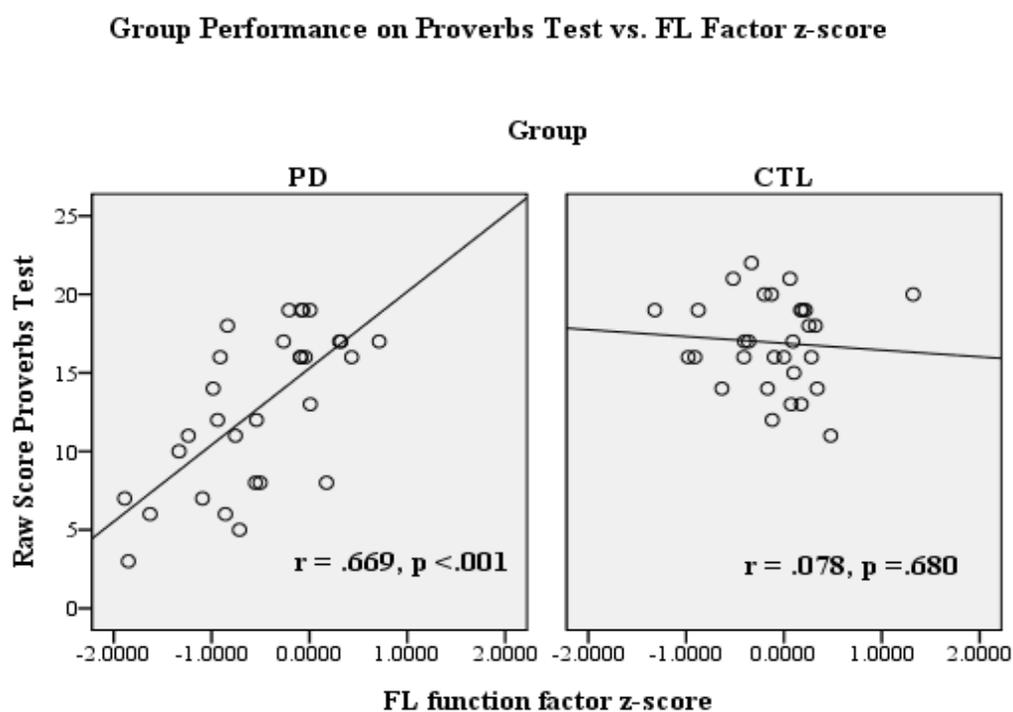


Figure 4: Separate scatter plots for each group illustrating the relation between performance on the Proverbs Test and performance on the FLFF.

Visual inspection of Figure 5 reveals an overall positive relation between performance on the Proverbs Test and performance on FLFF $r = .52, p < .001$.

Group Performance on Proverbs Test vs Performance on FLFF

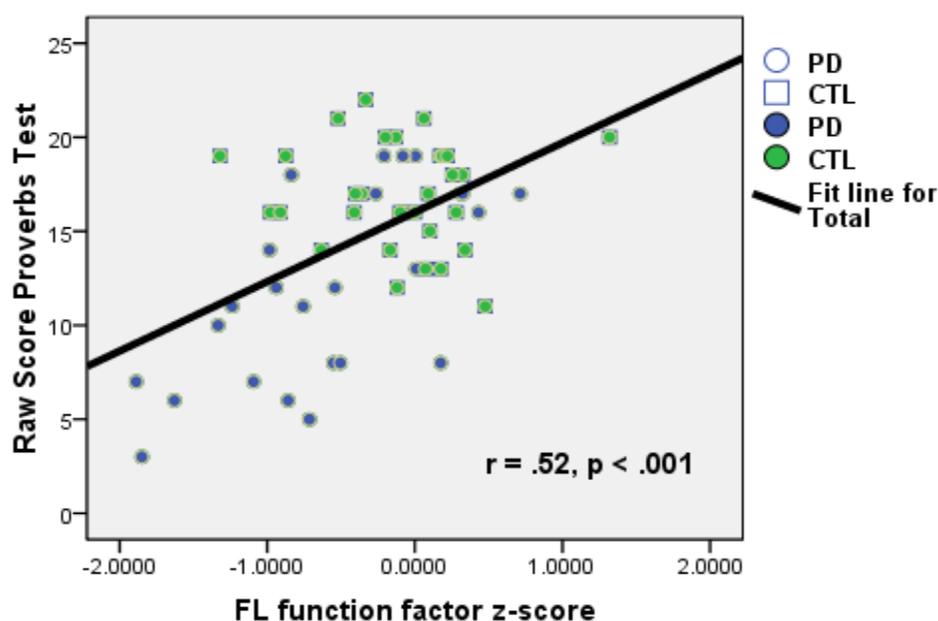


Figure 5: Scatter plot of all data points for both groups.

The overall regression analysis revealed that performance on the Proverbs Test was significantly correlated with score on the MMSE, group, and FL function z-score. Performance on the FL function factor, as reflected in the z-score, was significantly correlated with performance on the MMSE, group, and performance on the Proverbs Test. Significant zero-order correlations are shown in Table 8.

Table 7: Significant zero-order correlations.

| Variable | Score on Proverbs Test | FL function z-score | MMSE |
|---------------------|------------------------------|---------------------|------|
| FL function z-score | $r(58) = .516$ $p < .001$ | | |

Table 7: Significant zero-order correlations.

| Variable | Score on Proverbs Test | FL function z-score | MMSE |
|----------|------------------------------|------------------------------|------------------------------|
| MMSE | $r(58) = .339$ $p = .008$ | $r(58) = .378$ $p = .003$ | |
| Group | $r(58) = .466$ $p < .001$ | $r(58) = .323$ $p = .006$ | $r(58) = .307$ $p = .009$ |

A stepwise multiple regression was conducted with performance on the Proverbs test as the criterion variable and ‘MMSE’, ‘group’, and ‘FL function z-score’ as predictor variables. Analysis revealed that ‘FL function factor z-score’ significantly predicted performance on the Proverbs test for which $R^2 = .266$, as did group membership for which R^2 change = .100, indicating that adding ‘group’ as a predictor accounted for an additional 10 percent of the variance in the criterion variable. R^2 for the model (i.e., a regression model models the relation between one variable (DV) and one or more other variables (IVs) by way of a linear transformation) encompassing the aforementioned predictors was .366, suggesting that these two variables accounted for approximately 37 percent of the variance in the criterion variable, $F(2, 57) = 16.426, p < .001$. Both predictors had significant standardized beta coefficients; for ‘FL function factor z-score’ $\beta = .408, t(57) = 3.658, p = .001$, and for ‘group’ $\beta = .334, t(57) = 2.993, p = .004$. Tolerance and variance inflation factor (VIF) levels were within acceptable limits for both predictor variables suggesting that multicollinearity was not a problem. The issue of multicollinearity is important because if the predictors are not linearly independent of one another, then one of the assumptions underlying regression analysis (i.e., homoscedasticity) would be violated. Multicollinearity does not reduce the predictive

power or reliability of the model as a whole; it only affects calculations regarding individual predictors. That is, a multiple regression model with correlated predictors can indicate how well the group of predictors predicts the criterion variable, but it may not give valid results about any individual predictor.

The regression equation for the entire cohort (i.e., N=60) using the two significant predictors would be:

$$\text{Performance on Proverbs Test} = 11.29 + .408 (\text{FL function factor z-score}) + .334 (\text{Group}).$$

Prior to conducting a separate regression analysis for the PD group, zero-order and partial correlations were examined to determine the influence of disease-specific variables such as ‘years since diagnosis’, ‘UPDRS score’, and ‘Total L-dopa equivalent’.

Performance on the Proverbs Test was negatively correlated with (a) score on the UPDRS, $r = -.465, p < .001$, (b) years since diagnosis, $r = -.334, p = .011$, and (c) L-dopa equivalent, $r = -.371, p = .005$. These negative correlations suggest that performance on the proverbs test declines as each of the above variables increases.

When ‘Proverbs test correct’, ‘Years since diagnosis’ and ‘UPDRS’ were entered, score on the UPDRS was negatively correlated with ‘Proverbs test correct’, $r = -.411, p = .002$, and positively correlated with years since diagnosis, $r = .628, p < .001$. When ‘Proverbs test correct’, ‘Total L-dopa equivalent’, and ‘UPDRS’ were entered, a significant zero-order correlation between UPDRS and Total L-dopa equivalent emerged, $r = .579, p < .001$, but no partial correlations were significant. Finally, when the variables ‘Proverbs test correct’, ‘Total L-dopa equivalent’, and ‘Years since diagnosis’ were

entered, a positive zero-order correlation between ‘Total L-dopa equivalent’, and ‘Years since diagnosis’ was found, $r = .566, p < .001$. When ‘Years since diagnosis’ was factored out, a significant negative correlation between ‘Proverbs test correct’ and ‘Total L-dopa equivalent’ was found, $r = -.279, p < .05$.

In contrast, when the three PD-specific variables (i.e., years since diagnosis, UPDRS, and total L-dopa equivalent) were used in calculations of zero-order and partial correlations between ‘Proverbs test correct’ and ‘FL factor z-score’ different results emerged. When ‘Proverbs test correct’, ‘Years since diagnosis’, and ‘FL factor z-score’ were entered, a significant zero-order correlation emerged for FL function z-score and proverbs test correct, $r = .678, p < .001$. When ‘years since diagnosis’ was factored out, the relation between ‘Proverbs test correct’ and ‘FL factor z-score’ remained significant at $r = .412, p = .002$. When ‘Proverbs test correct’, ‘FL factor z-score’ and ‘Total L-dopa equivalent’ were entered and ‘Total L-dopa equivalent’ was factored out, the correlation between ‘Proverbs test correct’ and ‘FL factor z-score’ increased to $r = .793, p < .001$. Likewise, when ‘Proverbs test correct’, ‘FL factor z-score’, and ‘UPDRS’ were entered, and ‘UPDRS’ was factored out, a significant correlation between ‘Proverbs test correct’ and ‘FL factor z-score’ remained, $r = .425, p = .001$.

This pattern of results suggests a robust relation between ‘Proverbs test correct’ and ‘FL factor z-score’ that is impervious to the effects of the three PD-specific variables used in this analysis.

3.3.2 Regression for the PD group

As above, the criterion variable in the regression analysis for the PD group was performance on the Proverbs test. Predictor variables in this analysis were: 'MMSE', 'FL function factor z-score', 'UPDRS', 'Years since diagnosis', and 'L-dopa equivalent'. Results of this stepwise regression revealed that only two predictors remained in the model – 'FL function factor z-score' and 'L-dopa equivalent'. Model $R = .777$ and $R^2 = .603$, suggesting that these two predictors accounted for approximately 60 percent of the variance in the criterion variable. Importantly, when 'FL function factor z-score' was the only predictor in the model, it had an $R^2 = .448$. Adding 'L-dopa equivalent' to the model resulted in a change in R^2 of .155. The change statistics were both significant; for FL function z-score $F(1, 19) = 15.410, p = .001$ and for L-dopa equivalent $F(1, 18) = 7.040, p = .016$. The ANOVA confirmed the model's significance with $F(2, 18) = 13.674, p < .001$.

The standardized beta coefficients were also significant. For 'FL function factor z-score', $\beta = .803, t(20) = 5.120, p < .001$. For L-dopa equivalent, $\beta = -.416, t(20) = |2.653|, p = .016$.

Tolerance and variance inflation factor (VIF) levels were within acceptable limits for both predictor variables [Tolerance: FL factor = .897; L-dopa equivalent = .897; VIF for both variables was 1.115] suggesting that multicollinearity was not a problem.

Using the significant predictors, the regression equation for the PD group would be:

Performance on Proverbs Test = 18.062 + .803 (FL function factor z-score) + (-.416 * L-dopa equivalent).

3.3.3 Regression for the control group

A separate regression analysis was not conducted for the control group because the correlation between performance on the Proverbs test and the 'FL function factor z-score' was not statistically significant, so there was no basis for conducting a regression.

DISCUSSION

The primary purpose of this study was to examine figurative language function and its relation to FL function in the NDPD population. Using proverbs as a vehicle to examine figurative language, the aim of the first research question was to compare the performance of people with and without idiopathic Parkinson's disease (PD) on a proverb interpretation task. The aim of the second research questions was to investigate whether performance on the proverb interpretation task was related to frontal lobe function in both the clinical and non-clinical populations studied herein. The discussion will be framed by addressing these two purposes.

Results of this study indicate a between-groups performance discrepancy such that PD participants performed more poorly than their control counterparts. This statistically significant difference in performance suggests that PD exerts a deleterious influence on proverb interpretation.

Further analysis revealed that performance on the FL function factor and Total Levodopa equivalent were significant predictors of performance on the proverb interpretation task for the PD group. For the controls there were no significant predictors of performance on the proverb interpretation task.

The general trend of these results confirms the hypothesis that there would be between-group differences in performance on the proverb interpretation task. The results also demonstrate a relation between performance on the FL function factor and performance on the proverb interpretation task in the PD group only.

4.1 Effect of PD on proverb interpretation

Having PD seemed to exert a deleterious effect on performance on a proverb interpretation task, as evidenced by the findings that (a) PD participants performed more poorly than controls on the experimental task, and (b) that group membership, along with FL function (for the PD group), influenced the outcome of the overall regression analysis.

Results of this study indicate a robust relation between performance on the proverb interpretation task and performance on the FL function factor in the PD population. This finding suggests that some aspects of proverb interpretation depend on intact cognitive function in general, and intact FL function in particular, both of which can be compromised even in the early stages of PD (Cooper et al., 1991; Dubois & Pillon, 1997).

That performance on the experimental task was negatively affected by PD dovetails with the finding that PD patients have difficulty with other aspects of figurative language, such as metaphor (Monetta & Pell, 2007), and adds to a growing body of evidence regarding a figurative language deficit associated with PD (Pell & Monetta, 2008).

Results of the present study suggest that PD participants either invoke fewer and/or less exacting strategies to tackle the task or that they are less efficient in their use of previously successful strategies. The latter interpretation favors a generally depressed cognitive profile not dissimilar to that seen in PD.

How PD participants approach the proverb interpretation task harkens back to the theories of proverb comprehension presented in the introduction. Although this study was

not designed to test one or another of these theories, it is helpful to revisit some of these theories as a way to explain some of the observed phenomena.

The PD group as a whole performed more poorly on the proverbs task than did the control group, and their performance was correlated with FL function. In the control group, the relation between performance on the proverbs task and FL function did not exist. Perhaps the experimental task did not tax controls, or perhaps controls access nonliteral interpretations more directly than their PD counterparts by effortlessly bypassing the literal interpretation. If this were so, it would refute the standard pragmatic model that suggests that a proverb is understood in stages (Honeck et al., 1998; Temple & Honeck, 1999) and instead lend credence to the concept of suppression as it relates to comprehension of figurative language. According to Gernsbacher and Robertson's (1999) notion of suppression, the literal meaning of an expression must be suppressed in order to reach the nonliteral meaning. It may be that controls expertly and automatically suppress the literal meaning of a proverb whereas PD participants may not be as able to effortlessly suppress the literal meaning. They then get "stuck", as it were, with this impoverished interpretation, and must ostensibly access the contents of working memory to reinvigorate the process of interpretation. If the by-product of the first attempt at interpretation is quite literal, trying to enhance it by making a second attempt at interpretation might not result in much progress if the literal meaning cannot be suppressed.

Alternately, it may be that controls arrive at the nonliteral interpretation of a proverb by proceeding quickly and seamlessly through the five stages contained in the

multistage assumption (i.e., construction of literal meaning, recognition that the literal meaning is not right and should be rejected, transformation of the literal meaning, construction of a figurative meaning, and instantiation of this meaning) (Temple & Honeck, 1999). PD participants, on the other hand, may begin this multistage process but not be able to complete it, resulting in an incorrect response. Some PD participants had insight into their performance on the proverbs task and remarked, "...that's not quite right, but I can't say it". According to the multistage assumption, these participants may have completed steps one and two but been unable to proceed.

Taken together, the evidence suggests that performance on the proverbs task lends itself to different theoretical interpretations. With the limited data from this study, it is not possible to adjudicate among these theories. More refined experimental tasks are needed to further delineate the processes involved.

4.1.1 Effects of dopamine on proverb interpretation

Although the focus of this study was not related to medication status, results of the regression analysis for the PD group indicated that 'total L-dopa equivalent' was a predictor of performance on the Proverbs Task. It is not possible, given the current data, to determine whether dosage played a role in the relation between predictor and criterion variables. However, participants were optimally medicated during testing for this study (e.g., approximately 2 to 3 hours after taking medication), suggesting that disease severity, as indexed by the L-dopa equivalent, influences performance on the Proverbs Test. Given that L-dopa can have both deleterious and beneficial effects on cognition, it

is unclear from the results of the regression where on that continuum these results might lie. It is also known that as the disease progresses, there is an increased likelihood of the cognitive decline becoming a more frank dementia. If total L-dopa indexes disease severity, it may serve as a marker to monitor with respect to cognitive function – something that is suggested by these data, most notably by the finding when ‘total L-dopa’ was factored out of the correlation between performance on the Proverbs Test and FL function z-score, the bivariate correlation increased beyond its base value. This result suggests that ‘Total L-dopa equivalent’ acted as a suppressor variable in this relation.

Data regarding three PD-specific variables (i.e., ‘years since diagnosis’, ‘score on the motor section of the UPDRS’, and ‘total L-dopa equivalent’) were collected. In aggregate, the PD-specific variables reflect some measure of disease severity and progression. Each of the PD-specific variables was negatively correlated with performance on the Proverbs Test, suggesting that both disease progression and severity are associated with increasingly poor performance on the dependent variable.

In attempting to determine whether medication status (i.e., either ‘ON’ or ‘OFF’) has any effect on proverb interpretation, a very small sample of PD participants agreed to participate in a second testing when they had been off their medication for a period of 12 hours. Owing to the fact that data from only three participants was available, it is not prudent to draw any conclusions. However, even in this limited sample, there was a high correlation between performance on the FL function factor in the ‘ON’ and ‘OFF’ state, $r=.995$, $p=.032$. No other significant correlations were found. Of the three subjects tested, two maintained their previous levels of performance on the Proverbs Test, and one

subject improved performance in the 'OFF' state. With such limited data, it is unclear whether similar effects might be found were a larger sample to be tested. Also, although caution was taken to have approximately two to three months between the two testing sessions, practice effects cannot be ruled out. At present, it is not possible to disentangle any potential interactions between medication status (i.e., ON or OFF) and practice effects.

4.2 Cognition and language in PD

The evidence implicating frontally-based cognitive dysfunction in the PD population prompted the second research focus of this study; namely, to determine whether performance on the proverb interpretation task was related to frontal lobe function. Although the groups were matched for age and education level, results indicated a robust relation between performance on the proverb interpretation task and performance on the FL function factor in the PD group only.

The frontostriatal circuits are highly influential with respect to both cognition and language function in PD. By virtue of the circuits' connections, the basal ganglia and the frontal lobes are also intimately involved in these functions. Monetta and Pell (2007) suggest that frontostriatal dysfunction in PD may underlie what they have called primary and secondary impairments, where primary impairments refer to the cognitive deficits that arise from progressive frontostriatal dysfunction and secondary impairments refer to the resulting impairments of language and communication.

When proverb interpretation is considered within the broader context of figurative language, there is considerable evidence for task-related neuropsychological correlates. Among the candidate cognitive processes implicated in proverb comprehension tasks are executive functions such as working memory (Moran, Gillon, & Nippold, 2006), set-shifting, and inhibition (Uekermann, Thoma, & Daum, 2008).

4.2.1 Working memory and proverb interpretation

Working memory appears to play an important role in the processing of figurative language. For example, PD participants with impaired working memory were reported to be impaired in processing metaphorical language (Monetta & Pell, 2007) and in inference generation (Monetta, Grindrod, & Pell, 2008), a finding echoed in the work of others (e.g., Berg et al., 2003; Levin et al., 1989; Moran et al., 2006). In turn, working memory has been related to language comprehension ability in both clinical and non-clinical populations (e.g., Daneman & Carpenter, 1980; Daneman & Merikle, 1996; King & Just, 1991; Qualls & Harris, 2003).

One prevailing notion with respect to the role of working memory in language comprehension is the limited capacity theory (Just & Carpenter, 1992; King & Just, 1991). As articulated by its authors, the limited capacity theory suggests that "...cognitive capacity constrains comprehension, and it constrains comprehension more for some people than for others." (Just & Carpenter, 1992, p. 122). The authors further explain that "...language comprehension is an excellent example of a task that demands extensive storage of partial and final products in the service of complex information

processing.” (Just & Carpenter, 1992, p. 122). In this view, working memory is active in a variety of task-related contexts – storage of items for later retrieval, storage of partial results or products of processing for later use, storage of the theme of the text or discourse, and maintenance of a representation of the sentence currently being processed. Because working memory is, in effect, multitasking in the limited capacity theory, the system makes trade-offs between storage and processing which degrade the by-products of processing either because forgetting has occurred or because processing is slowed and /or incomplete. The limited capacity hypothesis provides one avenue of explanation with respect to the performance of the PD group on proverb interpretation in that it suggests that processing may be incomplete, especially when WM is taxed.

Proverb comprehension is a demanding language task that requires the integration of semantic, syntactic, pragmatic, and metalinguistic information in order to be successful. Glisky and Kong (2008) suggest that the FL factor used in this experiment may be capturing some aspect of WM that facilitates integration of information across different cognitive or perceptual domains. Were the ability to integrate information across different cognitive domains to go awry, it might predispose someone to commit errors in interpretation. In the case of proverb interpretation, this might be reflected in difficulty moving beyond a concrete interpretation towards the requisite nonliteral one. That the FL function factor used in this study taps into some aspects of integration of information across cognitive domains perhaps explains why the score on the FL function factor was predictive of performance on the proverbs task in the PD group only. For controls, the integrative processes tapped by the FL function factor remained intact or were not taxed

enough by the proverbs task to yield a predictive effect of performance on the proverbs task. In contrast, for PD participants, the FL function factor may have been tapping a significant problem with WM that then had a negative impact on proverb interpretation.

Evidence to support the claim that results of this experiment *may* be explained by difficulty with integration of information in WM can be drawn from research suggesting that the basal ganglia are intimately involved in WM from an anatomical standpoint (e.g., Alexander et al., 1986; Middleton & Strick, 1994). Additional research indicates that basal ganglia dysfunction may give rise to some of the WM deficits observed in PD such as difficulty with inhibitory processes (Frank, Loughry, & O'Reilly, 2001; Hazy, Frank, & O'Reilly, 2007; Monchi, Taylor, & Dagher, 2000). Friederici and colleagues (2003) reported that in an electrophysiological experiment conducted with PD participants results suggested that the basal ganglia do not support early syntactic processing during comprehension; rather, they support processes of syntactic integration which occur later in time.

Although it is premature to conclude anything with respect to the cognitive and neuropsychological underpinnings of integration, there are clear indicators that WM plays a role in language comprehension for controls as well as in the PD population (e.g., Daneman & Merikle, 1996; Friederici, Kotz, Werheid, Hein, & von Cramon, 2003). With respect to the NDPD population, it is conceivable that difficulty with WM may destabilize language comprehension processes just enough to make what was previously automatic no longer so, resulting in the reported problems in processing figurative language.

4.2.2. Neural and neuropsychological correlates of proverb interpretation

Although consensus regarding both the neural and the neuropsychological correlates of proverb comprehension has not yet been reached, converging evidence from behavioral (e.g., Burgess & Chiarello, 1996; Van Lancker, 2006) and neuroimaging studies (e.g., Lauro et al., 2008; Zempleni et al., 2007) suggest that higher-level language processing is dependent on intact frontostriatal systems; the same systems that are vulnerable to the effects of PD even early in its course.

Similarly, although the literature does not address the locus of proverb comprehension per se, studies of other forms of figurative language converge on a number of distinct neuroanatomical regions. Across a variety of neuroimaging experiments, a homolog of Wernicke's area in the right temporal lobe (Pobric, Mashal, Faust, & Lavidor, 2008) and the left inferior frontal gyrus have been identified as playing crucial roles in metaphor processing (Eviatar & Just, 2006; Mashal, Faust, & Hendler, 2005; Kircher, Leube, Erb, Grodd & Rapp, 2007; Rapp, Leube, Erb, Grodd, & Kircher, 2004; 2007; Stringaris, Medford, Giampetro, Brammer, & David, 2007).

When processing of idioms is examined, research implicates left prefrontal regions (Lauro, Tettamanti, Cappa, & Papagno, 2008; Mashal, Faust, Hendler, & Jung-Beeman, 2008; Oliveri, Romero, & Papagno, 2004; Rizzo, Sandrini, & Papagno, 2007). Moreover, Fogliata and colleagues (2007) suggested that the prefrontal region is involved in both the retrieval of a figurative meaning from semantic memory as well as in the response-monitoring and inhibition of alternative interpretations. If this is indeed the case, damage to frontostriatal circuitry would interrupt one or all of these processes. In

the case of proverb interpretation, this might result in an inability to retrieve a proverb's figurative meaning, or to inhibit a more literal meaning, both of which would result in an incorrect response.

Taken together, the neuroimaging evidence suggests a pivotal role for the prefrontal cortex in at least two forms of figurative language processing, and underscores the nature of frontal lobe participation in this endeavor. Although it is premature to speculate about the neural correlates of proverb comprehension based on the results of the present study, and the dangers inherent in inferring function from dysfunction, it is likely that PFC will continue to be a focus of inquiry in this regard.

Regardless of theoretical orientation, lines of converging evidence suggest that successful higher-level language processing depends critically on intact frontostriatal systems. Performance by the PD group in this study on both the proverbs task and the FL function factor reflects this relation. That this relation held regardless of participant educational achievement suggests that the cognitive deficit in PD is pervasive and has far-reaching implications for cognitive and communicative function.

In conclusion, results of this experiment revealed a between-groups difference with respect to performance on a proverb interpretation task for the PD group in the ON medication state. In the PD group, performance on the proverb interpretation task was related to performance on a FL function factor, which may reflect difficulty with integration of information across conceptual domains within working memory. It is likely that an interaction between the symptomatology of PD and some degree of dissolution of

relevant cognitive processes exists which manifests in the performance decrement in evidence here.

4.3 Limitations of the study

Although the dependent measure used in this study, *Gorham's Test of Proverbs*, has been validated and used across a variety of populations (Elmore & Gorham, 1957; Gorham, 1956a; 1956b), its scoring rubric is relatively vague and limited by its three point span (i.e., 0, 1, and 2). A number of authors have suggested different scoring schemes in tandem with other assessment tools (e.g., Brundage & Brookshire, 1995). Adoption of a different scoring scheme might provide more detailed and accurate information about performance than is currently available using this test.

In addition to the scoring issue, the presentation of test items in a decontextualized setting poses a threat to ecological validity. Typically, proverbs occur as part of normal discourse, and as such, are context-dependent and often culturally bound (Haas, 2008). Thus, one's ability to understand a proverb is girded by context without which the task is that much more demanding. The modifications made to the test for its non-standardized administration in this study did not reflect real world situations where proverbs occur in conversation.

The composition of the study population might limit its external validity in that the entire sample was of Caucasian origin, and many were well-educated (across group average, $M = 16.68$ years of education). Thus, results from this study may apply to other similarly constituted populations, but may not apply to samples of other ethnic or

educational background. Likewise, the cross-sectional design of this study might confound cohort effects with real age and/or pathology-based effects.

Care was taken to exclude potential PD participants who evidenced frank signs of dementia as determined by the referring neurologist. Given the cross-sectional nature of this study, it is unlikely that anybody progressed to PDD from the time of recruitment to the time of testing (a period not usually longer than two weeks). Were this study to be replicated, it would be necessary to safeguard against inclusion of participants with incipient dementia.

Another limitation of the study is the use of the MMSE as a coarse measure of cognition. The one point between-groups difference on the MMSE proved to be statistically significant. Although the cut-off score for inclusion in this study was 24, none of the participants in the PD group achieved this score – the lowest score in that group being 25. Of the four PD participants with a score of 25 on the MMSE, two also scored quite low on the FL function factor (i.e., z-scores of -1.85 and -1.33), and three of the four scored below the 50% mark for the Proverbs test. For the PD group, performance on the MMSE was correlated with performance on the FL function factor, $r = .398$, $p = .015$, a correlation that did not apply to the control group. Were this study to be replicated with a different sample, perhaps a cut-off of 25 might provide adequate coverage of the population in question.

Recent research indicates that using a more sensitive measure (e.g., the *Montreal Cognitive Assessment – MoCA*; Nasreddine, Phillips, Bedirian, Charboneau et al., 2005) might aid detection of early cognitive impairment in PD, even when MMSE scores

suggest normal cognitive function (Gill, Freshman, Blender & Ravina, 2008; Nazem, Siderowf, Duda, Ten Have et al., 2009; Zadikoff, Fox, Tang-Wai, Thomsen et al., 2008).

In a related vein, Mamikonyan, Moberg, Siderowf, Duda and colleagues (2008) reported that mild cognitive impairment (MCI) is common in PD patients with normal MMSE scores, with concomitant memory, attention, and executive impairments. In the Mamikonyan et al. study, increasing age and disease severity as well as use of anti-anxiety medication and increasing severity of daytime sleepiness were all independent predictors of cognitive impairment.

In highly educated individuals (i.e., those with 16 or more years of self-reported education), specific cut scores for optimizing sensitivity and specificity using the MMSE for detecting dementia in older white adults have recently been reported (O'Bryant, Humphreys, Smith, Ivnik et al., 2008). The present study sample was comprised largely of educated adults ($M = 16.9$ years in the PD group; $M = 16.47$ years in the NC group). It is therefore important to consider that MMSE scores in the normal range might reflect mild cognitive impairment in highly educated persons with PD, and that scores of 26 and below might signal the onset of dementia.

This growing body of evidence strongly suggests that using an instrument more sensitive to the nature of cognitive impairment even in early PD would be prudent.

4.4 Clinical implications

Language is a sophisticated code by means of which people convey information and intent. When language goes awry in some way, the impact on communication can be

quite dramatic. The language deficit that accompanies NDPD is non-aphasic but is comprised of more subtle difficulties involving figurative language. As PD progresses with its incipient cognitive decline, it is important that clinicians and caregivers alike are aware that types of figurative language may not be understood when used in conversation. This lack of understanding may go undetected if the conversation provides enough scaffolding that both parties can continue without pause, or it may lead to communication breakdown if continuation of the conversation hinges on adequate understanding.

In addition, although results of this study suggest that people with PD performed less well than their control counterparts on the Proverbs Test, it is important to remember that there was variability in the sample. Participants were optimally medicated during testing, which may have influenced their performance. As such, medication status as well as medication dosages should be considerations whenever language testing is undertaken in this population.

Further, although depression did not figure in a statistically significant manner in this study, it is certainly a variable of interest in the PD population. It is unclear at this time whether even a mild depression that is treated with medication might influence cognitive and communicative behaviors. It will continue to be important to monitor depression status in PD patients across the course of their disease, and note if or how the cognitive and behavioral sequelae of depression influence figurative language function.

Another clinical consideration in this regard relates to the expression and understanding of prosody and emotion by people with PD. Recent research suggests that

some PD patients may experience difficulties in both the expression and comprehension of non-verbal cues such as facial expressions (Cheang & Pell, 2007; Pell & Leonard, 2003; Pell & Monetta, 2008). Subtle but pervasive deficits such as these may further complicate communication when figurative language is involved because of the need to apprehend all aspects of the communication situation in order to understand the message being conveyed.

Results of this study demonstrated a robust relation between performance on the Proverbs Test and on the frontal lobe function factor. Poor performance on the FL factor correlated with poor performance on the Proverbs Test. Likewise, performance on the FL function factor was an important predictor of performance on the Proverbs test in the PD population. Thus, it is incumbent on clinicians to be aware that cognitive decline may be the harbinger of deficits in higher-level language function. Clinicians would then be in the role of providing education and perhaps counseling to patients as well as other involved parties.

In this vein, it is important to be aware that much of the literature on figurative language testing in PD shows that deficits emerge when cognitive resources are stressed. Without, for example, pushing working memory to its limit, deficits might remain obscured. In concrete terms, this means that informal assessment of communication skills based on a language sample might not reveal the true extent of the impairment. A range of assessment tasks at various levels of difficulty would be more appropriate in this situation.

4.5 Theoretical implications

Results of this study highlight the relation of frontostriatal circuitry to competency in language processing, and further support the role of subcortical functions in language (Crosson, 1985; Crosson, Zawacki, & Brinson, 1997). In particular, frontostriatal circuits seem to subserve at least some aspects of figurative language processing, and as such, are important with respect to the broad range of social and pragmatic skills involved in the use of figurative language.

At present, it is not known specifically how dopamine depletion in the frontostriatal circuits affects language function across the course of the disease. What is suggested by the literature is that frontostriatal systems influence cognitive processes such as working memory, recruitment of cognitive control (Liston, Watts, Tottenham, Davidson, Niogi et al., 2006) and other executive type functions (Heyder, Suchan, & Daum, 2004). As the pathology of PD progresses and the frontostriatal systems become increasingly involved, there may be a commensurate decline in the cognitive processes that subserve communication (Pell & Monetta, 2008). As such, it is important to consider how to better capture the effects of frontostriatal system deterioration as it relates to language function.

Results of this study highlight the intimate coupling of FL function and proverb interpretation in the PD population. This relation was found across a range of participants, some of whom were relatively early in the disease process. This suggests that even early in the disease when motor symptoms tend to predominate, a cognitive component is likely to exist, and may exert a deleterious effect on higher-level language

functions. Likewise, this study adds to the growing body of literature supporting the presence of a figurative language deficit alongside the other motor and non-motor symptoms of the disease.

4.6 Directions for future research

Many gaps remain in our understanding of the interaction between cognition and language in the PD population. Results of this cross-sectional study suggest a number of directions for future research one of which is horizontal (i.e., along similar/parallel lines), the other beginning vertical (i.e., beginning at the same point but having different endpoints). In the horizontal realm, a longitudinal study in which a single cohort of subjects is followed over time and tested at regular intervals might offer greater insight into the relation between language and cognition in this population and how or whether it changes over time. Longitudinal studies confer the additional advantage of allowing individual patterns of change over time to complement extant information from group studies. A note of caution in this regard, though: participants must be thoroughly and carefully screened at the outset to exclude those with PDD and those with incipient dementia. In addition, comparison of the performance of young onset versus older onset (as used in this study) PD patients on the same study protocol might yield information regarding age-of-onset and time until deficits are in evidence, information not currently available with respect to figurative language processing in PD.

Given the robust relation between performance on the frontal lobe function factor and performance on the Proverbs test in this study, it would be both interesting and

clinically relevant to determine whether performance on a proverbs type task might be used to predict cognitive decline in the PD population. Were such a relation to be found, speech and language clinicians could monitor progress over time and involve other professionals in a timely manner.

In the vertical realm, it is unclear at present whether the relation found in this study holds true for other neurodegenerative diseases with identified frontal lobe involvement (e.g., amyotrophic lateral sclerosis (ALS), multiple sclerosis (MS), and Huntington's disease (HD)). Because frontal lobe dysfunction manifests differently across disorders, elucidation of potential cognitive and language relations in each of these populations would contribute to both theoretical as well as clinical endeavors.

The arena is open to further explore whether or not deep brain stimulation (DBS) affects cognition in general and proverb comprehension in particular.

Neuroimaging data would complement the above-outlined behavioral data. Specifically, determining neuroanatomical correlates of proverb comprehension would complement the extant literature regarding the neural substrates of different forms of figurative language. Such information would further our understanding of how and where proverbs are processed in the brain, in both normal and PD participants.

Results of this study add to the growing body of evidence characterizing the language deficit that accompanies PD. Together with a well-established syntactic comprehension deficit, nondemented persons with PD are known to demonstrate marked difficulty with comprehension of figurative language (e.g., metaphor, ambiguous sentences), high level verbal reasoning tasks, discourse comprehension and pragmatic

function. Comprehension of proverbs is also vulnerable to the effects of PD, and is related to frontal lobe function. Whether this relation holds true across time and across other groups of subjects awaits confirmation.

APPENDIX A**Gorham's Test of Proverbs Form II**

1. He who stumbles twice over one stone deserves to break his shins.
2. Don't judge a book by its cover.
3. The proof of the pudding is in the eating.
4. One may ride a free horse to death.
5. A rolling stone gathers no moss.
6. Strike while the iron is hot.
7. All is not gold that glitters (All that glitters is not gold).
8. Easy come, easy go.
9. All's well that ends well.
10. Let sleeping dogs lie.
11. Great bodies move slowly.
12. Better be happy than wise.

APPENDIX B

Data Tables

The following pages contain data for each of five categories for both groups – PD and Controls. The five categories are: demographic data, screening data, FL function factor scores and z-score data, proverbs and familiarity data, and HMGT data. For the PD group, there is one additional data table that contains PD-specific variable data.

Table B1: Demographic Data – PD

| Subject | Gender | Age (yrs) | Education (yrs) | AQ |
|----------------|---------------|------------------|------------------------|--------------|
| 1301 | F | 78 | 16 | 98.4 |
| 1302 | M | 80 | 20 | 98.2 |
| 1303 | M | 65 | 18 | 97.8 |
| 1304 | F | 80 | 12 | 95.6 |
| 1305 | F | 71 | 18 | 99 |
| 1306 | M | 74 | 16 | 98.2 |
| 1307 | M | 67 | 20 | 99.2 |
| 1308 | F | 67 | 14 | 99.2 |
| 1309 | M | 78 | 20 | 98.8 |
| 1310 | F | 72 | 18 | 98.6 |
| 1311 | M | 71 | 16 | 96.8 |
| 1312 | M | 82 | 16 | 99 |
| 1313 | F | 70 | 18 | 99.6 |
| 1314 | F | 76 | 18 | 98.6 |
| 1315 | M | 82 | 20 | 96.8 |
| 1316 | F | 80 | 20 | 97.8 |
| 1317 | M | 69 | 20 | 98.4 |
| 1318 | M | 71 | 16 | 99.4 |
| 1319 | M | 75 | 12 | 99.4 |
| 1320 | M | 69 | 20 | 96.6 |
| 1321 | F | 85 | 12 | 99.2 |
| 1322 | M | 83 | 16 | 99.2 |
| 1323 | M | 73 | 18 | 99 |
| 1324 | F | 67 | 12 | 98 |
| 1325 | F | 67 | 20 | 98.8 |
| 1326 | M | 66 | 18 | 99.2 |
| 1327 | F | 76 | 14 | 97.2 |
| 1328 | M | 71 | 19 | 99.6 |
| 1329 | F | 69 | 14 | 99.6 |
| 1331 | M | 83 | 16 | 98.8 |
| | MEAN: | 73.9 | 16.9 | 98.45 |
| | S.D.: | 5.97 | 2.7 | 1.01 |

Means and standard deviations for the PD group for the variables age, education, and score on the WAB-R AQ.

Table B 2: Demographic Data – Controls

| Subject | Gender | Age (yrs.) | Education (yrs.) | AQ |
|----------------|---------------|-------------------|-------------------------|--------------|
| 2301 | F | 65 | 18 | 97.7 |
| 2302 | M | 72 | 18 | 99 |
| 2303 | M | 67 | 20 | 100 |
| 2304 | F | 72 | 18 | 100 |
| 2305 | M | 76 | 16 | 95 |
| 2306 | F | 70 | 12 | 98.2 |
| 2307 | M | 74 | 18 | 98.8 |
| 2308 | F | 65 | 20 | 98.4 |
| 2309 | F | 75 | 16 | 100 |
| 2310 | F | 80 | 13 | 99.6 |
| 2311 | M | 70 | 19 | 99.6 |
| 2312 | F | 79 | 16 | 99.6 |
| 2313 | F | 70 | 16 | 98.2 |
| 2314 | F | 68 | 16 | 100 |
| 2315 | F | 75 | 18 | 99.6 |
| 2316 | F | 71 | 14 | 98.4 |
| 2317 | M | 70 | 16 | 96.8 |
| 2318 | F | 70 | 14 | 98.6 |
| 2319 | F | 66 | 16 | 99.4 |
| 2320 | F | 67 | 14 | 99.2 |
| 2321 | M | 70 | 16 | 98.2 |
| 2322 | M | 75 | 20 | 99.2 |
| 2323 | M | 74 | 16 | 98.2 |
| 2324 | F | 80 | 18 | 97 |
| 2325 | F | 82 | 12 | 98.8 |
| 2326 | F | 79 | 14 | 99.2 |
| 2327 | M | 81 | 20 | 99.6 |
| 2328 | F | 80 | 16 | 99.2 |
| 2329 | M | 82 | 20 | 99.6 |
| 2330 | F | 71 | 14 | 100 |
| | MEAN | 73.2 | 16.47 | 98.84 |
| | S.D. | 5.37 | 2.4 | 1.13 |

Means and standard deviations for the control group for the variables age, education (years), and score on the WAB-R AQ.

Table B 3: Screening data – PD

| Subject | MMSE | Hearing | GDS |
|----------------|--------------|----------------|-------------|
| 1301 | 30 | Pass | 1 |
| 1302 | 26 | Pass | 2 |
| 1303 | 28 | Pass | 0 |
| 1304 | 29 | Pass | 2 |
| 1305 | 28 | Pass | 5 |
| 1306 | 29 | Pass | 3 |
| 1307 | 27 | Pass | 2 |
| 1308 | 27 | Pass | 0 |
| 1309 | 27 | Pass | 4 |
| 1310 | 28 | Pass | 2 |
| 1311 | 25 | Pass | 4 |
| 1312 | 25 | Pass | 4 |
| 1313 | 29 | Pass | 1 |
| 1314 | 25 | Pass | 3 |
| 1315 | 27 | Pass | 1 |
| 1316 | 30 | Pass | 3 |
| 1317 | 25 | Pass | 9 |
| 1318 | 29 | Pass | 6 |
| 1319 | 28 | Pass | 2 |
| 1320 | 30 | Pass | 0 |
| 1321 | 29 | Pass | 2 |
| 1322 | 29 | Pass | 11 |
| 1323 | 29 | Pass | 6 |
| 1324 | 29 | Pass | 1 |
| 1325 | 29 | Pass | 1 |
| 1326 | 29 | Pass | 2 |
| 1327 | 28 | Pass | 7 |
| 1328 | 30 | Pass | 2 |
| 1329 | 28 | Pass | 3 |
| 1331 | 30 | Pass | 1 |
| MEAN: | 28.07 | | 3 |
| S.D. | 1.6 | | 2.63 |

Means and standard deviations for the PD group for the MMSE and the GDS-SF. The MMSE is scored out of a possible 30 points, and the GDS-SF is out of 15, with a score of five or greater being a caution for depression. The hearing screening yielded pass/fail data.

Table B 4: Screening data – Controls

| Subject | MMSE | Hearing | GDS |
|----------------|--------------|----------------|-------------|
| 2301 | 30 | Pass | 0 |
| 2302 | 30 | Pass | 1 |
| 2303 | 30 | Pass | 1 |
| 2304 | 29 | Pass | 7 |
| 2305 | 29 | Pass | 8 |
| 2306 | 29 | Pass | 2 |
| 2307 | 30 | Pass | 1 |
| 2308 | 26 | Pass | 0 |
| 2309 | 29 | Pass | 2 |
| 2310 | 30 | Pass | 0 |
| 2311 | 29 | Pass | 0 |
| 2312 | 30 | Pass | 1 |
| 2313 | 30 | Pass | 3 |
| 2314 | 28 | Pass | 1 |
| 2315 | 28 | Pass | 0 |
| 2316 | 28 | Pass | 3 |
| 2317 | 28 | Pass | 0 |
| 2318 | 28 | Pass | 2 |
| 2319 | 30 | Pass | 0 |
| 2320 | 30 | Pass | 0 |
| 2321 | 30 | Pass | 1 |
| 2322 | 28 | Pass | 0 |
| 2323 | 30 | Pass | 1 |
| 2324 | 28 | Pass | 3 |
| 2325 | 29 | Pass | 4 |
| 2326 | 26 | Pass | 2 |
| 2327 | 30 | Pass | 6 |
| 2328 | 27 | Pass | 0 |
| 2329 | 30 | Pass | 3 |
| 2330 | 30 | Pass | 2 |
| MEAN | 28.97 | | 1.8 |
| S.D. | 1.22 | | 2.12 |

Means and standard deviations for control group for the MMSE and the GDS-SF. The MMSE is scored out of a possible 30 points, and the GDS-SF is out of 15, with a score of five or greater being a caution for depression. The hearing screening yielded pass/fail data.

Table B 5: Frontal Lobe Function Factor Test Scores and z-scores – PD

| Subject | Arithmetic | WCSTcat | Digitspan | FASTtotal | MControl | FLFzscore |
|----------------|-------------------|----------------|------------------|------------------|-----------------|------------------|
| 1301 | 15 | 5 | 9 | 36 | 19 | 0.004097 |
| 1302 | 6 | 0 | 6 | 35 | 26 | -1.09346 |
| 1303 | 9 | 6 | 8 | 35 | 16 | -0.71495 |
| 1304 | 9 | 1 | 6 | 8 | 16 | -1.62972 |
| 1305 | 17 | 6 | 8 | 65 | 24 | 0.71181 |
| 1306 | 14 | 3 | 9 | 47 | 22 | -0.06938 |
| 1307 | 14 | 5 | 8 | 39 | 20 | -0.2648 |
| 1308 | 8 | 1 | 7 | 31 | 31 | -0.91229 |
| 1309 | 17 | 6 | 6 | 20 | 21 | -0.20848 |
| 1310 | 12 | 6 | 7 | 45 | 22 | -0.08221 |
| 1311 | 8 | 1 | 4 | 22 | 15 | -1.85039 |
| 1312 | 6 | 1 | 5 | 28 | 21 | -1.33317 |
| 1313 | 16 | 6 | 10 | 38 | 23 | 0.308399 |
| 1314 | 8 | 6 | 5 | 30 | 20 | -0.75738 |
| 1315 | 15 | 3 | 8 | 34 | 26 | 0.008808 |
| 1316 | 14 | 6 | 9 | 50 | 21 | 0.430908 |
| 1317 | 12 | 2 | 8 | 22 | 20 | -0.98544 |
| 1318 | 10 | 4 | 6 | 28 | 22 | -0.83776 |
| 1319 | 17 | 5 | 7 | 30 | 29 | 0.174239 |
| 1320 | 17 | 2 | 4 | 32 | 18 | -0.93905 |
| 1321 | 11 | 4 | 5 | 27 | 15 | -0.85901 |
| 1322 | 12 | 4 | 7 | 49 | 20 | -0.09547 |
| 1323 | 12 | 6 | 7 | 37 | 36 | 0.323097 |
| 1324 | 6 | 1 | 5 | 47 | 23 | -1.23797 |
| 1325 | 14 | 6 | 7 | 36 | 26 | -0.08667 |
| 1326 | 8 | 6 | 4 | 46 | 26 | -0.55211 |
| 1327 | 6 | 1 | 4 | 21 | 15 | -1.88864 |
| 1328 | 15 | 6 | 9 | 23 | 24 | -0.04217 |
| 1329 | 10 | 5 | 7 | 40 | 21 | -0.50485 |
| 1331 | 13 | 3 | 7 | 37 | 15 | -0.542 |
| MEAN | 11.7 | 3.9 | 6.73 | 34.6 | 21.78 | -.5175 |
| S.D. | 3.68 | 2.12 | 1.7 | 11.38 | 4.95 | .676 |

Means and standard deviations for the PD group for each of the five tests comprising the FL function factor and for the FL factor z-score. The five tests comprising the FL factor are – ‘Arithmetic’ denotes score on Mental Arithmetic, ‘WCSTcat’ denotes categories achieved on the Wisconsin Card Sorting Test (WCST), ‘Digitspan’ denotes score on Digit Span Backward, ‘FASTtotal’ denotes the total number of words achieved on the FAS test, and ‘MControl’ denotes score achieved on the Mental Control test.

Table B 6: Frontal Lobe Function Factor Test Scores and z-score data – Controls

| Subject | Arithmetic | WCSTcat | Digitspan | FASTotal | MControl | FLFzscore |
|----------------|-------------------|----------------|------------------|-----------------|-----------------|------------------|
| 2301 | 14 | 5 | 9 | 53 | 21 | 0.061407 |
| 2302 | 16 | 6 | 4 | 44 | 28 | 0.101873 |
| 2303 | 19 | 3 | 5 | 31 | 22 | -0.51978 |
| 2304 | 9 | 6 | 8 | 61 | 28 | 0.321192 |
| 2305 | 13 | 6 | 6 | 36 | 18 | -0.33238 |
| 2306 | 9 | 5 | 7 | 30 | 14 | -0.97859 |
| 2307 | 16 | 6 | 8 | 47 | 26 | 0.477237 |
| 2308 | 12 | 6 | 9 | 49 | 26 | 0.172002 |
| 2309 | 14 | 6 | 9 | 44 | 20 | 0.188888 |
| 2310 | 11 | 6 | 9 | 28 | 20 | -0.16815 |
| 2311 | 13 | 4 | 6 | 39 | 18 | -0.63427 |
| 2312 | 15 | 4 | 9 | 40 | 26 | 0.255722 |
| 2313 | 12 | 2 | 8 | 23 | 21 | -0.91063 |
| 2314 | 14 | 1 | 3 | 38 | 16 | -1.32045 |
| 2315 | 9 | 6 | 7 | 52 | 29 | 0.175718 |
| 2316 | 10 | 5 | 6 | 49 | 22 | -0.36188 |
| 2317 | 12 | 6 | 6 | 15 | 18 | -0.87623 |
| 2318 | 13 | 6 | 5 | 29 | 25 | -0.40296 |
| 2319 | 14 | 6 | 8 | 37 | 22 | -0.12926 |
| 2320 | 15 | 3 | 8 | 49 | 29 | 0.07268 |
| 2321 | 15 | 5 | 9 | 43 | 22 | 0.090381 |
| 2322 | 15 | 6 | 6 | 45 | 20 | -0.00085 |
| 2323 | 16 | 3 | 10 | 39 | 16 | -0.2 |
| 2324 | 12 | 4 | 6 | 50 | 23 | -0.12 |
| 2325 | 7 | 4 | 8 | 49 | 18 | -0.41 |
| 2326 | 12 | 3 | 8 | 57 | 19 | -0.1 |
| 2327 | 14 | 5 | 5 | 60 | 23 | 0.22 |
| 2328 | 10 | 6 | 6 | 68 | 24 | 0.34 |
| 2329 | 17 | 6 | 6 | 76 | 34 | 1.32 |
| 2330 | 13 | 6 | 9 | 40 | 28 | 0.28 |
| MEAN | 13.03 | 4.87 | 7.10 | 44.03 | 22.53 | -.1129 |
| S.D. | 2.697 | 1.432 | 1.749 | 13.09 | 4.65 | .5178 |

Means and standard deviations for the control group for each of the five tests comprising the FL function factor and for the FL factor z-score. The five tests comprising the FL factor are – Mental Arithmetic, categories achieved on the Wisconsin Card Sorting Test (WCST), Digit Span Backward, Total number of words achieved in the FAS test, and Mental Control (abbreviated in the data table as ‘MControl’).

Table B 7: Proverbs Test and Familiarity Index Data – PD

| Subject | Proverbs | Familiarity | FamIndex |
|----------------|-----------------|--------------------|-----------------|
| 1301 | 19 | 10 | 0.833 |
| 1302 | 7 | 9 | 0.75 |
| 1303 | 5 | 8 | 0.667 |
| 1304 | 6 | 7 | 0.583 |
| 1305 | 17 | 8 | 0.667 |
| 1306 | 19 | 8 | 0.667 |
| 1307 | 17 | 8 | 0.667 |
| 1308 | 16 | 9 | 0.75 |
| 1309 | 19 | 12 | 1 |
| 1310 | 19 | 8 | 0.667 |
| 1311 | 3 | 11 | 0.083 |
| 1312 | 10 | 11 | 0.083 |
| 1313 | 17 | 8 | 0.667 |
| 1314 | 11 | 8 | 0.667 |
| 1315 | 13 | 9 | 0.75 |
| 1316 | 16 | 12 | 1 |
| 1317 | 14 | 11 | 0.083 |
| 1318 | 18 | 8 | 0.667 |
| 1319 | 8 | 8 | 0.667 |
| 1320 | 12 | 10 | 0.833 |
| 1321 | 6 | 10 | 0.833 |
| 1322 | 16 | 8 | 0.667 |
| 1323 | 17 | 8 | 0.667 |
| 1324 | 11 | 7 | 0.583 |
| 1325 | 16 | 8 | 0.667 |
| 1326 | 8 | 8 | 0.667 |
| 1327 | 7 | 11 | 0.083 |
| 1328 | 16 | 10 | 0.833 |
| 1329 | 8 | 8 | 0.667 |
| 1331 | 12 | 8 | 0.667 |
| MEAN: | 12.77 | 8.97 | .606 |
| S.D. | 4.932 | 8.31 | .693 |

Means and standard deviations for the PD group for the variables ‘raw score on the Proverbs Test’, ‘Familiarity’, and the ‘Familiarity Index’. A total of 24 points is possible on the Proverbs Test. A total of 12 points is possible (one for each of the 12 proverbs on the test) for the ‘Familiarity’ variable. The ‘familiarity index’ is the proportion of familiar proverbs on the test, and ranges from 0 to 1.

Table B 8 : Proverbs Test and Familiarity Index Data – Controls

| Subject | Proverbs | Familiarity | FamIndex |
|----------------|-----------------|--------------------|-----------------|
| 2301 | 21 | 9 | 0.75 |
| 2302 | 15 | 8 | 0.667 |
| 2303 | 21 | 9 | 0.75 |
| 2304 | 18 | 9 | 0.75 |
| 2305 | 22 | 8 | 0.667 |
| 2306 | 16 | 7 | 0.583 |
| 2307 | 11 | 9 | 0.75 |
| 2308 | 19 | 8 | 0.667 |
| 2309 | 19 | 8 | 0.667 |
| 2310 | 14 | 8 | 0.667 |
| 2311 | 14 | 9 | 0.75 |
| 2312 | 18 | 9 | 0.75 |
| 2313 | 16 | 10 | 0.833 |
| 2314 | 19 | 9 | 0.75 |
| 2315 | 13 | 8 | 0.667 |
| 2316 | 17 | 10 | 0.833 |
| 2317 | 19 | 8 | 0.667 |
| 2318 | 17 | 6 | 0.5 |
| 2319 | 20 | 8 | 0.667 |
| 2320 | 13 | 8 | 0.667 |
| 2321 | 17 | 8 | 0.667 |
| 2322 | 16 | 8 | 0.667 |
| 2323 | 20 | 8 | 0.667 |
| 2324 | 12 | 8 | 0.667 |
| 2325 | 16 | 8 | 0.667 |
| 2326 | 16 | 8 | 0.667 |
| 2327 | 19 | 8 | 0.667 |
| 2328 | 14 | 8 | 0.667 |
| 2329 | 20 | N/A | N/A |
| 2330 | 16 | 9 | 0.75 |
| MEAN: | 16.93 | 8.31 | .693 |
| S.D.: | 2.85 | .806 | .067 |

Means and standard deviations for the control group for the variables ‘raw score on the Proverbs Test’, ‘Familiarity’, and the ‘Familiarity Index’. A total of 24 points is possible on the Proverbs Test. A total of 12 points is possible (one for each of the 12 proverbs on the test) for the ‘Familiarity’ variable. The ‘familiarity index’ is the proportion of familiar proverbs on the test, and ranges from 0 to 1.

Table B 9: PD-Specific Variables

| Subject | UPDRS | Time since diagnosis of PD (yrs.) | Ldopa equivalent (mg) |
|----------------|--------------|--|------------------------------|
| 1301 | N/A | 3 | 600 |
| 1302 | 10 | 10 | 1200 |
| 1303 | 10.5 | 5 | 1600 |
| 1304 | 27 | 3 | 360 |
| 1305 | 12.5 | 2 | 1160 |
| 1306 | 16.5 | 5 | 690 |
| 1307 | N/A | 5 | 690 |
| 1308 | 39 | 10 | 920 |
| 1309 | 22.5 | 5 | 1300 |
| 1310 | 4 | 1 | 300 |
| 1311 | 25 | N/A | 250 |
| 1312 | 21.5 | 13 | 800 |
| 1313 | 19 | 3 | 3600 |
| 1314 | 28 | 6 | N/A |
| 1315 | 20.5 | 9 | 2200 |
| 1316 | 5 | 5 | 760 |
| 1317 | 21 | 4 | N/A |
| 1318 | 19 | 13 | 1700 |
| 1319 | N/A | 10 | 5600 |
| 1320 | 25 | 10 | 1320 |
| 1321 | 21 | 2 | N/A |
| 1322 | N/A | 6 | 960 |
| 1323 | 16 | 25 | 1080 |
| 1324 | 16 | 2 | 600 |
| 1325 | 25 | 4 | 2700 |
| 1326 | N/A | 10 | 2150 |
| 1327 | 25 | 6 | 530 |
| 1328 | 27.5 | 2 | 50 |
| 1329 | 14 | 9 | 3900 |
| 1331 | 15 | 2 | N/A |
| MEAN: | 19.42 | 6.55 | 1423.85 |
| S.D.: | 7.82 | 4.98 | 253.07 |

Means and standard deviations for the three PD-specific variables. 'UPDRS' refers to the score attained on the motor subscale of the UPDRS, 'Time since diagnosis of PD' refers to the years since diagnosis, 'Ldopa equivalent' refer to Total L-dopa equivalent expressed in milligrams. N/A denotes data not available.

Table B 10: HMGT data – PD

| Subject | HMGT |
|----------------|--------------|
| 1301 | 10 |
| 1302 | 8 |
| 1303 | 14 |
| 1304 | 5 |
| 1305 | 11 |
| 1306 | 11 |
| 1307 | 10 |
| 1308 | 10 |
| 1309 | 11 |
| 1310 | 15 |
| 1311 | 3 |
| 1312 | 9 |
| 1313 | 14 |
| 1314 | 10 |
| 1315 | 14 |
| 1316 | 12 |
| 1317 | 11 |
| 1318 | 11 |
| 1319 | 13 |
| 1320 | 9 |
| 1321 | 10 |
| 1322 | 13 |
| 1323 | 10 |
| 1324 | 8 |
| 1325 | 12 |
| 1326 | 13 |
| 1327 | 6 |
| 1328 | 9 |
| 1329 | 14 |
| 1331 | 14 |
| MEAN: | 10.67 |
| S.D.: | 2.83 |

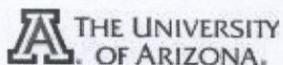
Mean and standard deviation for the PD group on the HMGT.

Table B 11: HMGT data – NC

| Subject | HMGT |
|----------------|-------------|
| 2301 | 11 |
| 2302 | 13 |
| 2303 | 14 |
| 2304 | 12 |
| 2305 | 10 |
| 2306 | 13 |
| 2307 | 13 |
| 2308 | 11 |
| 2309 | 13 |
| 2310 | 11 |
| 2311 | 13 |
| 2312 | 10 |
| 2313 | 13 |
| 2314 | 10 |
| 2315 | 15 |
| 2316 | 13 |
| 2317 | 13 |
| 2318 | 12 |
| 2319 | 12 |
| 2320 | 14 |
| 2321 | 10 |
| 2322 | 13 |
| 2323 | 13 |
| 2324 | 10 |
| 2325 | 10 |
| 2326 | 11 |
| 2327 | 14 |
| 2328 | 13 |
| 2329 | 16 |
| 2330 | 10 |
| MEAN: | 12.2 |
| S.D.: | 1.65 |

Mean and standard deviation for the control group on the HMGT.

APPENDIX C - Project Approval Letter



Human Subjects
Protection Program

1235 N. Mountain Ave.
P.O. Box 245137
Tucson, AZ 85724-5137
Tel: (520) 626-6721
<http://www.irb.arizona.edu>

21 March 2008

Michelle Guttman, MS
Advisor: Brad Story, PhD
Department of Speech, Language, & Hearing Sciences
PO Box 210071

RE: **PROJECT NO. 08-0098-02** PROVERB COMPREHENSION AND FRONTAL LOBE
FUNCTION IN PARKINSON'S DISEASE

Dear Michelle Guttman:

We received your 17 March 2008 letter and revised Project Review Form, revised Geriatric Depression Rating Scale, revised Subject's Consent Form [Parkinson's and Controls versions 03/17/08], revised PHI Authorization Form [version 03/17/08], revised Recruitment Flyers, and Participant Information form for the above referenced project. All of the conditions as set out in our 26 February 2008 letter to you (relevant to the **25 February 2008 Full Board review** of this project) have been met. Therefore approval for this **subjects-at-minimal-risk** project is granted with an **expiration date of 25 February 2009**.

Note that approval of this project also includes the following documents: stamped Informed Consent forms (Parkinson's Disease and Controls) and stamped PHI Authorization Form.

The Institutional Review Board (IRB) of the University of Arizona has a current **Federalwide Assurance** of compliance, **FWA00004218**, which is on file with Department of Health and Human Services and cover this activity.

Approval is granted with the understanding that no further changes or additions will be made either to the procedures followed or the consent form(s) used (copies of which we have on file) without the knowledge and approval of the Institutional Review Board. Any research related physical or psychological harm to any subject must also be reported to the appropriate committee.

A university policy requires that all signed subject consent forms be kept in a permanent file in an area designated for that purpose by the Department Head or comparable authority. This will assure their accessibility in the event that university officials require the information and the principal investigator is unavailable for some reason.

Sincerely,

Elaine G. Jones, RN, PhD
Chair, Social and Behavioral Sciences Committee
UA Institutional Review Board (IRB)

EGJ:maa
cc: Departmental/College Review Committee



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