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Cognitive and affective processing in hemiparkinson's disease

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Cognitive and Affective Processing in Hemiparkinson's Disease

by

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Abstract

COGNITIVE AND AFFECTIVE PROCESSING

IN HEMIPARKINSON'S DISEASE

by

John St. Clair

Advisor: Joan C. Borod, Ph.D.

Twenty-three patients with Parkinson's disease (PD) on one side of the body, known as hemiparkinson's disease (HPD), were compared to 11 normal control (NC) subjects on a battery of 15 neuropsychological tests assessing left, right, and frontal lobe functions. ANOVAs revealed no significant differences between patients with Parkinson's disease on the right side of the body (RPD, N=11) and patients with Parkinson's disease on the left side of the body (LPD, N=12). When combining LPDs and RPDs into one group ("early PD") and comparing them to NCs (N=11), cognitive deficits often seen in PD were found. These results support other studies that have failed to find differences in neuropsychological functioning between LPDs and RPDs, and also support studies indicating that there are neuropsychological deficits present in the early stages of PD when compared to Ncs.

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Introduction

Parkinson's disease was first described by James Parkinson, an English physician, in 1817 (Stern & Lees, 1990). He wrote of six patients with a slowly progressive physical disease as characterized by "involuntary tremulous motion, with lessened muscular power, in parts not in action even when supported, with a propensity to bend the trunk forward and to pass from a walking to a running pace" (Knight, Godfrey, & Shelton, 1985, p. 392). This disease state is now known as Parkinson's disease (PD).

There are three salient features of PD. The first is tremor (e.g., shaking of the limbs). This usually, though not always, occurs at rest. The second major feature of PD is bradykinesia, defined as a slowing or cessation of movement. The third feature is rigidity. This is seen in stiffness of the muscles and joints, noted by a resistance to passive movements of a limb, such as the wrist or elbow. Often, this rigidity manifests itself as a regular rhythmical jerking movement. When this is seen, it is referred to as "cogwheel rigidity". Other physical symptoms often seen in PD include postural changes, decreased arm swing or dragging of one leg when walking (many patients report this to be

their first recollection of the presence of the disease), difficulties in the initiation or cessation of movement, an expressionless face (often referred to as a "Parkinsonian mask"), impaired dexterity for skilled tasks (especially those involving rapid, repetitive movements), and "micrographia" (noted by small, often illegible handwriting [Pearce, 1992; Turnbull, 1992]).

When James Parkinson first described the physical symptoms of what was to become known as Parkinson's disease, he made a point of excluding any changes in mental functioning. He wrote, for example, "throughout the course of the illness the senses and intellects were preserved" (Parkinson, 1817/1955, p. 153). Today, we know there are many "intellectual" changes that may be seen in patients with PD, even at the onset of the disease. Parkinson's disease and its associated features can be studied from various methodological approaches. As often happens with research, new areas of interest have emerged. One relatively recent research area has been in hemiparkinsonism, which is the presence of Parkinson's disease symptomatology lateralized either exclusively or primarily to one side of the body. By definition, HPD is an

early, almost always transient stage in the development of PD (Chouza et al, 1984). With very few exceptions, HPD always progresses into PD with bilateral symptoms. Right hemiparkinsonism (RPD) refers to motor disturbances being more prevalent on the right side of the body, suggesting more left- than right-sided subcortical pathology. Conversely, left hemiparkinson's disease (LPD) refers to motor disturbances being more prevalent on the left side of the body, suggesting more right- than left-sided subcortical pathology. The current project investigated cognitive and affective processing in hemiparkinson's disease (HPD).

Etiology and Pathophysiology of PD

Before addressing the neuropsychological aspects of PD, an overview of the etiology and pathophysiological substrates of PD will be reviewed. Although the terms "PD" and "parkinsonism" are often used interchangeably, parkinsonism refers to a clinical syndrome characterized by four major symptoms: tremor, rigidity, bradykinesia, and postural disturbances. The term "Parkinson's disease" refers specifically to those cases where the etiology is unknown. This type of parkinsonism is often called idiopathic PD and accounts for the vast majority of

parkinsonian cases. Other cases of parkinsonism (where the etiology is known) include drug-induced parkinsonism (particularly from the use of phenothiazines and butyrophenones), post-encephalitic parkinsonism (which now is relatively rare but resulted in the incidence of many cases stemming from an influenza epidemic between 1917 and 1926), and MPTP toxicity (which resulted from the use of synthetically-produced "designer drugs" in the early 1980's [Caird, 1991]). Other disease states that may have parkinsonism associated with them include progressive supranuclear palsy, olivopontocerebellar atrophy, strionigral degeneration, Shy-Drager syndrome, Alzheimer's disease, multiple cerebral infarcts, and head injury (Caird, 1991).

In idiopathic PD, various factors have been investigated regarding possible causes, but there has been no identifying agent(s) found to be responsible for its occurrence. Slow viral infections have been investigated, but studies have found no evidence for links between viruses and PD. It does not seem to be pathophysiologically related to the normal aging process, although the incidence of PD does increase with age and peaks at about 1% in 80-year old

populations. Environmental toxins have long been a suspected possible contributing factor, especially with the observation that while other neurological conditions have been observed and recorded for thousands of years, descriptions of PD are comparatively recent, coinciding with the onset of the industrial revolution. Mercury, manganese, carbon monoxide, and carbon disulfate have all been suspected causes, but the most implicated causal agent is that of agricultural pesticides. It has been documented that there is an increased incidence of PD in rural dwellers, users of well water, and users of herbicides and pesticides, but not all studies have been able to confirm these findings (Caird, 1991).

Along the same lines, there is no substantial evidence for increased numbers of cases of PD patients associated with particular geographical areas or time periods. Hereditary factors, including data obtained from twin studies, have also proved inconclusive. In fact, one twin study (Ward, Duvoisin, Ince, et al., 1983) actually found that the prevalence of disease in non-twin siblings and parents was <u>greater</u> than that in co-twins.

The neuropathology of PD indicates specific deficits in both neuroanatomical substrates as well as the neurotransmitters associated with them (the neuropathology of HPD is assumed to be the same as in PD, except that it is unilaterally expressed). The primary deficit found in PD is the loss of the majority of large neuromelanin-containing neurons of the substantia nigra (Calne, 1989). These large neurons of the substantia nigra utilize dopamine as their neurotransmitter. Parkinson's disease is a result of the loss of these dopaminergic fibers that feed into the caudate nucleus and putamen (collectively known as the striatum) of the basal ganglia. Up to a 50% degeneration of the substantia nigra/basal ganglia complex is a normal age-related event. Parkinson' disease seems to occur in those cases where degeneration reaches approximately 80%. What factors are responsible for this heightened loss of cells in some aged individuals but not others is unknown. Although this is the primary pathological basis of PD, other neuroanatomical and neurochemical abnormalities are seen throughout the CNS in parkinsonism.

While depigmentation, neuronal loss, and gliosis of the substantia nigra (especially the pars compacta) and locus

coeruleus are found in PD (Teuber & Proctor, 1964), one also often finds atrophy of the cortical gyri as well as enlarged ventricles, but this is thought to be due to the normal aging process and not to the PD itself (Pearce, 1992). Also observed in parkinsonism is neuronal degeneration in the substantia innominata. Invariably, Lewy bodies are found in the brains of PD patients. Although non-diagnostic (they are found in other CNS disease states, for example, Alzheimer's disease), Lewy bodies and glial foci are the major features on microscopic examination and are found in practically every case of PD (Pearce, 1992). Lewy bodies are pink acidophilic blobs, with a central core and a peripheral halo. When viewed under an electron microscope, they show "radiating filaments resembling Van Gogh's sunflowers" (Pearce, 1992). They are found all throughout the CNS, but are especially dense in the compact zone of the substantia nigra and in the pigmented noradrenergic locus coeruleus of the midbrain. Other areas showing Lewy bodies include the autonomic ganglia, the substantia innominata, the amygdala, the hypothalamus, and the dorsal motor nucleus of the vagus. They are often found throughout the cerebral cortex as well, although in smaller numbers.

As has been stated, dopamine (DA) is the primary neurotransmitter affected in PD. However, other neurotransmitters are also found to be disturbed in parkinsonism. As a result of the striatal depletion of DA, acetylcholine (Ach) becomes the dominant neurotransmitter. Treatments of PD typically focus on increasing DA and decreasing Ach. However, there is not an actual increase in the production of Ach. Acetylcholine activity seems to increase because of the dopaminergic decrease. Normally, these two neurotransmitters work in tandem and regulate each other. When the dopaminergic inputs decrease, an imbalance ensues, resulting in a functional increase of Ach activity. Whereas a functional increase in Ach may occur in the striatal area, Meynert's nucleus (which is cholinergic) is found to have depletions of Ach. Some suspect this may be related to the memory loss seen in some PD patients. However, this memory loss could also result from the anticholinergic medications taken by PD patients receiving treatment.

Two other neurotransmitters and a group of neuropeptides have also been found to be altered in PD. In post-mortem studies in patients with Parkinson's disease,

Serotonin (5-HT), as well as its metabolic byproduct, 5-hydroxyindoleacetic acid (5-HIAA), are found to be depleted in the basal ganglia, hypothalamus, hippocampus, and frontal cortex. At present, the clinical significance of this is unclear, although it is thought that it may play a role in the depression often seen in parkinsonism. At least one study has found results supporting this hypothesis. Mayeaux, Stern, Cote, and Williams (1984) found that 5-HIAA levels were lower in depressed than nondepressed PD patients. They conclude that their data suggest that the serotonergic alterations found in PDs may identify a subgroup of patients who are prone to depression.

The noradrenergic system, especially in the locus coeruleus and to a lesser extent in the cortex, is depleted. Again, clinical significance is unclear, but possible effects may include the akinesia and freezing often found in PD, as well as depression. A decrease in neuropeptide levels accompanies neuronal degeneration in the basal ganglia. Five neuropeptides have been identified: met-enkaphalin, leu-enkaphalin, cholecystokinin, somatostatin, and substance P. Once more, clinical significance is uncertain, although depletion of somatostatin levels in the

cortex have been suggested to account for the presence of dementia found in some PD patients (Agid, Ruberg, and Raisman, 1990).

Neuropsychological Deficits in Parkinson's Disease

The neuropsychological deficits seen in PD have been well documented (for reviews, see Brown & Marsden, 1990; Raskin, Borod, & Tweedy, 1992).

Visuospatial functioning. One of the most commonly cited deficits reported in PD is that of visuospatial functioning. There are various ways to measure visuospatial integrity. One approach that has been used by some researchers has been to study the response of patients to Aubert's phenomenon (Brown & Marsden, 1990). When a normal adult is placed in a dark room and is asked to place a luminous rod into a vertical position, the task is performed without difficulty. However, when instructed to do this with the head tilted to one side, subjects tend to incline the rod in an angle opposite to the direction their head is tilted. This is known as Aubert's phenomenon. In one study, when PD patients were tested using this procedure, the amount of error was slightly greater for PDs than for normal controls (NCs) when setting the rod to vertical

seated in an upright position, but the error was significantly greater for PDs than NCs when made with the body in a tilted position.

Although many studies have indicated a visuospatial deficit in patients with PD, these findings have been recently challenged by a number of investigators. For example, Ransmayr, Schmidhuber, Karamat, Eigler-Plorer, Poewe, and Leidlmair (1987) gave subjects a task involving line drawings of cubes with three faces showing. On each face was a different geometric design. The subjects were asked to match this cube with one of five others, the correct solution being a rotated version of the same cube. They found no impairment in the PDs' performance, as would be expected if patients with Parkinsonism had problems in processing visuospatial information. The authors state that the important feature here was not that the task was visuospatial, but that the subject had the opportunity to choose the correct answers from a number of alternatives. When a response must be self-generated, impairment is more likely to occur.

Other researchers have begun to question whether the deficits that have been found in PD are purely visuospatial,

or whether they are more indicative of problems in the ability to shift set mentally. Raskin et al. (1992) compared 20 PD patients to 20 NCs on a series of neuropsychological measures assessing visuospatial functioning and set-shifting abilities. The set-shifting tasks were designed to minimize visual-spatial demands, and the visuospatial tasks were designed to minimize any possible set-shifting components. They found a significant difference between the NCs and the PDs on tests assessing set-shifting abilities, but no differences on tests assessing visuospatial functions. In a si%wlar vein, several studies have found deficits in Parkinsonian patients on various subcategories of the Wisconsin Card Sorting Test, a test often given to assess mental flexibility and frontal lobe functioning (e.g., Flowers & Robertson, 1985; Lees & Smith, 1983).

Memory. A second area of impaired neuropsychological functioning that has been found in PD is memory. Specifically, when deficits are found in Parkinsonian patients, impairments tend to be seen on tests of recall but not on tests of recognition. Most studies also indicate that when fairly simple non-effortful recall tasks are

given, no impairment is seen. Tweedy, Langer, and McDowell (1982) administered several memory tests to PDs, right-hemisphere stroke patients, and normal controls. They found that PDs performed significantly worse than the stroke group and the NCs on a memory task that contained an interference-filled delay period. Weingartner, Burns, Diebel, and LeWitt (1984) demonstrated memory deficits in a small sample of patients tested in the early stages of Parkinson's disease. They found no impairment on "automatic" memory processes (like word fluency), but PDs showed deficits compared to NCs in learning a list of 12 unrelated words. Weingartner et al. concluded that memory deficits are present in Parkinson's disease but only with more complex or difficult tasks.

Some researchers suggest that, in contrast to recall and learning tests, recognition is a "passive" memory situation (Flowers, Pearce, & Pearce, 1984). They assert that, in recognition tasks, the subjects must simply pick between fixed alternatives provided for them by the experimenters. There are no demands to either manipulate or mentally scan the materials. Retrieval deficits exhibited by PDs then can be seen as occurring in tasks that require

active participation and manipulation of stimuli by the subjects. This concept of "active" vs. "passive" processing (referred to by others as "internal vs. external locus of control") is not unique to memory tasks and can be applied to many tasks assessing different neuropsychological processes.

Language. Language functioning in PD is usually reported to be "intact". However, there have been a few studies citing some evidence for language dysfunction in Parkinson's disease patients. It is important to define and specify what type of language deficit one is referring to here. Language abilities associated with the musculature that controls the motoric components of speech are often affected in PD, resulting in less audible output and sometimes in inappropriate periods of silence (Darley, Brown, & Swenson, 1975). Language deficits involving the musculature of the mouth and tongue area (e.g., dysarthria) are fundamentally different from deficits involving language comprehension and processing (e.g., the various aphasias). Most studies investigating the latter aspect of language dysfunction have not shown prominent deficits. One study that did find language deficits (Matison, Mayeaux, Rosen, &

Fahn, 1982) found that PDs performed significantly worse than NCs on the Boston Naming Test, as well as on a word fluency task (which required that subjects generate as many words as possible belonging to a specific semantic category in a set amount of time [i.e., 60 seconds]).

Frontal lobe/Executive functioning. A fourth area of impairment that has been found in PD involves executive functioning or what is sometimes referred to as "frontal lobe syndrome". Actually, frontal lobe syndrome encompasses many functions. In neuropsychology, specific, discernible deficits are usually described in behavioral terms (Brown & Marsden, 1990). That is, when neuropsychological deficits are described, they usually center on one functional category, like the three previously described deficits found in Parkinson's disease (visuospatial, memory, and language). In frontal lobe syndrome, a group of behaviors are categorized according to a specific anatomical region of the brain--the frontal lobes. The frontal lobes are thought to be the least lateralized of the brain's lobes and, as of yet, have resisted the specificity of function found in other areas of the brain (Brodal, 1981). Nauta (1971) states that the frontal lobes have "remained the most

mystifying of the major subdivisions of the cerebral cortex". In their review of neuropsychological deficits in PD, Brown and Marsden (1990) reviewed more than 80 articles that have demonstrated the overlap between cognitive deficits seen following damage to the frontal lobes and in at least some patients with PD. They note impaired performance in both groups on the following tasks: mental rotation, personal orientation, trail-making, the Stroop, delayed response, the Wisconsin Card Sorting Test (WCST), problem-solving, verbal fluency, judgment of visual-vertical under conditions of body tilt, recency discrimination, anomia (tip-of-the-tongue phenomenon), and decreased control of Necker cube alterations.

Brown and Marsden (1990) propose that an area of dysfunction that seems to typify PD and can apply to various specific neuropsychological categories can be addressed under an "internal versus external locus of control of attention" category. This is similar, in theory, to the previously discussed concept of "active" versus "passive" processing. Brown and Marsden initially proposed a deficit in the ability of PD patients to switch set when they had to rely on internal as opposed to external cues. Brown and

Marsden generalized this concept to areas other than set-shifting, asserting that PDs were impaired on cognitive functioning which calls on more internal than external locus of control.

Bradyphrenia. Another area of dysfunction that may typify PD is seen in what has been described as "bradyphrenia". This refers to the slowing down of thought and action. There is a decrease in the ability to attend and focus, a diminution in spontaneous interest and initiative, a decline in the ability to work, slight decreases in memory, and reports of decreases in energy, and tendencies to fatigue easily. This is akin to the controversial concept of subcortical dementia. The incidence of general dementia and the issue of subcortical dementia in Parkinson's disease will be addressed shortly.

Depression. A commonly reported phenomenon in PD is that of depression. Estimates of depression in PD vary greatly, with figures ranging from 15% to 50% (Dakof & Mendelsohn, 1986). In a recent review, Cummings (1992) surveyed the literature on depression in PD and devised a neurobiological model relating structural and biochemical changes to the behavioral manifestations exhibited in

Parkinson's disease. He states that approximately 40% of PDs show depression. He also lists risk factors, including lower cerebral spinal fluid (CSF) levels of 5-hydroxyindoleacetic acid (5-HIAA), a past history of depression, and increased levels of functional disabilities (e.g., lowered levels of performance at work or disturbances in social and personal relationships). Other possible risk factors include being female, early age of onset of PD, and greater left- than right-hemisphere involvement. In terms of specific criteria for depression, Cummings states that approximately one half of the PDs who show depression fit the DSM-III-R criteria for major depression, while the other half would meet the criteria for dysthymia. Depression in PD and HPD will be addressed more thoroughly in a later section.

Dementia. The last area of dysfunction often reported in PD is that of dementia. The term "dementia", like that of frontal lobe syndrome, encompasses not one but many aspects of behavior and neuropsychological performance. Dementia can be defined as an acquired persistent impairment of intellectual functioning, with compromise in at least three of the following spheres of mental activity:

language, memory, visuospatial skills, emotion and personality, or cognition (e.g., abstraction, calculation, judgment) (Cummings, Benson, & LoVerne, 1980). Like depression, the incidence of dementia in PD varies greatly from study to study. Mayeux, Denaro, Hemenegildo, & Marder (1992) investigated the prevalence of dementia in PD patients in the borough of Manhattan in New York City. They developed a registry of PD by placing announcements in local newspapers in Manhattan for over a two-year period. Of the patients identified as having idiopathic (unknown or unspecified etiology) PD, over 40% had dementia. Benson, (1984) reviewed various studies investigating the presence of dementia in PD and found rates to range from 20% to 93%. To account for these differences, he maintains that certain factors should be accounted for, including age of the patient, (the older the patient, the greater chance of seeing cognitive impairment), as well as the criteria used for assessing dementia. This study screened for the presence of dementia using the Mini Mental State exam (MMS). There is some research indicating that the kind of dementia found in PD and other diseases typified as subcortical (such as Huntington's chorea) may be different than the disease

states typified as more cortical (such as Alzheimer's disease). This concept of subcortical dementia (reviewed earlier) is controversial. Some researchers assert that it is misleading, lacks clinical validation, and has a questionable pathological basis.

In one study, over 100 patients with Alzheimer's, Parkinson's, or Huntington's disease (with each group subdivided into three functional disability stages) were administered a brief neuropsychological battery (Mayeaux, Stern, Rosen, & Benson, 1983). They found that Parkinson's and Huntington's disease patients were less intellectually impaired than Alzheimer's patients at each functional stage. Using the criteria for dementia obtained from the Diagnostic and Statistical Manual of Mental Disorders (DSM-111) (American Psychiatric Association, 1980), Mayeaux et al. found dementia present in all of the Alzheimer's patients, but in only half of the Huntington's and Parkinson's disease patients. Depression, however, was absent in the Alzheimer's group, but present in the Huntington's and Parkinson's disease groups, and was correlated with intellectual decline in both the Huntington's and Parkinson's disease groups. Although

research investigating the validity of two distinct profiles of dementia (cortical and subcortical) has not been conclusive, there is a possibility that the dementia seen in PD patients may be of a different type than that seen in other cortical diseases. The screening test that was administered in this study (the MMS) was designed to assess dementia as it is defined in the DSM-III-R. Although it is theoretically interesting, it was beyond the scope of this study to test for the possible presence of cortical versus subcortical dementia.

Hemiparkinson's Disease

Parkinson's disease is a complex of symptoms which is characterized by rigidity, tremor, and bradykinesia. A relatively recent observation is that of PD patients exhibiting unilateral symptoms, from which emerged a new classification scheme (Blonder, Gur, Gur, Saykin, & Hurtig, 1989: Trabucchi, Albizzati, Frattola, & Scarlato, 1979). Some PD patients can be divided into subgroups based upon a right or left "hemiparkinson's" pattern. In some PD patients, symptoms are basically limited to one side of the body. This is thought to be the unilateral expression of Parkinson's disease (Chouza et al., 1984). Right

hemiparkinson's disease (RPD), then, refers to the typical motor dysfunctions being seen more on the right than the left side of the patient's body, presumably reflecting left basal ganglia pathology (or at least more left than right basal ganglia dysfunction). Conversely, left hemiparkinson's disease (LPD) denotes left-sided motor dysfunction reflecting a right-sided subcortical deficit.

Research in cognitive and affective processing among HPD subjects is relatively sparse. Unfortunately, of the studies that have been conducted, there have been contradictory and inconsistent findings. This could be due, in part, to some methodological issues that are inherently problematic to the investigation of hemiparkinson's disease. These methodological issues will be reviewed in a later part of this section.

Before discussing the literature investigating Hemiparkinson's disease, the occurrence of HPD itself should be addressed. Hemiparkinson's disease is not seen in every PD patient. When it is seen, it is almost always an initial, transient stage that develops into full-blown PD with bilateral symptoms (Chouza et al., 1984). The presence of HPD can last from a few months to several years. In the

present study, the duration of HPD was based upon the first time the subject recalled his/her first symptom of PD up until the time of the administration of our neuropsychological battery. It was observed in the literature that when other studies provided information on the duration of HPD, it was not reported whether the starting point was considered to be the first time the patient remembered their first PD symptom or if it was considered to be the first time the diagnosis of PD was made. Other than the original study of Hoehn and Yahr (1967), statistics are not available regarding the average duration of unilateral symptoms. This is probably due to the relative lack of research in this area, as well as varying operational definitions as to what are considered to be acceptable criteria in defining HPD. Table 1 illustrates the stage and duration of illness in PD in the Hoehn and Yahr study.

Hemiparkinson's disease can range from purely unilateral, indicated by a Hoehn-Yahr scale rating of "I" (Hoehn and Yahr, 1967), to a state where there is bilateral involvement, but with one side more affected than the other (indicated by a Hoehn-Yahr scale rating of II or III).

Table 2 lists the five stages of the Hoehn-Yahr scale, with a description of the criteria for each stage.

In the literature investigating HPD, only two studies (Hietenan and Teravainen, 1989; Huber, Freidenberg, Shuttleworth, Paulson, & Clapp, 1989) used exclusively stage I patients. This is most probably because of the large difficulty in obtaining HPD patients (hemiparkinsonism can be detected in Hoehn-Yahr stages I, II, and III), let alone obtaining HPD patients only in stage I.

All other studies, including the present study, used patients in stages I, II, and/or II of the Hoehn-Yahr scale. By definition, stage I is totally unilateral. Stage II indicates predominant but not exclusive unilateral symptomatology. Stage III indicates more severe motoric dysfunction, but also allows for the presence of some unilateral symptoms.

By definition, HPD is usually thought to represent the incipient stages of the disease. Logically, since this is the expression of the disease at its onset, symptoms tend to be less severe than when the disease has developed into its more serious and disruptive stages. Not all patients with Parkinson's disease show cognitive deficits. Any cognitive

changes associated with hemiparkinson's disease might be expected to be more subtle, since the disease is still in its earliest stages. The question of whether neuropsychological changes in the early part of PD do not yet exist or whether our neuropsychological instruments are simply not sensitive enough to detect them is an issue worth bearing in mind.

Neuropsychological Deficits in Hemiparkinson's Disease

Some studies indicate that bilateral or left HPDs (i.e., more right than left-hemisphere pathology) tend to do more poorly on various cognitive tasks than do right HPDs (Bowen, Hoehn, & Yahr, 1972; Direnfeld, et al., 1984; Fleminger, 1991; Hietanen & Teravainen, 1989; Villardita , Smirni, & Zappala, 1983). Direnfeld et al. (1984) examined 10 patients with Senile dementia of the Alzheimer's type (SDAT), 10 PDs (five characterized as LPD, four as RPD, and one bilateral), and 12 NCs on a variety of neuropsychological functions, including memory, visuospatial processing, language, and mental control. They derived an overall dementia score by combining the scores from these four domains. A mini-mental status exam was also given to assess dementia, and a Beck Depression Inventory was given

as a measure of depression. The patients with LPD scored worse than NCs on tests of memory and visuospatial functioning, and had lower overall dementia scores. RPDs scored lower than NCs only in visuospatial functions. Looking at LPDs versus RPDs, LPDs had an overall dementia score that tended to be lower ($p < .10$) than the one for RPDs. They also point out that, although LPDs and RPDs did not significantly differ in any of the domains tested, LPDs scored consistently lower than RPDs.

Villardita et al. (1983) compared 31 PDs (14 bilateral, 7 right, 10 left) on a visual cancellation test. Here, a line-crossing-out test was given. It consisted of 94 lines approximately two centimeters long, drawn in different directions. The task was to bisect each line, and four lines (on the top and bottom left- and right-hand corners) were marked by the examiner as examples. Scores were derived by looking at omissions of left, center, and right quadrants of the entire stimulus array. They found visual neglect only in the bilateral and LPD groups but not in the RPD group. Villardita et al. use these findings to support the hypothesis of subcortical structures in

attentional mechanisms as being mediated by the right hemisphere.

Fleminger (1991) looked at depression and anxiety in 30 HPDs (17 right, 13 left), using both a self-rating scale and a semistructured interview. LPDs exhibited more symptoms of depression and anxiety than did RPDs. Hietanen and Teravainen (1989) compared seven untreated LPDs with five untreated RPDs in the following domains: cognition (Similarities, Picture Completion, and Block Design WAIS-R subtests); cognitive flexibility (Part B of the Trail-Making Test, and parts 2 and 3 of the Stroop); memory (Wechsler Memory Scale subtests of Digit Span, Logical Memory, Associative Learning, and Visual Reproduction); depression (Beck Depression Index), and psychomotor functioning (four various reaction time tasks). LPDs performed less well on the WAIS-R Picture Completion subtest and the Stroop test (parts 3, and part 3 minus part 2) than did the RPDs. Like Villardita et al. (1983), Hietanen and Teravainen interpreted the results as supporting the hypothesis that right hemisphere dopaminergic structures may be important in mediating attentional processes.

Only one study showed RPDs performing at lower levels than LPDs (Spicer, Roberts, & LeWitt, 1988). Here, seven RPDs and eight LPDs were tested on dominant and nondominant hemispheric functions. Dominant hemisphere assessment was tested by serial digit learning, confrontation naming, and verbal associative fluency tasks. Nondominant hemisphere assessment was tested using form sequence learning, line orientation, and facial recognition tasks. The results indicated that patients with signs lateralized to the right side of the body were impaired on all three of the "dominant hemisphere" tests compared to patients with signs lateralized to the left. It is interesting to note that, even though this study had a relatively small sample size, two of the tests were significant at the .05 level, and one test (serial digit learning) was significant at the .01 level. (It should be noted that they utilized a one-tailed and not a two-tailed test.) None of the "nondominant hemisphere" tests were significant.

The rest of the studies reviewed failed to find any differences between RPDs and LPDs on neuropsychological measures or found differences consistent with lateralization of function (i.e., RPDs impaired on left hemisphere tasks,

and LPDs impaired on right hemisphere tasks) (Agniel., 1991; Blonder, et al., 1989; Chouza et al., 1984; Huber, et al., 1989; Riklan, Stellar, & Reynolds, 1990; Starkstein, Seiguarda, Gershanik, & Berthier, 1987).

In what is probably one of the best methodologically designed, executed, and comprehensive studies of neuropsychological functioning in hemiparkinsonism, Blonder et al. (1989) administered a standardized neuropsychological battery to 21 HPDs (14 right, 7 left) and 17 NCs. Their battery was divided into the following sections: (a) Intellectual-Cognitive (Verbal -- WAIS-R Information and Vocabulary subtests; Spatial -- WAIS-R Block Design subtest and Judgment of Line Orientation); (b) Memory (Wechsler Memory Scale); (c) Attention-Concentration (WAIS-R Digit Span subtest and Wechsler Memory Scale Mental Control subtest); (d) Language (Comprehension of Complex Ideational Material and Animal Naming subtest from the Boston Diagnostic Aphasia Examination (BDAE) and the Boston Naming Test); and (e) Sensorimotor (Fingertip Number Writing and Finger Tapping Test). While the authors found that both patient groups performed less well on almost all of the tests when compared to NCs, only two tests yielded

differences between LPDs and RPDs: Animal Naming (more impairment in RPDs) and the Wisconsin Card Sorting Test (WCST) # correct (more impairment in LPDs). Starkstein et al. (1987) gave nine LPDs and nine RPDs a neuropsychological battery tapping frontal, temporal, and parietal lobe functions. They found slight (but significant) differences between groups, with RPDs performing worse than LPDs on the Verbal subtests of the WAIS-R and LPDs performing worse than RPDs on a line bisection task. Although some consider line bisection to be a right hemisphere task, this study had only one "pure" right hemisphere task in its neuropsychological battery, the Benton Visual Retention Task.

One of the first studies to look at neuropsychological functions in HPD was conducted by Chouza et al. (1984) in the mid-1980s. They assessed 13 right and 11 left hemiparkinson's patients, none of whom were receiving L-DOPA. Various measures were used with this group of patients, including a neuropsychological battery and a series of computerized tomography studies (CT-Scans). The neuropsychological battery consisted of what some might view as "nonconventional" tests. For intelligence, Piaget's Genetic Tests of Physical Amounts and Combinatories were

used. Also in this category was the Similarity Trial from the Wechsler-Bellevue Test, given here to assess abstraction capacity. The second category included tests assessing verbal, visually supported verbal, and visuospatial memories. For verbal memory, the "Test auf Phrases" and the Barbizet story were used. Visually-supported verbal memory was assessed with the 20-object series of Barbizet. Visuospatial memory was assessed using the "Constructional Praxia Model". Language was examined by the Benton-Spreen Battery (adapted to Spanish). Various apraxias were also analyzed. One of Chouza et al.'s stated goals was to try to find a neuropsychological profile of left and right hemiparkinsonism. They found that in RPD, as compared to LPD, apraxia was more prevalent and that there was a tendency for lower "intelligence values" (specifically on the Piagets Tests of Physical Amounts). LPDs were found to have more memory impairment, especially involving the visuospatial domain. They concluded that in RPD, features were similar to bilateral Parkinsonism, while in LPD, dysfunction was consistent with right brain damage.

A few studies have looked at hemiparkinsonism and found no differences between left and right patient populations.

These studies will be described briefly here with the caveat that, in general, most scientific journals tend not to report "negative" findings (i.e., studies where statistical significance is not found), so the number of studies conducted that have found no differences may actually be underreported.

Agniel et al. (1991) looked at cognitive functioning and cerebral blood flow in 23 lateralized Parkinson's disease patients. They failed to find a correlation between laterality of motor symptoms and cognitive hemisphere-asymmetry scores or cerebral blood flow scores. Only one neuropsychological test, the WAIS Object Assembly Subtest, differentiated LPDs and RPDs. There were no significant differences between hemispheres for LPDs and RPDs in either cortical or subcortical CBF scores.

Huber et al. (1989) looked at 23 PDs with exclusively unilateral symptoms (stage I of the Hoehn-Yahr Rating Scale) Thirteen of these PDs had symptoms exclusively on the right, and 10 had symptoms exclusively on the left. The authors assessed visuospatial skills, mood, memory, cognition, language, and word- list generation. Only two of the tests, the attention/calculation component of the Mini Mental Exam

and the Digit Span subtest, differentiated the two groups. They concluded that no real neuropsychological differences between early hemiparkinson's disease groups were evident. They then did a second experiment with PDs in stages II to IV of the Hoehn-Yahr Scale, that is, those patients showing relative, but not exclusive, asymmetries of motor dysfunction. Neuropsychological deficits were found in both groups but were not related systematically to side of symptoms. Their final conclusion was that, with advancement of PD, overall cognitive impairment increases, but neuropsychological deficits are not different with respect to laterality of symptoms.

Riklan et al. (1990) came up with the same conclusion of neuropsychological deficits being indicative of disease severity but not of side of symptom in PD. They assessed memory functions (using a modified Randt memory test) and cognition (using seven verbal and non-verbal subtests of the WAIS-R). The left (N=15) and right (N=10) HPD groups did not differ on a host of demographic items (e.g., age at onset, education) but did differ significantly in bradykinesia and functional impairment, with RPDs being more impaired in both of these categories. They then performed

concurrent analyses of variance and covariance, the latter to take into account the observed differences in bradykinesia and functional disability. Before adjusting for symptom severity, RPDs were impaired on five of the 12 tests of memory and cognition. After adjusting for symptom severity, no differences were found. They conclude that the severity of the disease, especially bradykinesia and functional disability, play a more significant role in the behavioral deficits seen in hemiparkinson's disease than left or right subcortical involvement, indicated by the side of motor impairment.

Affective Processing in PD and HPD

In addition to cognitive functions, affect has also been investigated in PD. The area of affective processing in PD and HPD can be divided into two major categories: (a) depression, and (b) emotional perception and production. Depression refers to the actual psychopathology that the PD patient experiences or manifests (i.e., actual DSM-111-R mood disorders). Emotional perception and production refer to PDs' ability to either output behaviors appropriate to specific emotions (e.g., happiness, fear, and surprise) or

their ability to accurately perceive various emotions. Each will be discussed separately in a later section.

There are various theories that have tried to explain where and how in the central nervous system emotion and affect are processed (e.g., Borod, 1992). Two leading hypotheses that have evolved regarding the lateralization of emotion are (a) the valence hypothesis, and (b) the right-hemisphere hypothesis. The valence theory asserts that the right hemisphere mediates negative emotions, while positive emotions are mediated by the left hemisphere (Ahern & Schwartz, 1979; Davidson, 1984). The right-hemisphere hypothesis states that the right hemisphere is dominant in the processing of both positive and negative emotions, and applies to both expression and perception (Borod & Koff, 1984; Campbell, 1983; Strauss & Moscovitch, 1981; Suberi & McKeever, 1977). Many studies have used brain-damaged populations to study the issue of lateralization for emotion (e.g., Borod, Andelman, Obler, Tweedy, & Welkowitz, 1992; Borod, et al., 1990).

Depression in PD and HPD

Cummings (1992) conducted an extensive review of the literature in depression (as measured by various depression

inventories such as the Beck or Zung scales) and PD, concluding that depression occurs in approximately 40% of PD patients, with numbers ranging from a low of 4% to a high of 70%. Risk factors include early age of onset, female gender, and greater left brain involvement. Depression in PD was distinguished from other depressive disorders by greater anxiety and less self-punitive ideation. Most investigators report that the profile of depressive symptoms found in PD patients is not exactly the same as that found in other populations where depression is seen. As previously noted, greater anxiety and less self-reproach were found in PD patients with depression. Other distinguishing features include a much lower incidence of delusions and hallucinations and a low suicide rate, even though there does seem to be a high rate of suicidal ideation. It is suggested that in PD there may be a subtly different form of depression than that of idiopathic mood disorders (and therefore a disease-specific depressive syndrome with distinct symptoms). Relationships between depression and motor/cognitive dysfunction have been investigated, with most studies reporting no correlation between depression and the various types of motor signs

(rigidity, bradykinesia, and tremor) seen in PD (e.g., Ehman, Beninger, Gawel, & Riopelle, 1990; Mayeaux et al., 1984). Disease severity has usually yielded more consistent findings in those PD patients showing significant levels of depression, with at least moderate correlations between levels of depression and the amount of functional impairment (Robinson & Price, 1982). Last, the occurrence of depression during the "on and off" phenomenon has been investigated. "On and off" refers to the fluctuations of motor symptoms that occur with the administration of L-Dopa drug therapy. "On" refers to an agitated or normal kinetic state, whereas "off" refers to decreases in kinetic states. In general, investigations suggest that in patients experiencing this "on-off" phenomenon, mood changes are not uncommon, with depression being reported more in the "off" condition.

Depression in HPD has received less attention than depression in PD, due mostly to the fact that HPD itself has been much less studied. However, some studies investigating lateralized PD have given a depression inventory, most often the Beck or the Zung, and found virtually equal levels of depression between RPDs and LPDs (Blonder et al., 1989;

Huber et al., 1989). When differences are found, data tend to support an association between RPD and higher levels of depression. For example, Direnfeld et al. (1984) administered the Beck Depression Inventory and found RPDs to score higher than LPDs, although it was not a statistically significant difference. Starkstein, Mayberg, Seiguarda, Preziosi, & Robinson, (1992) found a trend for higher depression scores in PDs with symptoms lateralized to the right, and Heitenan and Teravainen (1989) also found a tendency for RPDs to have slightly higher Beck scores (i.e., more depressive symptoms) than LPDs. Although these studies all show depression to be more associated with RPD, it should be kept in mind that none of these findings were statistically significant. One study was found indicating a trend for LPDs to have higher (Beck) depression scores than RPDs (Spicer, 1988).

Only one study was found that looked specifically at depression in HPD (Fleminger, 1991). Seventeen right and 13 left hemiparkinson's disease patients were tested. They conducted semi-structured interviews and administered self-rating scales for depression and anxiety. Their results are difficult to interpret, however, as they are contrary to

those from other studies investigating depression indicating more left brain involvement in HPD (with the single exception of the Spicer et al. study that reported a trend for LPDs to exhibit more depression than RPDs). Results from the Fleminger study indicate that LPDs have significantly higher levels of depression and anxiety than do RPDs. However, most other studies that have measured depression in left and right HPD have found no significant differences between these groups. When trends were found, they usually indicated higher levels of depression in right rather than left hemiparkinson's disease.

To summarize, two studies indicate more depression in LPDs than in RPDs. The first study to suggest this was Fleminger (1991), in which LPDs showed significantly higher levels of depression (as well as anxiety) when compared to RPDs. The second study that suggests more depression in LPDs as compared to RPDs was conducted by Spicer et al. (1988). In this study, trends, but not significant differences, were found indicating higher levels of depression in LPDs when compared to RPDs. Other studies that have looked at depression in Hemiparkinsonism show trends indicating that RPDs show higher levels of depression

than LPDs (e.g., Cummings, 1992; Direnfeld et al., 1984; Hietanen and Teravainen, 1989; Starkstein et al., 1987). It should be noted here, however, that studies supporting higher levels of depression in RPD as compared to LPD all show trends, not significant differences, between these two groups.

Significance

This study was designed to investigate cognitive and affective processing in Hemiparkinson's disease patients. The results from this study can be applied to various areas of research. Cognitive and emotional deficits in PD are important to understand in any clinical treatment program. Studying these potential deficits in the incipient stages of this disease could be applied to early behavioral management techniques. Secondly, one can examine laterality issues, particularly the contribution of subcortical substrates to cognitive and affective processes. Finally, information from this study could provide added insight and understanding into the development and progression of Parkinson's disease.

Hypotheses

Based on the literature reviewed above, the following hypotheses were asserted:

1) Right hemiparkinson's disease patients (RPDs) will exhibit more deficits than left hemiparkinson's disease patients (LPDs) and normal controls (NCs) on tasks assessing left hemisphere functioning (e.g., language processing).

2) LPDs will exhibit more deficits than RPDs and NCs on tasks assessing right hemisphere functioning (e.g., visuospatial and affective processing).

3) LPDs will exhibit more depressive symptoms than RPDs.

4) Early PDs (i.e., LPDs and RPDs taken together as an "early parkinsonian" group) will exhibit deficits in neuropsychological functioning when compared to NCs. These deficits include impairments in memory, visuospatial, and frontal lobe functioning.

Method

Subjects

The 23 PD patients tested for this study were recruited from Columbia Presbyterian Hospital (CPH) in Manhattan. The first step involved reading through medical charts at the Movement Disorder Clinic at CPH. From here, each patient with a diagnosis of Parkinson's disease was identified, and their latest Hoehn-Yahr scale score (from I to V) was recorded. If the Hoehn-Yahr scale score was III or below, side of asymmetry was recorded, and histories were then examined to screen for inclusion and exclusion criteria. The criteria required for participation in this study included the following:

a) English as a native language

b) No second language acquired before the age of 10

c) Right-handedness (as defined by self-report)

d) No history of psychiatric illness

e) No history of excessive recreational drug use

f) No history or current use of psychotropic medications

g) No history of neurological disorders other than PD (e.g., stroke, closed head injury resulting in loss of consciousness)

f) No one under 50 or over 85 years of age

g) For the PDs, a Hoehn-Yahr scale score of III or below

Approximately 80 patients were eligible for participation in this study after these criteria were screened for. Hoehn-Yahr scales were then examined, and along with reports from attending physicians, two lists were formed. List A (N=65) included "first choice" subjects most of whom had Hoehn-Yahr scale scores of I or II, indicating very clear cut presence of HPD, and with symptoms being either totally or extremely unilateral. List B (N=25) included "second choice" subjects, most of whom had Hoehn-Yahr scale scores of II or III, still indicating the presence of HPD, and with symptoms being exhibited more on one side of the body than the other, but not as clearly unilaterally expressed as for subjects on list A. Both lists were comprised of subjects who met the criteria of HPD, and no one with a Hoehn-Yahr scale over III+ was

considered for this study. (Of the 23 HPD patients actually tested in this study, 20 were from list A and 3 were from list B).

From these lists, 12 LPDs and 13 RPDs agreed to participate in the study. Of these subjects, one RPD discontinued testing before completion of the battery, and one RPD was not tested after failing to score a minimum of 23 (indicating the presence of dementia) on the Mini-Mental State exam. This left a final patient pool of 12 LPDs and 11 RPDs. All patients were receiving Cinemet (L-Dopa) at the time of testing. While patient use of certain medications was acceptable in this study (e.g., high blood-pressure medication), no subject was taking anti-cholinergics or anti-depressants.

In the LPD group, 7 were male and 5 were female. In the RPD group, 5 were male and 6 were female. The mean age for the RPD group was 66.6 years (s.d. 8.5), mean level of education was 15.1 years (s.d. 1.8), and the mean for the duration of symptoms was 3.6 years (s.d. 2.1.). The mean age for the LPD group was 72.5 years (s.d. 10.2), mean level of education was 15.9 years (s.d. 3.4), and the mean for the duration of symptoms was 3.7 (s.d. 2.1). (In this study,

duration was defined as the time the subject first noticed the presence of their first PD symptom up until the patient was administered the neuropsychological battery.) The mean of the Hoehn-Yahr scale scores for the RPDs was 2.0, s.d. 0.0, and for the LPDs the mean was 2.4, s.d. 0.5.

Normal control (NC) subjects were also recruited for this project. These NCs were obtained through a list of available NCs who had indicated they would be interested in participating in research projects being conducted at Columbia Presbyterian Hospital. They were matched with the PD groups for age, education, and gender. The same exclusion criteria were applied for the NCs as for the PD groups. A total of 12 NCs were tested. (One subject was dropped from the NC group because of consistently low performance and extremely slow response times throughout the administration of the battery.) The final NC group consisted of 6 male and 5 female right-handed subjects. The mean age of the NC group was 66.6, s.d. 10.8, and the mean years of education was 13.6, s.d. 2.4.

All three groups (RPD, LPD, and NC) were right-handed by self report. Here, although a formal handedness inventory was not administered, in order to assure that the

subject was truly right-handed, during the pretest interview the subjects were asked if they now or ever had used their left hand or foot for any activity such as writing, eating, throwing, or kicking. The PD patients' handedness was also confirmed by physician's reports of handedness as listed in their medical chart. One subject was not tested upon the discovery that she was left-handed.

The number of subjects selected was initially set at a minimum of 10 per group. This was based partly on other studies investigating HPD, as well as practical considerations, notably the great difficulty in locating and recruiting eligible Parkinson's disease patients. All Parkinson's disease patients participation was on a voluntary basis. Normal control subjects received twenty dollars for participation in this study.

Materials

Sixteen neuropsychological tests were administered to each subject. A list of the tests and whether they assess left, right, or frontal lobe functioning are presented below.

Right Hemisphere Tests (8 tests, 17 separate measures)

1. Wechsler Adult Intelligence Scale-Revised (WAIS-R) (Wechsler, 1981)
    a.) Picture Completion Subtest
2. Visual Cancellation Test (Hamsher, 1976)
    a.) 1 (left side of page)
    b.) 2 (middle of page)
    c.) 3 (right side of page)
3. Wechsler Memory Scale-Revised (WMS-R) (Wechsler, 1987)
    a.) Visual Reproduction Subtest
        1.) Immediate recall
        2.) 30-minute delayed recall
4. Stroop Test (45-second protocol) (Stroop, 1935)
    a.) Word Section
    b.) Color Section
    c.) Word-Color Section
5. Facial Emotional Identification Task (Borod, Martin, Alpert, Brozgold, & Welkowitz, 1993)
6. Emotional and Nonemotional Word Identification Task (Borod, Andelman, Obler, Tweedy & Welkowitz, 1992)

7. Benton Visual Form Discrimination (Benton, Hamsher, Varney, & Spreen, 1978, 1983)
8. Odd Man Out Test (Flowers & Robertson, 1985)
   a.) Trial 1
   b.) Trial 2
   c.) Trial 3
   d.) Trial 4
   e.) Trials 1-4

Left Hemisphere Tests (8 tests, 20 separate measures)

1. WAIS-R Vocabulary Subtest (Wechsler, 1981)
2. WAIS-R Digit Span Subtest (Wechsler, 1981)
   a.) Digits Forwards
   b.) Digits Backwards
3. Boston Diagnostic Aphasia Examination (BDAE) (Goodglass & Kaplan, 1983)
   a.) Animal Naming Subtest
4. Auditory Verbal Learning Test (RAVLT) (Rey, 1964)
   a.) Trial 1
   b) Trial 2
   c.) Trial 3
   d.) Trial 4
   e.) Trial 5

f.) Trial 6 (Interference trial)

g.) Immediate Recall

h.) 30-Minute Delayed Recall

i.) Total Recall (Trials 1-5)

5. Controlled Oral Word Association Test (Benton & Hamsher, 1976)

a.) "F" (one minute)

b.) "C" (one minute)

c.) "L" (one minute)

d.) "F, C, L" (Total)

6. Alternating "A-S" (Benton, 1974)

7. Nonemotional Word Identification Task (Borod et al., 1992)

8. Self-Rating Depression Scale (SDS) (Zung, 1965, 1967)

A major review of the literature in HPD was conducted in order to select the appropriate tests used in this study. In most cases, those tests that were found to significantly differentiate between LPDs and RPDs were used to construct our neuropsychological battery. In addition, measures of

frontal lobe functioning were included based on research conducted by Raskin et al. (1992).

To assess affective functioning, we employed a standard measure of depression (Zung, 1965) and two measures of emotional perception associated with right-hemisphere functioning (Facial Emotional Identification Task [Borod et al., 1993], and the Word Emotional Identification Task [Borod et al., 1992]). A general test to screen for dementia, the Mini-Mental State (MMS) (Folstein, Folstein, & McHugh, 1975), was administered to all subjects before proceeding with formal testing on the neuropsychological battery. If a subject failed to score 22 or above on the MMS (Folstein et al., 1975), testing was discontinued. One RPD patient was not given the neuropsychological battery after failure to score above the cut off score of 22. Scores on the MMS ranged from 26 to 30 for the LPD group and from 27 to 30 for the RPD and NC groups.

Appendix A lists whether the tests were considered to assess left hemisphere, right hemisphere, or frontal functioning. Pertinent rationales for a given test being included in the battery are also provided. Two major rationales were kept in mind for inclusion in this study.

First, neuropsychological tests that were thought to assess laterality of function were selected. Second, tests that previous research had indicated could differentiate between LPDs and RPDs were included. The latter gives this study the advantage of checking for the reliability (i.e., replication of statistically significant results [$p<.05$] or trends [$p<.10$]) of previous research.

Appendix B lists each test and describes whether the task was designed to assess left hemisphere, right hemisphere, or frontal lobe functioning.

Procedures

Each subject was tested at Columbia Presbyterian Hospital (CPH) in Manhattan, with the exception of two subjects (HPDs) who were tested at home sites. Before testing, each subject was given a brief description of the testing procedures and informed that any questions pertaining to the tests could be addressed in a debriefing period following completion of the battery. A CPH approved signed-consent form was read and signed before testing (see Appendix C). A brief Mini-Mental Status exam (MMS) was administered to screen for dementia. If the subject scored 23 or above out of 30, the neuropsychology battery was then

administered. One subject (an RPD patient) was discontinued for failure to reach this minimum score. The tests comprising this battery can mostly be categorized as left- or right-hemisphere tasks, with the exception of three that are categorized as frontal tasks. In general, left- and right-hemisphere tasks were alternated during administration. All subjects received the full set of tests in the same order, with the exception of the Emotional and Nonemotional Word Identification Tasks, which were always administered at the same point in the battery but were randomized between themselves. Total testing time varied depending upon the subject, but averaged approximately two hours (testing time ranged from one-and-a-half hours to two hours and 45 minutes). Each subject was told before testing began that the session would take approximately 2 hours, and that if they felt fatigued or needed a break, to inform the examiner. Each subject (both NCs and HPDs) completed the test without requesting a break. All subjects were tested by the same examiner.

Demographic Variables

Table 3 lists each individual subject and their respective age, education, and gender, as well as the side

of HPD, the Hoehn-Yahr rating score, and the duration of illness for each RPD and LPD.

Because of the known influence of some factors on neuropsychological performance, an attempt was made to keep each of the three groups (LPD, RPD, and NC) balanced for gender, age, and years of education. (Actual matching of subjects between groups was not possible because of the difficulty of procuring eligible left and right hemiparkinson's patients that met all the requirements for this study). A one-way analysis of variance (ANOVA) was conducted on the subject group factor (3) for each variable. None of the results was statistically significant. Table 4 lists the data for these variables.

Only patients obtaining a score of either stage I or II on this scale (an indication of the degree of lateralization of motor disturbances---see Table 2) were used.

As briefly discussed before, this study also controlled for the presence of dementia. The first test given to each subject was a Mini-Mental State examination (Folstein et al., 1975), used here as a screening test. If a subject scored below a score of 22 out of 30 (based on norms [Folstein et al., 1975] indicating the presence of

dementia), he or she was excluded from this study. An ANOVA was conducted on the mean dementia rating scores for the LPDs (M=28.42), RPDs (M=28.46), and NCs (M=28.55). No significant group differences were found (F=0.026; d.f.= 2, 31; p=.974).

Results

This study was designed primarily to determine if there are differences between left and right hemiparkinson's disease patients in cognitive and affective processing abilities. Specifically, the main objective here was to determine if LPDs are more deficient than RPDs in processing information usually mediated by the right hemisphere, and conversely, if RPDs are more deficient than LPDs in processing information usually mediated by the left hemisphere. A second objective was to see if there were differences in the degree of depression between LPDs and RPDs. A third objective was to see if these two groups, taken together and then viewed as an "early PD" group would show general cognitive deficits compared to an NC group.

Analyses of Variance between RPD, LPD, and NC groups

In order to test our primary hypothesis concerning test performance differences between left and right HPDs, an initial analysis of variance (ANOVA) was conducted on subject group (LPDs, RPDs, NCs) for each of the 37 variables from the test battery administered. Table 5 provides the results of this analysis, as well as the mean scores for

each measure for each of the three subject groups. Among the 37 ANOVAs conducted, there were two significant ($p<.05$) findings (Rey Delay subtest, Zung Depression Inventory) and two trends ($p<.10$) (Facial Emotional Identification Task, and Rey Total subtest).

Next, on an exploratory basis, post-hoc t-tests were conducted, comparing LPDs to RPDs. Table 6 provides the results from this analysis.

Of the 20 separate measures of left-hemisphere functioning and the 17 separate measures of right-hemisphere functioning, no significant differences were found. Two measures had p-values indicative of a trend ($p<.10$): the Zung Depression Inventory ($p=.099$) and Facial Identification Task ($p=.096$). On the Zung Depression Inventory, RPDs ($M=51.82$) had higher depression scores (indicative of higher levels of depression) than LPDs ($M= 47.33$). On the Facial Identification Task, RPDs ($M=18.73$) had higher scores (indicative of less impaired functioning) than LPDs ($M=16.67$). The results from these analyses indicate that there were no significant differences between the left and right HPDs in their ability to perform on these measures of left-hemisphere or right-hemisphere functioning.

Analyses of Variance between early PD and NC groups

Our secondary hypothesis concerned the performance of early PD patients on our neuropsychological battery compared to that of NCs. Therefore, LPDs and RPDs were collapsed together to form one group (called "early PD"), which was then compared to the NC group. Table 7 provides the results of one-way ANOVAs comparing early PD and NC performance on each test.

When analyzing the data in this way, significant differences ($p<.05$) as well as trends ($p<.10$) were found. Although not the primary focus of this study, it was hypothesized that when comparing both left and right HPDs to NCs, deficits consistent with PD in general would be found (for specific deficits, see the Hypotheses Section in the Introduction).

As can be seen in Table 7, there were significant differences for parts Trial 2, Trial 3, Trial 4, the 30-minute delayed recall, and the total score of the Rey AVLT. One part of the Verbal Fluency Task (the letter "F") reached significance. The Zung Depression Inventory was significant at the .001 level. Visual Form Discrimination also reached significance. In all tests where significance

was reached, the early PD group was impaired compared to the NC group. All of these tests represent functioning that has been found to be impaired in some PD patients (i.e., memory, verbal fluency, visuospatial processing, and depression). Although not quite significant, four trends were also detected. In all cases but one (Facial Emotional Identification), PDs were impaired relative to NCs (Animal Naming, Rey AVLT Trial 5, and Rey AVLT Immediate Recall). Again, these tests reflect functions that have been found to be compromised in some PD populations.

Analyses of Covariance (ANCOVAs)

In order to take into account the possible effects of some of the demographic variables on test performance, a series of ANCOVAS were conducted for age, education, and depression. The ANCOVAS were conducted between LPDs, RPDs, and NCs, as well as between early PD (LPDs and RPDs together) and NCs. An analysis of covariance for the Zung Depression Scale was conducted using age and education (together) as the covariates. For all other measures, the ANCOVAs used age, education, and depression simultaneously as the covariates. Table 8 lists the results for the ANCOVAS conducted between the LPD and RPD groups, and again

between the early PD and NC groups. As can be seen, no significant differences or trends occurred between LPDs and RPDs, with one exception. An analysis of covariance for the Zung Depression Inventory, using age and education as covariates, showed a trend ($p<.10$) with RPDs showing higher levels of depression than LPDs. (When age was covaried without education, a significant difference in the same direction between LPDs and RPDs [$p=.05$] was found.) All other findings were nonsignificant. With few exceptions, an ANCOVA between early PD and NC groups yielded approximately the same results as did the ANOVAS (See table 8). That is, the tests indicating impaired performance by early PDs when compared to NCs were not significantly changed by covarying for age, education, and depression. Specifically, ANOVAs and ANCOVAs on the right hemisphere tasks both showed significant differences between early PDs and NCs for Visual Form Discrimination. Facial Identification, which showed a trend with an ANOVA, failed to show significance or a trend when an ANCOVA was performed ($p=.907$). ANOVAs and ANCOVAs on the left hemisphere tasks both showed significant differences between early PDs and NCs for immediate subtests of the Rey AVLT and the Zung Depression Inventory. The Rey

AVLT delayed recall subtest was significant (p=.010) with an ANOVA, but showed a trend with an ANCOVA (p=.061). On one measure of verbal fluency, word fluency with the letter "F", an ANOVA showed a significant difference between groups (p=.038), but failed to show either significance or a trend when an ANCOVA was performed (p=.156). On a second measure of verbal fluency, Animal Naming, an ANOVA yielded a trend (p=.057), but failed to reach significance when an ANCOVA was performed (p=.132).

Motor Scores and Laterality Index for LPDs and RPDs

In order to determine if there were differences between the severity of symptoms of the LPDs compared to the RPDs, motor scores were determined, and a laterality index (i.e., ratio score) was computed. Each Hoehn-Yahr Scale provides scores for both the left and right sides of the body in evaluating rigidity, bradykinesia, and tremor. Scores for the left-sided and right-sided symptoms of the RPDs were added together to derive a total symptom severity score (R + L). This was done separately for tremor, rigidity, and bradykinesia, and then together for a mean of all three measurements. This (R + L) score allowed a comparison of total symptom severity between the LPDs and RPDs. A ratio

score was then calculated by dividing the right minus the left symptom score (R - L) by the combined right and left symptom score (R + L). This procedure was then repeated for the LPDs. Table 9a and 9b list the motor scores and ratio scores for RPDs and LPDs, respectively. Table 10 presents the mean total and ratio scores for both subject groups.

T-tests were then conducted to determine if there were differences in the severity of motor symptoms between LPDs and RPDs for the rigidity, tremor, bradykinesia, and total severity scores. No analysis for any test reached significance ($p<.05$). Finally, to see if one group had symptoms that were more strongly lateralized than the other group, t-tests on the laterality scores were performed between the LPD and RPD groups. No significant differences were found. The results of these t-tests are shown in Table 10.

Discussion

In researching neuropsychological functioning in hemiparkinson's disease (HPD), the literature is relatively small and quite equivocal. The results of this study support the view that there are no differences in neuropsychological functioning between patients with PD on the left side of the body compared to patients with PD on the right side of the body. However, the results also tend to support the idea that when one collapses across left and right HPD, forming an "early PD" group, that some of the neuropsychological dysfunctions most commonly seen in advanced PD are already present.

Cognitive and Affective Functioning in Left vs. Right HPD

The primary purpose of this study was to investigate, elucidate, and clarify any neuropsychological differences that may exist between PD patients with symptoms primarily on the right side of the body compared to PDs with symptoms on the left side of the body. In the literature, the least rigid acceptable definition of most (but not all) researchers of what constitutes HPD is that there be a preponderance of motor symptoms on one side of the body

compared to the other. However, operational definitions of what constitutes HPD can vary greatly and may account for much of the seemingly contradictory findings in the study of hemiparkinson's disease. Some studies use the Columbia Rating Scale (CRS) (Duvoisin, 1979) to define HPD, while others use the Hoehn-Yahr Rating Scale. Even when comparing studies that use the same scale, one often finds different criteria for what is an acceptable score for inclusion in a given study. For example, Starkstein et al. (1987) used the CRS to assess prospective subjects for their study. Only PDs who had at least a 3 to 1 ratio of symptoms on one side of the body versus the other were included. Spicer et al. (1988) also used the CRS, but with a minimum criteria of a 2 to 1 ratio. Appendix B lists each study reviewed for this project and its criteria for diagnosing HPD.

When looking through the approximately 15 studies investigating neuropsychological functioning in HPD, about a third indicate deficits in LPDs as compared to RPDs, another third show the opposite pattern (i.e., RPDs are impaired relative to LPDs), and the last third show no differences between the two groups. The current study confirms previous studies that indicate that while LPDs and RPDs show deficits

when compared as a group to NCs, there are no significant differences between RPDs and LPDs in cognitive and affective processing.

The current study carefully selected 16 tasks assessing left-hemisphere (linguistic and cognitive), right-hemisphere (visuospatial and affective), and frontal-lobe functions. When contrasts were conducted comparing only the LPD and RPD groups, no significant differences were found on any of the tasks. These findings are in accordance with at least three studies reporting negative findings (i.e., a lack of significant differences) between left and right hemiparkinson's groups (e.g., Agniel et al., 1991; Huber et al., 1989; Riklan et al, 1990).

Agniel et al. (1991) administered five right-hemisphere tests and four left-hemisphere tests in a study designed to assess the existence of cerebral blood flow (CBF) lateral asymmetries in HPDs (10 LPDs, 13 RPDs) to see if they correlated with the neuropsychological differences sometimes reported in these patients. They failed to find any relationship between HPD and both cognitive and CBF asymmetries. In looking at just side of symptom and test performance, only one test was shown to be significantly

different between the groups. Of the five right-hemisphere tests and four left-hemisphere tests administered, the WAIS-R Object Assembly subtest was found to show lower performances in the LPD group. While this does fit a profile of right-hemisphere pathology interfering with visuospatial performance, they point out that the other four right-hemisphere tests (letter recognition, Benton Facial Recognition, WAIS-R Block Design, and Light Pattern) yielded no significant differences between groups, nor were there any differences in any of the tests assessing left-hemisphere pathology (Letter Search, WAIS-R Digit Span, Benton Verbal Fluency, and Light Sequence). In addition, LPDs and RPDs showed no significant differences in CBF in either cortical or subcortical areas. The findings from the current study are in accordance with the findings of a lack of significant differences between LPDs and RPDs in cognitive processing.

Riklan, Stellar and Reynolds (1990) devised a study in response to questions raised about the severity of disease and disability in HPD and how they may relate to Direnfeld et al.'s findings (1984) that LPD groups were more impaired than RPDs on tasks assessing memory, visuospatial

performance, language and mental control. In the Riklan et al. study, 15 left- and 10 right-sided dominant patients were identified according to ratings for tremor, rigidity, and alternating movement impairments. They then combined ratings of bradykinesia and impaired function to derive a total symptom severity scale to test their hypothesis that right and left differences between HPDs may well be due to total severity of symptoms and not just to side of symptoms. Before adjustment for symptom severity, the "right-side dominant group" (that is, the RPDs) scored significantly lower on five of the 12 tests assessing cognition. After adjustments for severity of symptoms, there were no significant differences between the groups. The authors conclude that in studies of HPD, severity of motor symptoms may be a more important factor than laterality of symptoms when assessing cognitive impairment.

However, while it is true that some of the studies in HPD did not take "severity of symptoms" into account, most did. In fact, the study that Riklan et al. (1984) cite as their impetus to examine this issue (i.e., Direnfeld et al., 1984) <u>did</u> list several symptoms. Looking at rigidity, tremor, bradykinesia, and gait, no significant differences

were found between the left and right hemiparkinson's groups. The category of "symptom severity", according to Riklan, should include bradykinesia and impaired function, not just tremor and rigidity. Although most of the studies listed rigidity, bradykinesia, and tremor, none took into account "impaired function", which is a clinical assessment of a patients ability to carry out activities of daily living. And while most studies conducted t-tests to assure that there were no significant differences between groups on these factors, none (with the exception of the Agniel et al. study) covaried for them. Finally, none of the studies had a "total severity rating" taking all factors into account.

Huber et al. (1989) also looked at neuropsychological functioning in HPD and found no differences between LPD and RPD groups. As in Riklan's study, they were concerned with severity of disease, as impairments in cognition and progression of disease are known to be positively related (Huber, Paulson, & Shuttleworth, 1988). They performed two experiments, first assessing HPDs in stage I of the Hoehn-Yahr scale. Second, they performed the same experiment on HPDs with Hoehn-Yahr scores between II and IV. Post-hoc comparisons yielded a few differences between controls and

HPDs in both sets of experiments, but no significant differences between LPDs and RPDs. The results of these experiments concur with the present study. In our study, only stage II HPDs were tested (some patients were initially obtained because of Hoehn-Yahr scores of I, but were assessed as stage II by the time of testing). It seems that our results are still in agreement with those of Huber et al., whether looking at their first (stage I) or second (stage II-IV) experiments.

In describing whether neuropsychological differences do exist between left and right HPDs, the authors' interpretation of their findings in these various studies needs to be considered. For example, Blonder et al. (1989) administered a large battery of neuropsychological and affective tests to 14 RPDs and 7 LPDs in stages I to III on the Hoehn-Yahr scale (17 stage I, 3 stage II, 1 stage III). Only two of the 35 separate analyses showed a statistically significant difference between left and right HPDs. However, when subjects' scores were transferred into Z-scores and grouped into various categories (e.g., Memory, Abstraction, etc.), and when repeated-measures ANOVAs were performed, the expected differences reflecting

lateralization of neuropsychological functions emerged. Specifically, they found a Diagnosis Subgroup X Function interaction, with RPDs being relatively more impaired in language, and LPDs having relatively greater impairment in memory and abstraction. They then note that the individual contrasts for the measures were not significant. Their major conclusion is that there are neuropsychological deficits consistent with the lateralization of motor symptoms in early PD. The choice of analyses and one's interpretation of these analyses should be taken into consideration.

One obvious area of consideration when trying to interpret nonsignificant findings is to look at the number of subjects tested. In general, the smaller the N, the greater likelihood of a failure to reach significance. When looking in the literature and contrasting the studies that found significance and those that did not, the opposite actually occurred. That is, studies with the smallest Ns were much more likely to find significance. Starkstein et al. (1987), Spicer et al. (1988), Direnfeld et al. (1984), and Villardita et al. (1983) all had Ns of less than 20 patients overall, yet all found statistically significant

differences in neuropsychological functioning between left and right hemiparkinson patients. Although the N is not, by itself, the sole factor in determining whether significance is found, the relationship between sample size and the magnitude of differences between the left and right HPDs is in the opposite direction of what one would expect (see Table 11).

In order to take into account other possible factors that may have influenced the results from our three groups, various analyses of covariance were conducted. Age, education, and depression were all covaried for (both separately and together) to determine if these variables were confounding the findings of this experiment. In looking at our main hypothesis concerning differences between left and right HPDs, our analyses of the data yielded no differences between these two groups for either left- or right-hemisphere tasks. The reported ANCOVAs for the present study used age, education, and depression simultaneously (See tables 8a and 8b). However, when an exploratory ANCOVA covarying for age only was conducted, one test yielded significant differences between left and right HPD groups: the Zung Depression Inventory. In the original

ANOVAs, a trend was seen for depression, with RPDs showing more depressive symptomatology than LPDs (p=.098). When age was covaried using an ANCOVA, the RPD group showed significantly more depression than the LPD group (p=.05). This is in accordance with an extensive literature indicating that general left hemisphere pathology is more associated with depression (e.g., Goldstein's classical description of "catastrophic reaction"; Gainotti, 1972; Starkstein & Robinson, 1988).

Although most studies failed to find differences in the depression rate between left and right parkinsonian patients, those that did found that RPD was associated with higher rates of depression than was LPD. Direnfeld et al. (1984) reported that RPDs tended to show more depression as measured by a Beck Depression Inventory when compared to LPDs. Starkstein et al. (1987) also reported a non-significant trend indicating that RPDs tended to be more depressed than LPDs (no p-value provided). Hietenen and Teravainen (1988) state that the Beck Depression indices of their LPD and RPD patients were compatible. However, in examining the depression scores, the RPDs showed higher depression rates (M=7.0 +/-5.3) than LPDs (M=6.3 +/-6.4).

If both left hemisphere pathology and subcortical components are involved in depression, this may well be the first neurocognitive or neuropsychiatric manifestation observed in RPD (as RPD denotes pathology in the subcortical structures of the left hemisphere). The lack of differences between left and right hemiparkinson's groups in many other areas of neuropsychological functioning could be explained by a combination of other factors.

One possible factor could be that HPD is almost always found at the onset of this disorder. Although asymmetries in motor dysfunctions can be seen throughout the course of Parkinson's disease, hemiparkinsonism is usually seen at the very first of this disease, when it is in its early, milder state. Differences between left and right hemisphere functioning are likely to be quite subtle at this stage. Differences, if any, could be difficult to detect. If cognitive changes are more likely to be mild, some of the standard neuropsychological tests may be unable to detect slight changes in cognitive processing. It could be that there are differential deficits other than depression between LPDs and RPDs, but that our instruments are not

designed or sensitive enough to detect such subtle differences.

Cognitive Functioning in Early PDs versus NCs

Analyses of variance on our data yielded no significant differences between right and left HPD. Covarying for factors such as age and education still yielded no differences between left and right HPD with the one exception of depression, in which RPDs were found to be significantly more depressed than LPDs. Our major hypothesis then, that right and left HPD may have cognitive and affective differences, was not supported.

A secondary hypothesis was that, if we collapsed across the left and right HPD groups (called "early PD"), and compared them to NCs, differences between these groups would be present. This hypothesis was based on previous research indicating clear neurocognitive and behavioral deficits in PD (for a review, see Brown & Marsden, 1989). Very few studies have looked specifically at the early stages of PD. Those that did found deficits in PD when compared to normal control groups (Canavan et al., 1989; Lees & Smith, 1983). The use of the term "early PD" should be used with caution, however. The same problems with operationally defining HPD

apply to defining early PD. In the Lees and Smith study, early PD patient groups were identified by testing newly-diagnosed patients. Inclusion criteria for their study consisted of six different variables (i.e., 65 years of age or under, no exposure to antiparkinsonian medications, predominantly right-handed, normal CT brain scan, no evidence of depression, and an ischemia score of less than 4 [Hachinski et al., 1975]). No specific duration time of the illness was used as a specific inclusion criteria. Later, in the methods section they list "the mean duration of disease from the first symptom was 2.4 years (range = six months to five years)...". In the Canavan et al. study, again, no set criteria were listed for what constitutes early PD. Estimated duration of PD symptoms was 33.7 months (range = six to 86 months). In both studies then, early PD could mean from six months to more than five or six years. It is with this in mind that the term "early PD" is used in this study to describe both LPDs and RPDs together as one group.

In our study, the average length of illness for the LPDs and RPDs was approximately 3.6 years (LPDs--M=3.66 years, s.d.=2.06; RPDs--M=3.63 years, s.d.=2.06). When

compared to the NCs, the early PD group demonstrated cognitive deficits on four of the 16 tests administered (and on eight of the 37 separate measure involved). These deficits were seen in short- and long-term verbal memory, word fluency, visual form discrimination, and depression. Trends were seen on one affective task (facial identification [p=.087]) and on one of the verbal fluency tests (animal naming [p=.057]).

Memory Functioning in PD

In the present study, two memory tests were administered; the Rey Auditory Verbal Learning Test (Rey AVLT) for the assessment of verbal memory and the Visual Reproduction subtest of the Wechsler Memory Scale-Revised (WMS-R) for the assessment of non-verbal memory. Both of these tests provide procedures for assessing short- and long-term memory. The Rey AVLT requires subjects to reproduce as many words as possible from a list of 15 words given to them verbally by an examiner. After each trial, the subject is required to repeat as many of the words from the list as possible. This list is repeated five times (a response was required after each trial), followed by a sixth trial of a different list of 15 words. The seventh trial

requires the subject to recall as many words from the first list as possible. The Visual Reproduction subtest of the WMS-R entails showing the subject four pictures (one at a time) for a 10-second period. After the 10-second period is over, the picture is taken away, and the subject is instructed to reproduce the picture as accurately as possible. Both the Rey AVLT and the WMS-R are administered again after a 30-minute delay period in order to assess long-term memory.

In this study, PDs and NCs showed no differences for either short- or long-term nonverbal memory processing. However, on both short- and long-term aspects of the Rey AVLT, PDs and NCs showed significantly different patterns of deficits. Even after covarying for age, education, and depression, deficits in short- and long-term memory produced by the PD group remained relatively constant.

Investigations of memory functions in PDs began in the late 1920's (see, for example, Chritchley, 1929) and have produced inconsistent results (for a review, see Knight et al., 1988). The results concerning verbal memory deficits from the present study are consistent with some studies indicating such deficits in PDs (Bowen et al., 1975;

Taylor, Saint-Cyr, & Lang, 1986). However, some studies have also found memory deficits in the nonverbal domain (e.g., Bowen et al., 1975), a finding our data do not support.

Cooper, Sagar, Jordan, Harvey, and Sullivan (1991) administered an extensive neuropsychological battery, including a large number of various memory tests, to 60 newly diagnosed, untreated, idiopathic PD patients and to 37 matched NCs. They found deficits for some, but not all, of the memory tasks. For example, the PDs showed deficits in immediate recall of verbal material, but after a one-hour delay could recall as much of their initial response as could normals. In other words, the information that PDs could initially recall was no more susceptible to decay than the information that NCs could initially recall. They interpret this as impaired short-term memory but intact long-term recall. However, this interpretation does not address the fact that the PDs could recall less information than NCs in the first place. After a one-hour delay, the PDs were able to recall as much of the initially-learned information as could the NCs, but they had less information to recall because they initially remembered less

information. A more accurate assessment might have been to have both groups learn the same amount of information (even if, as one would suspect, it would take the PDs longer to learn) and then test their recall after a one-hour delay.

The results of the current study agree with Cooper et al. in finding impairments in immediate short-term memory. However, our results indicate that there is also a deficit in recall after a 30-minute delay, a finding inconsistent with the Cooper et al. study. It is possible that these discrepancies could be accounted for by the fact that in the Cooper et al. study, none of the PDs were receiving any medication, unlike the PDs in the present study, who were receiving Sinimet, a dopamine agonist. It is known that levodopa treatments can affect performance on neuropsychological performance. For example, Gotham, Brown, and Marsden (1990) found that performance on a sequencing task was impaired in PD patients on levodopa, but the same patients were unimpaired when compared to NCs after the discontinuation of their medication. Also, the Cooper et al. study excluded any PD patient showing depression or dementia. While our study did screen for dementia, it did not screen for depression (although a subsequent analysis

using depression as a covariate was performed). As mentioned above, our patients (M=49.6) were depressed relative to NCs (M=41.2) and were also receiving medication, both of which may contribute to memory deficits. It should be noted here, however, that when the current study covaried for depression, memory deficits were still present, weakening the argument of depression being a possible factor responsible for memory deficits.

In summary, results of impairments in memory in PD populations after a delay period are inconsistent. In the present study, both short-term and long-term verbal memory were shown to be compromised in PDs as compared to NCs. Some studies have indicated an impairment in memory after a delay period. For example, Levin, Llabre, and Weiner (1989) found deficits in both short-term and long-term recall, although they point out the proportionate decline relative to immediate recall is not greater than that of NCs. Other studies, however, show relative preservation of long-term memory in the presence of impaired immediate recall (Sullivan & Sagar, 1991; Taylor et al., 1986).

Cooper et al. (1991) assert that impaired performance in both short- and long-term memory can be seen as

indicative of deficits in processes affecting the registration of information (like attention or encoding) or retrieval. Impaired performance in short-term memory but normal performance in long-term memory could reflect adequate registration and suggest deficits in the speed, but not accuracy, of registration. Put in the context of an information-processing model, this would permit registration processes to be inefficient, but function at a level adequate enough to allow what has been encoded to achieve normal long-term memory performance. The results of this study support the former hypothesis, that is, that in early PD there are deficits in the registration and/or retrieval of information. This deficit is seen in the disruption of normal verbal short- and long-term memory in early PD.

Theoretically, this argument should hold for both verbal and nonverbal information. Our study found deficits in verbal but not nonverbal short- and long-term memory. Considering the evidence of visuospatial, as well as memory, deficits often reported in PD, one would not be surprised to find deficits in the visual memory domain. However, no deficits in nonverbal memory were found in this study.

Recent studies indicate that previously reported visuospatial deficits may actually reflect a disruption of set-shifting abilities (Raskin et al., 1992). Also, it is extremely difficult to equate verbal memory tests with nonverbal memory tests in terms of comparable levels of complexity and difficulty. It could be that in the present study, the memory test used to assess verbal functioning demands more difficult levels of processing than the memory test used to assess visual functioning. These factors may account, in part, for our finding of short- and long-term deficits in verbal, but not nonverbal, memory functions.

Visuospatial Functioning in Early Parkinson's Disease

Various measures of right-hemisphere/visuospatial functioning were administered to our PD and NC groups. Among them were the Picture Completion subtest of the WAIS-R, a visual cancellation test, the visual memory subtest of the WMS, a facial identification task, a word emotion task, and a visual form discrimination task. ANOVAs and subsequent ANCOVAs on all tasks were performed. No analysis was statistically significant (or revealed any trends) for any of the tasks except for the Visual Form Discrimination Task. An ANOVA showed a p value of .022, and a subsequent

ANCOVA for age, education, and depression simultaneously indicated a p-value of .008. Studies of neuropsychological functioning in PD have revealed cognitive changes in various areas. Early investigations indicated, among other deficits, the presence of visuospatial difficulties. One study (Pirozzolo, Hansch, Mortimer, Webster, & Kuskowski, 1982) stated that the visuospatial deficits seen in PD were considerably higher than any other cognitive change, occurring at a rate of up to 93%. Other studies conducted before the mid-1980's seemed to confirm the presence of visuospatial deficits in PD, although the prevalence of such deficits was not as high as in the Pirozzolo study (Boller et al., 1980, 1984; Proctor, Riklan, Cooper, & Tueber, 1964).

In the past decade, the phenomenon of visuospatial deficits in PD populations has come into question. Some studies have failed to find visuospatial deficits at all (Brown & Marsden, 1990; Raskin et al., 1992; Sala et al., 1986). What have commonly been considered to be visuospatial deficits in PD may actually be more related to set-shifting capacity or to the specific demands of a given task than to pure visuospatial deficits (Brown & Marsden,

1986). For example, Ransmayr et al. (1987) administered two visuospatial tasks to PDs, one involving choosing the correct answer from a number of alternatives, the other necessitating that the answer be self-generated. The PDs were impaired on the latter (self-generated) but not the former (alternatives provided). This and other studies (Flowers et al., 1984; Weingartner et al., 1984) suggest that the problem may not be visuospatial, but a deficit in tasks requiring internal as opposed to external control.

Another line of reasoning suggests that the visuospatial deficit commonly reported in PD patients reflects not a visuospatial problem, but a problem in shifting set (Brown & Marsden, 1990; Cooper et al., 1991). Raskin et al. (1992) devised a set of visuospatial tests without set-shifting demands and a set of set-shifting tasks without visuospatial demands. Their results indicate a lack of visuospatial deficits in PD, but the presence of set-shifting deficits was found. They interpret this finding as evidence for "frontal-lobe" types of dysfunction in PDs.

The present study looked at several right hemisphere tasks, listed earlier in this section. The only task to show impairment was that of visual form discrimination.

This agrees with earlier studies of visuospatial functioning, but is in contrast to more recent, methodologically advanced studies. Considering that the Visual Form Discrimination Test involves selecting the correct answer from four alternatives, one would expect that if the previously discussed theory of internal versus external locus of control was operating, no deficits would be found. One might have expected to see deficits in picture completion, nonverbal WMS tasks, or the visual cancellation task, as these all require active participation by the subject. However, these tests were found to be unimpaired, so this explanation cannot be applied here. Likewise, the set-shifting theory would predict deficits on tests assessing frontal lobe functioning, such as the OMO or the alternating A-S task, but these were found to be unimpaired. The visual form task has no set-shifting demands, however. This theory then is also unable to account for the finding in the present study of deficits in the visual form discrimination task.

Sala et al.(1986) tested 25 nondemented, mildly impaired PD patients. They found no evidence of specific spatial deficits. Knight et al. (1988) suggest that this

may indicate that visuoperceptual deficits may be primarily characteristic of the later stages of the disease. With the exception of the Visual Form Discrimination Test, this could account for the general lack of visuospatial deficits found in the present study, as our PD patients were also in the early, mild stages of Parkinsonism.

Frontal Lobe Functioning in Early Parkinson's Disease

Research in PD has revealed a striking similarity in the neuropsychological deficits seen with damage to the frontal lobes and those often seen in PD patients (Cooper et al., 1991; Gotham et al., 1987; Knight et al., 1988). Brown and Marsden (1990) reviewed the literature on cognitive functioning and found more than 50 studies showing the same type of impairment following damage to the frontal lobes as is found in PD.

Although the present study was mostly interested in lateralized differences between left and right hemiparkinsonism, we included two measures of frontal lobe functioning. The first measure was the Odd Man Out Test (OMO). This is similar in format and task demands to the Wisconsin Card Sorting Test (WCST). The second set of measures was verbal fluency. Included here were a

controlled oral word association test (i.e., "FCL"), an alternating letter test ("A-S"), and animal naming. The FCL and animal naming tasks were initially included in this battery as measures of left-hemisphere functioning because of their obvious dependence on language. Along these lines, Matison et al. (1982) noted that word fluency deficits in PD could actually reflect a "language problem". However, these tests are also known to be sensitive to frontal-lobe functioning. The alternating letter task is thought to be a more sensitive measure of frontal lobe functioning than the other two fluency tasks, because it taps not only verbal fluency but the ability to rapidly shift set, a function known to be disrupted by frontal lobe dysfunction (Raskin et al., 1992).

Initial ANOVAs of data in the current study contrasting early PDs to NCs found some differences between groups on verbal fluency. Specifically, ANOVAs revealed poorer performance for PDs than NCs on verbal fluency with the letter "F" but not with the letters "C" or "L". More interestingly, when asked to alternate the letters "A" and "S", PDs performed as well as NCs. One would have predicted that if there are frontal lobe deficits in PD, the

alternating letter task would have been more compromised than the single letter tasks, as the alternating letter task taps not only verbal fluency but also the ability to shift set. When ANCOVAs were performed on the "FCL" tasks, "C" and "L" remained statistically nonsignificant, as before. The ANCOVA (for age, education, and depression) on the letter "F" revealed a trend. Neither ANOVAs nor ANCOVAs on "A-S" reached statistical significance nor indicated trends.

The other test of verbal fluency, animal naming, showed a trend (p=.057) when the ANOVA was conducted. An ANCOVA using age, education, and depression simultaneously was performed; significance was not reached (p= .132). However, when exploratory ANCOVAs for animal naming were performed for education alone and for age and education combined, statistical significance was reached (p for education = .001; p for age and education = .008). Considering that animal naming findings went from statistically nonsignificant to significant with an ANCOVA, and that "F" went from statistically significant to nonsignificant with an ANCOVA, the data are difficult to interpret.

Gotham et al. (1987) suggest that different areas of prefrontal cortex are involved in various tasks and that frontal levels of dopamine in PD may vary between areas of the cortex and the caudate nucleus. In their study, various frontal lobe tests were differentially affected depending on whether patients were "on" or "off" levodopa treatment. They found that associative conditional learning and subject-ordered pointing were impaired in PDs (compared to NCs) only when on levodopa. Verbal fluency was impaired only when off levodopa. Finally, the WCST showed impairment both on and off levodopa. They propose various explanations for these discrepancies, suggesting that the most likely explanation is that these tests assess different aspects of frontal function, and that only certain aspects are compromised in patients who are not on dopaminergic medication.

Although all of the patients in the present study were receiving levodopa medication, it is possible that verbal fluency as assessed by letter-word fluency is mediated (and/or affected) by different frontal areas than a verbal fluency task, such as animal naming, which is different in that it provides additional semantic structure.

Neuroanatomical Substrates in PD

In order to explore possible interpretations of our data on neuropsychological functions in HPD vis-a-vis underlying CNS pathology, a discussion of the neuropathological substrates involved in PD will be discussed. After this discussion, attempts to relate brain structure with cognitive processing will be presented.

Recent studies indicate at least five or more parallel but independent caudatoprefrontal loops by which this processing of different types of cognitive function may occur. The first two loops are motor in nature, and probably do not mediate any specific cognitive function(s). The first circuit is called the "motor loop", and links the putamen with the supplementary motor cortex (Delong, Georgopoulos, & Crutcher, 1984). Another motor circuit involving the control of eye movement has been described. The remaining three circuits are described by their anatomical structures and complementary projection sites, as the functional significance of each is as yet uncertain. The first is the dorsolateral prefrontal circuit. The head (dorsolateral) and tail (rostrocaudal) of the caudate nucleus receive inputs from the dorsolateral prefrontal

cortex, posterior parietal cortex, and arcuate premotor area. The caudate, in turn, sends information back to the prefrontal area via two routes. The first is from various thalamic nuclei as well as from the globus pallidus. The second is from the thalamus and the substantia nigra. Both project to different areas of the prefrontal cortex. The second loop is the lateral orbitofrontal circuit. There, the prefrontal cortex projects to a section of the head and tail of the caudate nucleus. Output involves the globus pallidus and substantia nigra, which project to the lateral orbitofrontal cortex. The last circuit is the anterior cingulate circuit. Parts of the striatum receive inputs from the hippocampus, amygdala, limbic cortex, and neocortex. Output from the ventral striatum runs from the globus pallidus and substantia nigra to various regions, including the anterior cingulate area, thus closing the loop (Gotham et al., 1987).

These recently discovered anatomical substrates may mediate different aspects of cognitive function in both the basal ganglia and the frontal lobes, which could possibly account for differences between somewhat but not completely similar neuropsychological processing abilities.

In a similar fashion, differences in actual dopaminergic loss in separate anatomical structures (presumably contributing to different cognitive abilities) may influence performance on these frontal tests. When damage occurs to the substantia nigra, as in PD, widespread loss of DA to the striatum ensues. PD also affects the mesocortical dopaminergic system. Postmortem studies have indicated the extent of the dopaminergic depletion in different projection areas. Dopamine depletion seems to be greatest in the neostriatum, with the putamen being the most susceptible to high levels of neurotransmitter loss. The putamen has been shown to be depleted to only 5% or less of normal values. Caudate dopaminergic depletion is at about 15-20% of normal levels (Agid, 1987). Relative levels of dopaminergic depletion in the areas of the caudate involved in the different caudocortical loops is not known, however. It is possible that, within individual patients, caudate areas involved in the dorsolateral prefrontal and lateral orbitofrontal circuits may have different levels of dopamine depletion.

If dopamine levels in both the nigrostriatal and mesocorticolimbic systems are differentially depleted, then

at least two possibilities exist as to how dopaminergic dysfunctions could lead to different cognitive disturbances in PD. The first is through either one or both of these prefrontal circuits. Dopamine depletion might disrupt the caudate nucleus, causing the basal ganglia input to the prefrontal cortex to be impaired. Another possibility is more direct. It could be that there is dopaminergic depletion in the frontal cortex innervated by the ventral tegmental area.

These different mesocortical pathways and differential dopaminergic depletions, along with individual differences in subcortical damage among PD patients evidencing similar motor symptoms could play a part in the finding of some frontal signs on certain tests in the absence of similar frontal signs on other tests.

Depression in Early Parkinson's Disease

The present study was designed primarily to detect differences between left and right HPDs. Accordingly, most of our tests were divided into either "left hemisphere" or "right hemisphere" tasks (See Appendix B). For this study, the Zung depression inventory was selected, and was included as a "left hemisphere" task. This was partly based on

research indicating that general left hemisphere pathology leads to depression (e.g., Goldstein's "catastrophic reaction" [Goldstein, 1942; Starkstein and Robinson, 1988]). A second reason for the inclusion of the Zung among the left hemisphere tasks is because the literature investigating depression in HPD indicates higher rates of depression in right hemiparkinsonism (i.e., left subcortical damage) than in left hemiparkinsonism (i.e., right subcortical damage).

Methodological Considerations Regarding Depression

Before addressing the results of this study, some methodological considerations concerning the issue of depression should be discussed. In the study of PD and HPD, there are various ways to deal with depression. The first is to screen patients for the presence of depression. This is often done in studies that are interested in investigating cognitive changes in PD populations. Depression is controlled for (via screening procedures prior to testing) because it is known that depression itself can cause deficits in cognitive functioning. Although it is understandable to screen out patients with depression when testing for neuropsychological characteristics, it

introduces the problem of selection bias factors. One estimate (and some estimates are higher) is that 40% of PD patients evidence depression (Cummings, 1992). If this figure is accurate, then a little less than 1/2 of potential PD patients in a given study will be excluded from testing. Again, although understandable, this can lead to selective biasing of ones sample, thus leading to less external validity of results.

Another approach is to test for the prevalence of depression alongside other neuropsychological variables. Here though, you run the risk of attributing any found cognitive deficits to the presence of PD, when in fact the deficits may be partially or even mainly due to depression. Many studies have been conducted documenting increased incidence of intellectual impairment in PDs with depression when compared to those without depression (Mayeaux, et al., 1981; Starkstein et al, 1992; Stern et al., 1986; Taylor et al., 1986). Starkstein et al. (1992) compared patients with major, minor, and no depression on a battery of neuropsychological tests. PDs with major depression showed a significantly higher rate of cognitive decline (as well as deterioration in ADLs [activities of daily living] and

further progression through the Hoehn-Yahr stages) when compared to PDs with minor or no depression.

In the present study, we wanted to test for the presence of depression between left and right HPDs as well as for the presence of cognitive deficits. To take into account the effect of depression on cognitive processing in PD, an ANCOVA was performed. At least two other studies investigating cognitive deficits in PD used this approach. Mortimer, Pirozzolo, Hansch, and Webster (1982) found that the correlations between motor symptom severity and cognitive performance were not greatly altered by partialling out depression scores (the Zung) in a covariance analysis. Boller et al. (1984) found PDs to show visuospatial deficits as well as depression. Correlational studies of their results suggested that poor performance on visuospatial tests was not related to depression.

The results of the differences in the occurrence of depression between RPDs and LPDs were previously discussed. RPDs showed a trend ($p=.098$) toward more depressive symptomatology than LPDs on a one-way analysis of variance. An analysis of covariance taking into consideration age and education showed a significant difference ($p=.05$) in the

same direction. ANOVAs and ANCOVAs (for age and education) show highly significant differences between early PD groups (that is, the LPDs and RPDs pooled together) and NCs (P=.001 for all analyses). The strongest and most consistent finding in the present study is the presence of depression in early PD.

Although the presence of depression in a neurologically debilitating disease is not completely surprising, a major question is whether the depression is reactive or endogenous. Perhaps a better way to phrase this should be when depression is found in PD, how much is due to the psychological impact of having the disease and how much may be due to the underlying anatomical and/or neurochemical alterations. In terms of PD being a reactive phenomenon, at least one study provides evidence that depression is most pronounced in the early stages of the disease and therefore may be related to dealing with the psychological trauma of a major neurological disease (Dakof & Mendehsohn, 1986).

Most research tends to support the view that depression in PD is at least partially mediated by endogenous factors and not solely a reactive phenomenon. One line of evidence for this comes from studies comparing

PD patients to other chronic diseases. When these comparisons are made, PDs typically have higher rates of depression (Todes & Lees, 1985; Warleurton, 1967). In a review of PD and depression, studies using the Beck Depression Inventory (BDI) were analyzed (Cummings, 1992). With the exception of a study using arthritis patients as a comparison group, BDI scores of PDs were higher than the scores of comparison subjects. Other comparison groups consisted of spouses, normal elderly, volunteers, non-neurological patients, and disabled patients. The BDI contains items that PDs may score high on due to motor changes. This issue was more fully addressed earlier in this paper, but studies (e.g., Levin et al. 1988) indicate that the BDI is an accurate assessment of depression in PD.

Most of the research on depression in PD supports the view that the depression seen in PD is not identical to that seen in patients with idiopathic depression. PDs have been found to have higher levels of dysphoria and pessimism about the future, irritability, sadness, and suicidal ideation. However, they evidence relatively low levels of guilt, self-blame, and feelings of failure or punishment (Brown et al., 1988; Huber, Miller, Bohaska, Christy, & Bornstein, 1992;

Taylor et al., 1986). Other features include an increased rate of anxiety symptoms and a low suicide rate in the face of high suicidal ideation (Brown & Marsden, 1990; Cummings, 1992). The discrepancies between depression in PD and idiopathic depression listed above indicate the possibility that depression in PD is not totally a psychological reaction, and therefore mediated by structural or neurochemical changes.

Practical Implications

Since 1964, when Hoehn and Yahr identified a subgroup of patients exhibiting unilateral symptoms (subsequently termed hemiparkinson's disease), some researchers have used this group to investigate laterality issues. Upon the testing and analysis of the data collected on left and right HPD groups, many studies, including the present study, have concluded that there are no differences between left and right HPD groups in neuropsychological functioning.

Initially, the identification of a group of patients with left and right HPD seemed an ideal group for the study of the lateralization of the CNS, especially concerning the contribution of subcortical structures. Upon closer

inspection, HPD might not be the ideal group it was thought to be.

First, when one looks at the structures that are impaired in Parkinson's disease, cortical as well as subcortical systems are affected. By the same token, several neurotransmitter groups as well as neuropeptide groups are also affected throughout the central nervous system.

Second, and more importantly, HPD more often than not represents a subgroup of PDs with symptoms on both sides of the body, with one side affected more than the other. In these cases, one is observing bilateral, not unilateral damage.

Even in those rare cases where it is possible to test HPDs with exclusively unilateral symptoms, one is still most likely dealing with patients with bilateral subcortical damage. PD occurs when the deterioration of the substantia nigra/basal ganglia complex reaches 80%. Since it has been observed that HPD is almost always a transient state that soon develops into bilateral PD (Chouza et al., 1984), a completely unilateral group of HPDs most likely has between 50 to 80% substantia nigra/basal ganglia damage on the

"unaffected" side (it is known that a 50% loss of the substantia nigra/basal ganglia fibers is a normal, age-related event). So whether one is assessing lateralization of cognitive function in either predominantly or exclusively unilateral HPD, one is almost assuredly assessing, to some extent, bilateral brain damage.

Perhaps the use of the term HPD is more useful as a description of a particular PD subgroup rather than as an opportunity to identify a group of patients used to test subcortical brain damage and its effect on neuropsychological functioning.

If future research in HPD is to yield more coherent and useful findings, certain methodological guidelines are suggested. First, studies investigating HPD should use the same assessment scale. It is suggested here that the Hoehn-Yahr scale be used in tandem with the Unified Parkinson's Disease Scale (UPDS). the UPDS is a scale listing separate measures (e.g., tremor, bradykinesia, etc.) for various body parts (e.g., upper extremities, lower extremities, neck, etc.). At the end of this scale is a Hoehn and Yahr stage score based upon the clinical findings of the UPDS. Using these two scales has the advantage of providing specific

information about the side and severity of all major PD motor symptoms, as well as yielding an overall indication of HPD (the Hoehn and Yahr scale score itself). If there are any differences between left and right hemiparkinson's disease, it is strongly suggested that researchers use the same scale to define HPD so that when results from separate studies are compared, one can assume that they are measuring the same disease state derived from standard, defined, and clear criteria. Second, some sort of consensus concerning the minimal ratio of left to right symptoms should be agreed upon. Some use a 2:1 ratio as a minimum score for acceptance of an HPD subject in a given study; others use a 3:1 ratio. It is suggested here that a more stringent ratio would probably be more prudent, in that ratio scores of 2"1 indicate that the symptomatology is lateralized, but perhaps too close to be able to detect differences in an incipient disease state that already presumably reflects some bilateral subcortical pathology (50% degradation of the substantia nigra/basal ganglia complex is a normal age-related event). In terms of practical application, this may be more easily said than done. Hemiparkinson's disease patients are not that easy to find, but if one compares a

study that uses a lax criterion for severity of symptoms to one that uses a more stringent criterion, it makes it more difficult to interpret any differences or similarities between studies that may be found. A few studies (e.g., Riklan et al. 1990) have indicated that severity of symptoms may be a more important factor in neuropsychological dysfunction in HPD than side of motor symptoms. It is for these reasons that a standard protocol is suggested if future research in HPD is to be conducted.

Conclusions

The results of this study support previous research in finding that various cognitive deficits may appear in the early stages of Parkinson's disease. However, the results of this study failed to find any differences in neuropsychological functioning between left and right hemiparkinson's disease patients. These results are in agreement with some recent research in PD also failing to find differences between LPDs and RPDs. While many possible factors were discussed as to why this study failed to find differences between left and right HPDs, the considerable variation in the diagnosis and criteria for defining HPD is thought to be a major factor in the inconsistent results

reported from various studies. It is suggested that further research proceed with a more clear cut definition of what is acceptable for the diagnosis of HPD. Without such a definition, comparisons between studies investigating HPD will be problematic, and will hinder a better understanding of cognitive and affective functioning in hemiparkinson's disease.

Table 1

Primary Parkinsonism: Stage and Duration of Illness

(from Hoehn and Yahr, 1967)

Total patients (183)	Stage	Median*	(--------duration in years--------) 0-4	5-9	10-14	15-19	20-24	25-29	30+
31	I	3.0+/-7.1	20	6	3	1	0	0	1
53	II	6.0+/-6.9	24	14	9	3	1	1	1
43	III	7.0+/-6.3	15	14	9	4	0	0	1
47	IV	9.0+/-7.2	11	18	10	4	2	1	1
9	V	14.0+/-3.4	0	2	5	2	0	0	0
			(-duration expressed in percentages-)						
31	I		65	19	10	3	0	0	3
53	II		45	26	17	6	2	2	2
43	III		35	33	21	9	0	0	2
47	IV		32	38	21	8	4	2	2
9	V		0	22	56	22	0	0	0

* Median indicates the number of years the patient has evidenced Parkinson's disease for a given Hoehn and Yahr stage.

Table 2

Hoehn-Yahr Scale (Hoehn and Yahr, 1964)

Stage I. Unilateral involvement only, usually with minimal or no functional impairment

Stage II. Bilateral or midline involvement, without impairment of balance.

Stage III. First sign of impaired righting reflexes. This is evident by unsteadiness as the patient turns or is demonstrated when he is pushed from standing equilibrium with the feet together and eyes closed. Functionally the patient is somewhat restricted in his activities but may have some work potential depending upon the type of employment. Patients are physically capable of leading independent lives, and their disability is mild to moderate.

Stage IV. Fully developed, severely disabling disease; the patient is still able to walk and stand unassisted but is markedly incapacitated.

Stage V. Confinement to bed or wheelchair unless aided.

Table 3

Demographics of LPDs, RPDs, and NCs

Subject	Side of Symptom	Age	Sex	Education	Hoehn-Yahr Rating	Duration of Illness
1.	L	65	F	12	- *	8
2.	L	85	F	12	2	2
3.	L	82	M	18	3- **	4
4.	L	85	M	22	3	2
5.	L	59	M	18	2	1
6.	L	81	M	19	2	2.5
7.	L	66	M	16	2	5
8.	L	67	M	19	2	3
9.	L	61	F	15	2	2
10.	L	67	F	16	3	6.5
11.	L	85	F	12	3	3.5
12.	L	67	F	12	2	4.5
13.	R	65	M	17	2	2
14.	R	68	M	15	2	5
15.	R	80	M	14	2	5
16.	R	79	M	16	2	2.5
17.	R	59	F	14	2	3
18.	R	61	M	19	2	7.5
19.	R	60	F	14	2	2
20.	R	57	F	13	2	5
21.	R	69	F	14	2	1
22.	R	76	F	16	2	5.5
23.	R	59	F	14	2	1.5
24.	NC	70	F	12		
25.	NC	68	M	13		
26.	NC	78	M	10		
27.	NC	79	F	13.5		
28.	NC	70	F	17		
29.	NC	68	F	12.5		
30.	NC	61	M	16		
31.	NC	57	M	16		
32.	NC	51	M	18		
33.	NC	50	M	16		
34.	NC	81	F	14		

* Subject number 1 was assessed as a LPD on the basis of clinical evaluation. No Hoehn-Yahr Scale score was provided.

** On occasion, a + or - score accompanies a Hoehn-Yahr scale score, indicating a slightly higher or lower score, but not enough to merit inclusion in the next stage.

Table 4

Means, standard deviations, and statistical values for demographic, neurological, and general cognitive variables for each subject group.

		Subject Group			Statisical Test	
Variable	Statistic	LPD (n=12)	RPD (n=11)	NC (n=11)	F or t Value	p-Value
Gender	Male\Female	7/5	5/6	6/5	n.a.	n.a.
Age	Mean	72.5	66.6	66.6	1.375	.268
	S.D.	10.16	8.5	10.8	(d.f.=2,31)	
Education	Mean	15.92	15.1	13.6	2.170	.131
	S.D.	3.4	1.8	2.4	(d.f.=2, 31)	
Duration of Illness	Mean	3.67	3.64	--	.001	.972
	S.D.	2.1	2.1	--	(d.f.=1, 21)	
Hoehn-Yahr Stage	Mean	2.4	2.0	--	n.a	n.a.
	S.D.	0.5	0.0	--	n.a	n.a.
Total Motor Severity Score*	Mean	3.94	4.33	--	0.198	>.500
	S.D	2.04	1.32	--	(d.f.=21)	
Total Laterality Ratio**	Mean	-.577	.574	--	0.011	>.500
	S.D.	.291	.204	--	(d.f.=21)	
Mini-Mental State	Mean	28.42	28.46	28.55	0.026	0.974
	S.D.	1.62	1.29	1.13	(d.f.=2,31)	

n.a.= not analyzed

*= sum of right-sided (R) plus left-sided (L) motor symptoms

**= (R-L)/(R+L)

Table 5a

Analysis of Variance for LPDs, RPDs, and NCDs, with means and p values: Right-hemisphere Tasks

	{----------means----------}			
Test	LPD	RPD	NC	p value
Pic Comp	15.08	15.27	14.36	.865
Vis Canc1	29.73	29.82	29.91	.670
Vis Canc2	29.91	30.00	29.91	.611
Vis Canc3	30.00	30.00	29.91	.380
WMS Immed	26.42	28.82	29.82	.614
WMS Delay	20.08	20.91	23.0	.811
Stroop W	92.17	89.18	97.00	.621
Stroop C	58.54	63.22	68.00	.697
OMO*	36.80	35.82	35.73	.382
Fac ID**	16.67	18.73	15.91	.065
Word Emot**	18.75	19.09	19.73	.614
Vis Form**	13.00	14.27	15.46	.111

The first subset of tasks listed above was selected from the literature in which LPDs were significantly impaired relative to RPDs.

** Tasks not uncovered by the literature review but tasks considered to assess right-hemisphere functiong.

* Included in lieu of the WCST which was found in the literature to indicate that LPDs were significantly impaired relative to RPDs.

Table 5b

Analysis of Variance for LPDs, RPDs, NCs, with means and p values: Left-Hemisphere Tasks

	{----------means----------}			
Test	LPD	RPD	NC	p value
Vocab	52.92	50.91	48.18	.435
WAIS Dig F	9.42	10.18	11.36	.324
WAIS Dig B	7.75	8.45	9.09	.593
Anim Naming	17.75	22.36	18.09	.137
Rey 1-5	38.42	48.18	40.40	.080
Rey 6	4.00	5.18	4.10	.340
Rey Imm	7.08	9.82	8.80	.130
Rey Delay	6.00	10.27	7.80	.033***
"F"*	14.67	18.82	15.09	.108
"C"*	14.17	17.64	14.64	.314
"L"*	14.08	15.91	14.18	.634
"FCL"*	42.92	52.36	43.91	.249
"A"-"S"**	13.17	14.82	13.46	.780
Word NonEmot	18.33	19.64	19.36	.370
Zung	47.33	51.82	41.18	.001***

The first subset of tasks was selected from the literature in which RPDs were significantly impaired relative to LPDs

* Tasks not uncovered by the literature review but tasks considered to assess left-hemisphere functioning.

** Included here due to it's verbal nature; it is generally thought to assess frontal-lobe functioning.

*** statistically significant

Table 6a

Post-hoc t-tests: p values for RPD vs. LPD
(Left Hemisphere Tasks)

	p Value RPD vs. LPD	F Ratio (ANOVA for L,R,NC)	
Vocab	.222	.435	0.86
WAIS Dig F	.137	.324	1.17
WAIS Dig B	.317	.593	0.53
Anim Naming	.892	.137	2.12
Rey (Trial 1)	.962	.589	0.54
Rey 2	.315	.056	3.18
Rey 3	.929	.211	1.64
Rey 4	.861	.053	3.25
Rey 5	.599	.162	1.94
Rey 6	.919	.348	1.09
Rey Immed	.259	.130	2.19
Rey Delay	.312	.033	3,81
Rey Total (1-5)	.677	.080	2.76
"F"	.846	.108	2.40
"C"	.847	.314	1.20
"L"	.963	.634	0.46
"FCL"	.873	.249	1.45
"A"-"S"	.910	.780	0.25
Zung	.098**	.001	8.22
Word Non Emot	.371	.370	1.03

* = statistically significant ($p<.05$)

** = trend ($.05<p<.10$)

Table 6b

Post-hoc t-tests: p values for RPD vs. LPD
(Right Hemisphere Tasks)

Test	LPD vs. RPD	ANOVA for L,R,NC P Value	F Ratio
WAIS Pic	.922	.865	0.14
Vis Canc (Tot)	.698	.670	0.40
WMS Immed	.502	.614	0.50
WMS Delay	.868	.911	0.21
Stroop W	.724	.621	0.48
Stroop C	.628	.697	0.37
Stroop WC	.745	.438	0.86
OMO 1	.161	.382	0.99
OMO 2	.892	.649	0.44
OMO 3	.312	.547	0.62
OMO 4	.867	.951	0.05
OMO Total	.634	.830	0.07
Facial ID	.096**	.065	2.99
Word Emotion	.754	.614	0.50
Vis Form Disc	.339	.111	2.37

* = Statistically significant (p<.05)

** = Trend (p<.10)

Table 7a

Analysis of Variance for Early PD (N=33) vs. NC (N=11) Means and p Values: Right Hemisphere Tasks

Test	Early PD (mean)	NC (mean)	p value
WAIS Pic Comp	15.2	14.4	.536
Vis Cancell1	29.8	29.9	.361
Vis Cancell2	30.0	29.9	-
Vis Cancell3	30.0	29.9	-
WMS Immed	27.6	29.8	.486
WMS Delay	21.5	23.0	.503
Stroop W	90.7	97.0	.328
Stroop C	60.9	68.0	.558
Stroop WC	31.7	39.6	.302
OMO1	8.86	8.18	.754
OMO2	9.05	8.73	.273
OMO3	8.90	9.09	.709
OMO4	8.95	8.82	.794
OMO TOTAL	8.94	8.77	.700
Fac ID	17.7	15.9	.087
Word Emotion	18.9	19.7	.299
Vis Form Dis	13.6	15.5	.022*

* = statistically significant

Table 7b

Analysis of Variance for early PD vs. NC: Left Hemisphere Tasks

Test	Early PD (mean)	NC (mean)	p value
Voc	50.6	50.9	.906
WAIS Dig For	10.4	10.2	.860
WAIS Dig Back	8.4	8.5	.976
Anim Naming	17.9	22.4	.057
Rey 1	5.18	5.82	.323
Rey 2	6.86	8.82	.040*
Rey 3	8.18	10.27	.043*
Rey 4	9.09	11.45	.012*
Rey 5	10.09	11.81	.073
Rey 6	4.1	5.2	.117
Rey Immed	7.9	9.8	.099
Rey 30 delay	6.9	10.3	.010*
Rey Total	39.4	48.2	.024*
"F"	14.9	18.8	.038*
"C"	14.4	17.6	.143
"L"	14.1	15.9	.354
"FCL"	43.4	52.4	.106
"A"-"S"	13.3	14.8	.496
Zung	39.6	32.8	.001**
Word Nonemot	18.8	19.6	.239

* = statistically significant

Table 8a

Analysis of Covariance Between RPDs, LPDs, and NCs, With Age, Education, and Depression as Covariates: Right Hemisphere Tasks

Test	(Adjusted Mean) LPD	NC	RPD	(p value) RPD vs. LPD	(p value) Early PD vs.NC
Pic Comp	15.68	13.64	15.35	.877	0.274
Vis Canc1	29.74	30.04	29.68	.808	0.118
Vis Canc2	29.95	29.87	29.99	-	-
Vis Canc3	30.02	29.90	29.97	-	-
WMS Imm	26.99	30.88	27.13	0.971	0.352
WMS Delay	20.58	25.62	17.75	0.610	0.186
Stroop W	60.65	65.39	62.19	0.891	0.790
Stroop C	92.75	96.84	88.70	0.666	0.462
Stroop WC	153.4	168.3	151.54	0.926	0.544
OMO1	9.27	9.06	8.67	0.225	0.871
OMO2	9.52	8.66	9.50	0.985	0.377
OMO3	9.23	9.26	8.44	0.188	0.520
OMO4	8.89	9.92	8.91	0.972	0.978
OMOtot	34.08	38.19	33.62	0.911	0.100
Fac ID	16.41	17.01	17.91	0.264	0.907
Word Emot	18.51	20.36	18.73	0.856	0.088
Vis Form	13.08	16.08	13.56	0.743	0.008*

* = significant at p<.05

Vis Canc2 and Vis Canc3 p values not computed because of lack of differences in mean values

Table 8b

Analysis of Covariance between LPDs, RPDs, and NCs: Left Hemisphere Tasks

Test	(Adjusted Mean) LPD	NC	RPD	(p value) LPD vs. RPD	(p value) Early PD vs. NC
Voc	52.68	52.78	46.57	0.159	0.424
WAIS DigF	9.59	10.44	10.92	0.352	0.904
WAIS DIgB	8.05	8.86	8.36	0.836	0.657
Anim Nam	18.10	22.36	17.71	0.889	0.132
Rey 1	5.29	5.93	4.93	0.640	0.322
Rey 2	6.32	9.23	7.06	0.485	0.035*
Rey 3	8.12	10.27	8.36	0.882	0.111
Rey 4	9.19	11.43	8.98	0.877	0.046*
Rey 5	9.94	11.59	10.22	0.829	0.243
Rey 6	4.03	5.58	3.62	0.705	0.061**
Rey Imm	7.20	9.64	8.86	0.318	0.264
Rey Delay	6.12	10.06	7.89	0.361	0.061**
Rey Tot	38.86	48.45	39.57	0.891	0.061**
"F"	15.53	18.41	14.56	0.689	0.156
"C"	14.74	17.73	13.91	0.760	0.227
"L"	14.48	15.72	13.94	0.819	0.539
"FCL"tot	44.75	51.87	42.41	0.734	0.238
"A"-"S"	13.70	15.04	12.65	0.709	0.513
Word NonE	18.29	19.99	19.05	0.551	0.128
Zung Depr	47.05	41.04	52.27	0.067**	0.002*

* = significant at p<.05
** = trend at p<.10

Zung Depression ANCOVA used only age and education covariates

Table 9a

Motor Scores for RPDs: Tremor, Rigidity, and Bradykinesia

Ss	Tremor				Rigidity				Bradykinesia			
	R	L	Tot	Ratio	R	L	Tot	Ratio	R	L	Tot	Ratio
1.	3	0	3	1.00	2	0	2	1.00	3	0	3	1.00
2.	7	1	8	0.75	2	2	4	0.00	6	0	6	1.00
3.	3	0	3	1.00	3	2	5	0.20	4	4	8	0.00
4.	1	0	1	1.00	3	1	4	0.50	4	1	5	0.60
5.	0	0	0	0.00	2	0	2	1.00	8	0	8	1.00
6.	0	0	0	0.00	2	0	2	1.00	8	3	11	0.45
7.	0	0	0	0.00	1	0	1	1.00	7	0	7	1.00
8.	7	1	8	0.75	2	1	3	0.33	6	0	6	1.00
9.	3	0	3	1.00	3	1	4	0.50	4	4	8	0.00
10.	1	0	1	1.00	3	3	6	0.00	5	6	11	-0.09
11.	1	1	2	0.00	2	1	3	0.33	4	1	5	0.60
M=	2.3	.27	2.64	.792	2.3	1.0	3.3	.533	5.4	1.7	7.1	.613
s.d.=			2.91	.478			1.49	.404			2.47	.424

Table 9b

Motor Scores for LPDs: Tremor, Rigidity, and Bradykinesia

Ss	Tremor				Rigidity				Bradykinesia			
	R	L	Tot	Ratio	R	L	Tot	Ratio	R	L	Tot	Ratio
1.**	-	-	-	-	-	-	-	-	-	-	-	-
2.	1	3	4	-.5	0	2	2	-1.0	0	6	6	-1.0
3.	1	2	3	-.33	2	2	4	0	6	6	12	0
4.	0	2	2	-1.0	1	2	3	-.33	4	4	8	0
5.	1	1	2	0	0	1	1	-1.0	0	0	0	-1.0
6.	0	2	2	-1.0	0	2	2	-1.0	0	4	4	-1.0
7.	0	0	0	0	2	2	4	0	1	4	5	-.60
8.	0	1	1	-1.0	5	7	12	-.17	1	9	10	-.80
9.	0	2	2	-1.0	0	0	0	0	2	5	7	-.43
10.	0	2	2	-1.0	2	3	5	-.20	4	8	12	-.33
11.	1	1	2	0	1	2	3	-.33	0	3	3	-1.0
12.	0	1	1	-1.0	0	2	2	-1.0	0	4	4	-1.0
M=	.36	1.5	1.9	.621	1.2	2.3	3.5	.457	1.6	4.8	6.5	.56

** Subject #1 not assigned a Hoehn-Yahr scale score

Table 9c

Mean Motor Scores for RPDs and LPDs*

{----------RPD----------}			{----------LPD----------}		
No.	Tot Score	Laterality Ratio	No.	Tot Score	Laterality Score
1.	2.67	1.00	**2.	4.00	-0.83
2.	6.00	0.58	3.	6.33	-0.11
3.	5.33	0.40	4.	4.33	-0.44
4.	3.33	0.70	5.	1.00	-0.67
5.	3.33	0.67	6.	2.67	-1.00
6.	4.33	0.48	7.	3.00	-0.20
7.	2.67	0.67	8.	7.67	-0.66
8.	5.67	0.69	9.	3.00	-0.48
9.	5.00	0.50	10.	6.33	-0.51
10.	6.00	0.30	11.	2.67	-0.44
11.	3.33	0.31	12.	2.33	-1.00
M=	4.33	0.57		3.94	-0.58
SD=	1.32	0.20		2.04	0.29

* Average value for tremor, rigidity, and bradykinesia.

** LPD subject number 1 is not included here due to the absence of a Hoehn and Yahr scale score. This subject was diagnosed as exhibiting LPD symptomatology on the basis of clinical observations as reported in his medical files.

Table 10

T-tests for Motor Symptoms for LPDs versus RPDs

	t value
Ratio Scores	
Tremor	.089
Rigidity	.265
Bradykinesia	.113
Total Ratio Score	.011
Right + Left Symptoms	
Tremor	.524
Rigidity	.099
Bradykinesia	.191
Total Symptom Score	.198

Table 11.

Sample size and significance in Hemiparkinson's disease studies

Study	Sample Size LPDs	Sample Size RPDs	Significance
Agniel et al.	10	13	No
Boller et al.	14	13	No
Huber et al. (1989)			
experiment 1	10	17	No
experiment 2	17	14	No
Huber et al. (1992)	10	12	No
Oyebode et al.	9	8	No
Riklan et al.	15	10	No
Blonder et al.	7	14	Yes
Chouza et al.	11	13	Yes
Direnfeld et al.	5	4	Yes
Heitenan et al.	7	5	Yes
Spicer et al.	8	7	Yes
Starkstein et al.	9	9	Yes
Villardita et al.	10	7	Yes

Appendix A

Description and Rationales for Neuropsychological Battery

The following is a list of the tests used in this study, presented in the order in which they were administered.

For each test, the following guide is used:

I. Approximate time of administration

II. Left hemisphere (LH), right hemisphere (RH), or frontal lobe task (if applicable)

*III. Rationale for the selection of the task

*In general, an attempt was made to alternate between RH and LH tasks.

---

1) The Mini-Mental Exam

I. 5'

II. Neither left, right, nor frontal lobe task. Used to sreen for dementia.

III. The mini-mental test was the first test administered, used as a screening test for dementia. Subjects scoring 22 or less (indicative of dementia) out of a possible score of 30 were excluded from further testing.

2) The WAIS-R: Picture Completion subtest

I. 10'

II. RH task

III. The Picture Completion subtest was administered because

a) It is one of the non-verbal subtests of the WAIS-R and generally thought to assess RH functioning.

b) Hietanen and Teravainen (1988) found that there were significant differences ($p<.05$) between left and right HPD patients, with LPDs performing more poorly than RPDs.

3) The WAIS-R: Vocabulary subtest

I. 10'

II. LH task

III. The Vocabulary subtest is thought to assess language (LH) functioning.

4) The WMS-R: Visual reproduction and copy after delayed recall

I. 10'

II. RH task

III. The WMS-R is a test designed to assess memory. functioning. The visual reproduction and copy after delayed recall assesses visual/nonverbal aspects of memory and is therefore usually considered an indication of RH memory functioning. There is a 30" delayed recall portion of this test, so it was administered early in the battery to allow for the delay period.

5) The Stroop Color and Word Test (45 second protocol)

I. 10'

II. Frontal lobe task

III. This task was included in this battery as an assessment of mental control and response flexibility, both thought to be mediated by the frontal lobes. Recent research indicates deficits in some PD patients in frontal lobe functioning.

5) WAIS-R Digit Span subtest

I. 5'

II. RH task

III. The WAIS-R Digit Span subtest was given because

a) It is thought to assess visual attention, perceptual speed, and scanning, which are RH functions.

b) Spicer et al. (1987) found that this test differentiated LPDs and RPDs, with LPDs being more impaired.

6) Facial Emotion Identification

I. 10-15'

II. RH task

III. This task has recently been found to differentiate between right and left brain-damaged patients (Borod, et al., 1990). Also, we were interested in the ability of HPDs to process emotion, an area that has received relatively little testing in studies of HPDs.

7) REY Auditory Verbal Learning Test and delayed recall

I. 15'

II. LH task

III. This test was included because

a) It is a test assessing verbal memory functioning.

b) Starkstein et al. (1987) found that RPDs performed at lower levels than LPDs ($p<.06$).

c) Administered at this point in the testing session to allow for a 30" delay period.

8) CFL and alternating A-S (word fluency)

I. 5'

II. LH/frontal lobe task

III. This test was administered to assess LH functioning, specifically linguistic processes. However, although it is verbal in nature, it is also considered a "frontal" test, as patients with frontal lobe pathology are often impaired on it.

9) Animal Naming (word fluency)

I. 3'

II. LH/frontal lobe task

III. a) See #8, FAS.

b) Blonder et al. (1989) found that RPDs performed more poorly when compared to LPDs.

10) Word Emotion Identification Test

I. 10'

II. RH task

III. This test was administered to assess the role of lexical aspects in the communication (identification) of emotion. Recent research (Borod, 199?) found RPDs impaired on this task when compared to LPDs.

10) Odd Man Out

I. 5-10'

II. Frontal lobe task

III. This test is similar in nature to the Wisconsin Card Sorting Test (WCST), and is a test of mentallexibility and set-shifting abilities, both thought to be mediated by the frontal lobes. Recent research indicates deficits in frontal lobe functioning in some PD patients.

11) Benton Visual Form Discrimination Task

I. 10'

II. RH task

III. This test was chosen to assess right hemisphere functioning, as well as to measure the visuospatial functioning often reported to be compromised in some PD patients.

12) Visual Cancellation

I. 5'

II. RH task

III. This task was chosen because

a) it is thought to be efficient in assessing the right hemisphere's role in visual attention.

b) Villardita et al. (1983) found deficits in bilateral PDs and LPDs, but not RPDs on this task.

13) The Zung Depression Inventory

I. 5'

II. This task is usually not conceptualized as assessing right or left hemisphere functioning, although in this study it may be indicative of left hemisphere pathology.

III. This task was included to provide an indication of depressive symptomatology in our patient and normal

control groups. Also, some research indicates that RPDs exhibit higher levels of depression than LPDs (Direnfeld et al.. 1984; Starkstein et al., 1987).

Appendix B

Criteria for diagnosing Hemiparkinson's disease

Study	Criteria
Agniel, et al., (1991) RPD=10 LPD=10	Parkinsonian motor symptoms were considered as asymmetrical if there was a side-to-side difference of at least two points in at least two of the three main symptoms of the Parkinsonian syndrome (that is, tremor, rigidity, akinesia) rated on the motor examination of the Unified Parkinson's Disease Rating Scale (UPDRS version 1, a close variant of UPDRS version 3, 1978).
Bentin, et al., (1981) RPD=5	Out of 32 PDs, five cases presented with greater involvement of the right and four cases with greater involvement of the left side of the body. No

PD=4	additional information provided.
Blonder et al., (1989) RPD=14 LPD=7	17 patients in Stage 1, 3 in stage 2, and 1 in stage 3 of the Hoehn-Yahr Scale participated in this study. The Diagnosis was made by attending physicians. No additional information given.
Boller et al., (1984) RPD=7 LPD=6	Only subjects in the first 3 stages of the disease form the Hoehn-Yahr Scale were used. No additional information provided.
Canavan, et al., (1989) RPD=6 LPD=3	On the basis of the motor signs six subjects were judged to have predominantly left-sided cerebral pathology, three predominantly right-sided pathology, and nine bilateral pathology. No additional information provided.

Chouza, et al., (1984) RPD=13 LPD=11	1. Intensity of motor symptoms above eight points on the Webster Scale (Scale provided in paper). 2. Evolution time of the disease must be a year or more 3. Lack of tremor in the nonaffected" side. 4. Acceptance of the existence of Froment's sign in the nonaffected side due to its almost constant presence. Also, "mild akinesia" accepted on nonaffected side.
Direnfeld, et al., (1984) RDP=4 LPD=5	The side of greater asymmetry was determined by history and physical examination. The patient was asked which side he believed was more affected by the disease, if any. Asymmetry of involvement was also determined by an examination. Of the three cardinal features, tremor, rigidity, and bradykinesia, it

	was bradykinesia that was given the most weight in determining the side of greater disease involvement. The side of greater disease involvement based on the history and examination was noted as being mild, moderate, or marked.
Hietanen and Teravainen (1989) RPD=5 LPD=7	Clinical disability and extrapyramidal symptoms were valuated using the Columbia University Parkinsonism Disability Rating Scale (CRS). Only patients with Parkinsonian symptoms and signs solely on one side of the body were accepted for the study. A table was provided showing means and standard deviations of each motor sign on the CRS. Exclusion criteria included the presence of rigidity and/or tremor on the intact side, history of tremor on the intact side, and/or clinically significant bradykinesia.

Huber, et al., (1989)	In their first experiment, all patients were rated as stage I on the Hoehn-Yahr Scale. In the second experiment, all
Exp. 1	patients were in stage II to IV on the
RPD=13	Hoehn-Yahr Scale. A table is provided
LPD=10	listing left and right characteristics of rigidity, tremor, tapping, and
Exp.2	foot agility. No additional information
RPD=13	is provided.
LPD=15	

Huber, et al., (1992)	Patients were categorized as having right- or left-predominant PD on the basis of evaluation. Symptoms were
RPD=12	rated on both sides using a scale of 0
LPD=10	(normal function) to 4 (severely impaired) according to the Unified Parkinson Scale (Fahn & Elton, 1987). Patients met criteria for clinical predominance if the side of original involvement was currently more severe on

	at least two of the three symptoms rated and there were no reversals from side to side. Patients were also rated for stage of disease according to the Hoehn-Yahr Scale.
Riklan, et al., (1990) RPD=10 LPD=10	The side of the body showing greater involvement was determined by totalling the ratings for tremor, rigidity and alternating movement impairment for each side. If the total score was one rating point or more different between sides, the side with the higher score was deemed primarily involved.
Spicer, et al., (1988) RPD=7 LPD=8	Determination of asymmetric status was based on the summed CRS ratings (modified from that of Duvoisin [1971]) for resting tremor, action tremor, rigidity, finger dexterity, foot tapping, and alternating hand movements.

	Subjects were assigned to a particular hemiparkinsonian disease group only if the sum of the ratings for one side of the body was at least twice that of the other side.
Starkstein, et al., (1987) RPD=9 LPD=9	A PD score was obtained on the basis of the CRS, but only those items evaluating unilateral signs were considered; bradykinesia was measured as the ability to perform rapid alternating movements. Only PD patients who had at least a 3 to 1 ratio in their CRS when the side of the symptomatic limb was compared with the other side were included.
Villardita et al., (1987) RPD=7 LPD=11	The degree of clinical disability was assessed on the Hoehn and Yahr scale. No additional information provided.

Yokochi, et al., (1986) RPD=14 LPD=13	Patients were selected with stage I to III on the Hoehn-Yahr Scale. The patients were divided into three groups based on the asymmetry of neurological signs between the left and right arms. Tremor and rigidity were rated clinically on a five point scale from 0 to 4. When a patient's total score of both signs on one side was at least twice that of the other side, he/she was classified into the group with lateralised signs.

Appendix C

CONSENT FORM

PERCEPTUAL MOTOR FUNCTION IN AGING

I. Purpose:

I understand that the purpose of this investigation is to evaluate some of the signs and symptoms of Alzheimer's, Parkinson's, Huntington's and vascular diseases. It will involve assessments of emotion, intellectual ability, and motor performance. Healthy individuals will serve as control subjects. This is a research evaluation and some of these procedures may not be part of my routine care.

II. Procedures:

I understand that the following apply to all people who participate in this study. The procedures include:

1. Paper and pencil tests of memory and other intellectualfunctions.
2. Tests that assess motor abilities.
3. Tests that assess emotional symptoms.

These procedures may be completed on separate visits, but can be completed in a single visit.

III. Risks and Benefits:

I understand that the procedures in this study involve minimal risks. I recognize that all reasonable attempts will be made to prevent risks and to minimize inconveniences and discomforts while I participate in this study. I also understand that information gathered in this study that may be useful for understanding my condition will be transmitted to by primary physician.

IV. Inquiries:

I know that attempts will be made to answer inquiries I have raised concerning procedures in this investigation, and that time has bee set aside during the study to answer my

questions. I understand that Drs. Stern and Richards are the principal investigators in this study, and that they will administer the tests which I will perform. I also understand that Dr. Stern and Dr. Richards will be available to answer subsequent questions I may have about this study. I will be given a copy of this form.

V. Consent

I agree to participate as a research subject in this study. I understand that I may withdraw at any time and with any reason without prejudice to my clinical care or treatment. I also understand that I may refuse procedures that my require my participation at any time during the investigation. I also understand that if I refuse any part of this investigation, I will no longer be a participant in this study. however, my medical care at CPMC will not be affected.

I have been informed that if I believe that I have sustained injury as a result of participating in this research study that I may contact the principal investigator, Dr. Stern, or Dr. Richards at 305-4646, so that I may review the matter and identify the medical resources that may be available to me.

I understand that:

a) The Presbyterian Hospital will furnish emergency medical care determined to be necessary by the medical staff of this hospital;
b) I will be responsible for the cost of such care, either personally or through my medical insurance or other form of medical coverage;
c) No monetary compensation for wages lost as a result of injury will be paid to me by Columbia Presbyterian Medical Center.
I will receive a copy of this consent form.

_____ _____
Signature of Subject Date

_____ _____
Signature of Investigator Date

The Institutional Review Board of the Columbia Presbyterian Medical Center has approved the solicitation of subjects to participate in this research project.

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