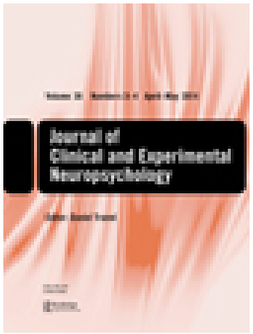

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Cognitive and Affective Functioning in Parkinson's Disease Patients with Lateralized Motor Signs*

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ABSTRACT

Eleven patients with Parkinson's disease (PD) and predominantly right-sided motor signs, 12 patients with PD and predominantly left-sided signs, and 11 demographically matched healthy controls were compared on tests assessing a range of cognitive and affective functions. Assuming a novel approach, our test battery was composed of measures drawn from ones previously used in the hemiparkinson's disease and lateralized PD literature. The two patient groups were similar in illness duration, severity of motor signs, and degree of lateralized motor deficits. Statistical analyses did not reveal significant differences between patient groups, consistent with other studies that have failed to find differences in neuropsychological functioning between PD patients with right- and left-sided motor signs.

In Parkinson's disease (PD), the onset of motor signs and symptoms (rigidity, bradykinesia, and tremor) can present itself primarily or exclusively on either the right or left side of the body. When the motor dysfunctions are exclusively unilateral, the disorder is referred to as Hemiparkinson's disease (HPD). When the motor dysfunctions are expressed bilaterally, but with one side of the body having more severe symptomatology, we suggest the disorder be referred to as lateralized Parkinson's disease. In most patients, lateralization of symptoms is a fairly transient condition associated with disease onset of Parkinsonism, while in others, it remains for years. In either HPD or lateralized PD, it is assumed that the underlying neuropathology is located mainly in contralateral subcortical regions.

Studies investigating neuropsychological functioning in HPD and lateralized PD have yielded mixed results. Some studies have demonstrated compromised cognitive functioning in patients with PD and left-sided signs (LPDs) compared to patients with PD and right-sided signs (RPDs) (Bowen, Hoehn, & Yahr, 1972; Direnfeld et al., 1984; Fleminger, 1991; Hietanen & Teravainen, 1989; Villardita, Smirni, & Zappala, 1983). In contrast, one study has

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shown that patients with RPD are cognitively more impaired than patients with LPD (Spicer, Roberts, & Lewitt, 1988). Other studies have found that group differences are consistent with lateralization of function (e.g., Blonder, Gur, Gur, Saykin, & Hurtig, 1989; Chouza et al., 1984; Starkstein, Leiguarda, Gershanik, & Berthier, 1987). That is, patients with RPD are impaired on ''left hemisphere'' tasks, whereas patients with LPD are impaired on ''right hemisphere'' tasks. Further, in at least two studies, there have been lateralized differences for one PD group but not the other (e.g., for patients with RPD [Huber, Miller, Bohaska, Christy, & Bornstein, 1992]; for patients with LPD [Villardita et al., 1983]). Finally, another set of studies has failed to show any significant neuropsychological differences between patients with RPD and patients with LPD (Agniel et al., 1991; Blonder, Gur, & Gur, 1989; Huber, Freidenberg, Shuttleworth, Paulson, & Clapp, 1989; Riklan, Stellar, & Reynolds, 1990).

The present study was designed to address contradictions in the literature regarding cognitive functioning in lateralized PD, using a unique approach to select the cognitive measures. Based on a review of the literature, tests shown to significantly differentiate between patients with LPD and patients with RPD were used to construct the battery for the current study. We reasoned that such a battery would be most sensitive to any potential differences between the two lateralized groups. Measures of affective processing and depression were also included. Although some research on lateralized PD and depression has been conducted (e.g., Blonder, Gur, & Gur, 1989; Cummings, 1992; Fleminger, 1991; Spicer, Roberts, & LeWitt, 1988; Starkstein, Mayberg, Leiguarda, Preziosi, & Robinson, 1992), relatively few studies (e.g., Blonder, Gur, & Gur, 1989) have examined more general affective functioning in lateralized PD.

The battery developed was used to test the hypotheses that patients with RPD would exhibit greater deficits than patients with LPD on measures assessing left-hemisphere functioning and that patients with LPD would exhibit greater deficits than patients with RPD on measures assessing right-hemisphere functioning. In addition, we determined whether PDs, relative to healthy controls, would exhibit deficits in cognitive and affective functions.

METHODS

Participants

Participants were 12 patients with LPD, 11 patients with RPD, and 11 healthy control (HC) adults. Participants were right-handed, native speakers of English ($n = 42$) or fluent by an early age ($n = 2$), with no history of neurological disorder (secondary for patients with PD), dementia, psychiatric illness, psychotropic medication use, or alcohol/substance abuse. The only PD medication administered to all patients was Sinemet, an L-dopa agonist.

Patients with PD were outpatients at a motor disorders clinic at a large urban medical center. The same neurologist (L.J.C.) examined each patient to confirm the diagnosis of PD and to rate motor-sign severity. Idiopathic PD was defined by clinical and research criteria, including the presence of two of the four cardinal features of PD (tremor, rigidity, bradykinesia, and postural instability; Hughes, Ben-Schlomo, Daniel, & Lees, 1992; Hughes, Daniel, Kilford, & Lees, 1992; Ward & Gibb, 1990). Healthy controls were recruited from a pre-existing research participant pool.

The three groups (LPD, RPD, and HC, respectively) did not differ significantly ($p<.05$) from each other on gender (58%, 45%, and 55% male), age (72.5 [10.2], 66.6 [8.5], and 66.6 [10.8] years), education (15.9 [3.4], 15.1 [1.8], and 13.6 [2.4] years), or global cognitive status (28.4 [1.6], 28.5 [1.3], and 28.6 [1.1], as evaluated by the Mini-Mental State Exam; Folstein, Folstein, & McHugh, 1975). Also, the RPD and LPD groups did not differ significantly on illness duration (3.7 [2.1] and 3.6 [2.1] years, respectively), disease stage (2.4 [0.5] and 2.0 [0.0]; Hoehn and Yahr scale, 1967), or total severity score for motor signs (3.8 [2.0] and 4.3 [1.3], as assessed by the Unified Parkinson's Disease Rating Scale [UPDRS; Stern & Hurtig, 1978] and averaged for bradykinesia, tremor, and rigidity).

Next, the total motor laterality ratio score ([R – L]/[R + L]) was examined. Ratio scores ranged from –1.000 (exclusively left-sided) to +1.000 (exclusively right-sided). When considering the mag-

nitude (via absolute values) of the laterality ratios, patients with LPD (M = .552; SD=0.291) and patients with RPD (M = .574; SD=0.204) did not differ (t = 0.08, df = 21, p > .500). However, when focusing on the degree/direction of lateralization, patients with LPD (M = –.552) and patients with RPD (M = +.574) were significantly different from each other (t = 4.20, df = 21, p < .01). Further, each PD group's ratio score was significantly (p < .01) different from a mean score of zero (i.e., no lateralization).

Procedures

Each participant was administered a neuropsychological battery, consisting of 15 tests (references provided in Table 1), based on a review of the HPD and lateralized PD literature. Tests found to significantly differentiate between LPD and RPD groups were used. Tests assessing affective processing (Facial and Word Emotional Identification Tasks) and depression (Self-Rating Scale) also were employed. To examine other functions frequently compromised in PD (Brown & Marsden, 1990; Flowers & Robertson, 1985; Raskin, Borod, & Tweedy, 1990; Stern, 1983), tests assessing executive/frontal-lobe functioning (Alternating A-S and Odd Man Out) and visuospatial processing (Visual Form Discrimination) were included in the battery.

These 15 tests were categorized as tapping predominantly right- or left-hemisphere functions (Table 1). For tests that emerged from the lateralized PD literature review, a test was categorized as a right hemisphere (RH) task if patients with LPD were significantly impaired and as a left hemisphere (LH) task if patients with RPD were significantly impaired. Facial and word emotional identification tests were included in the RH list due to selective deficits for patients with right-brain damage on these tests (Borod, Andelman, Obler, Tweedy, & Welkowitz, 1992; Borod et al., 1990, 1998). The depression test was included in the LH list due to its frequent association with left-brain damage (Gainotti, 1972; Starkstein & Robinson, 1988). The visuospatial processing test was assigned to the RH list. One frontal test (Odd Man Out) was assigned to the RH list due to its visual characteristics, and the other (Alternating A-S) to the LH list due to its verbal nature. Altogether, there were eight predominantly RH tests, involving 12 separate measures, and seven predominantly LH tests, involving 13 separate measures. RH and LH tests were alternated during administration in a fixed order.

RESULTS

A series of one-way ANOVAs was conducted on Group (LPD, RPD, and HC), separately for each of the 25 measures under study. To test specific hypotheses, post hoc contrasts (LPD group vs. RPD group; PD group vs. HC group) were conducted (Rosenthal & Rosnow, 1985) for each one-way ANOVA yielding significance. To adjust for experimentwise error rate for the omnibus F tests, the Bonferroni correction was used (i.e., p = .05/25 or .002).

Of the 25 ANOVAs conducted, only the one for the Zung Depression Scale was significant, F (2,31) = 8.22, p = .001 (see Table 1 for group means and ANOVA values). When the post hoc contrast between PD groups was conducted, although patients with RPD (M = 51.8; SD = 5.3) had higher Zung scores than patients with LPD (M = 47.3; SD = 7.0), the comparison was not significant, F (1,20.34) = 2.99, p = .099. When the contrast between the PD group (M = 49.5; SD = 6.6) and the HC group (M = 41.2; SD = 5.9) was conducted, the PD group endorsed significantly more depressive symptoms than the HC group, F (1,20.44) = 14.39, p = .001.

DISCUSSION

The purpose of this study was to elucidate and clarify neuropsychological differences that might exist between PD patients with primarily right-sided and left-sided motor signs. To date, the literature in this area has been equivocal. The results of the current study, which incorporates many of the measures used previously, support the view that there are no significant differences in cognitive and affective functioning between patients with RPD and LPD.

From a neurophysiological perspective, our results may not be that surprising. When considering HPD, one is most likely dealing with a disorder involving bilateral subcortical damage. PD occurs when deterioration of the substantia nigra/basal ganglia complex reaches 80%. As it has been observed that HPD is almost always a transient state that soon develops into bilateral PD (Chouza et al., 1984), a completely unilat-

Table 1. List of Tests, Measures, and References.

Test	Reference	LPD vs. RPD Source	Individual Measure	Possible Score Range	LPD *M* (*SD*)	RPD *M* (*SD*)	HC *M* (*SD*)	ANOVA for all 3 groups *F*	ANOVA for all 3 groups *p*
Right-Hemisphere Tasks (8 tests, 12 measures)									
WAIS-R	Wechsler, 1981	H,T	Picture Completion Subtest	0–20	15.1 (5.7)	15.3 (3.1)	14.4 (2.9)	0.15	.865
Visual Cancellation	Hamsher, 1976	V,S,Z	Left side of page	0–30	29.7 (0.6)	29.8 (0.4)	29.9 (0.3)	0.41	.670
			Middle of page	0–30	29.9 (0.3)	30.0 (0.0)	29.9 (0.3)	0.50	.611
			Right side of page	0–30	30.0 (0.0)	30.0 (0.0)	29.9 (0.3)	1.00	.380
Memory Scale-Revised	Wechsler, 1987	B,G,G,S,H	Vis. Rep. Immediate Recall	0–41	26.4 (8.8)	28.8 (8.1)	29.8 (8.5)	0.50	.614
			Vis. Rep. Delayed Recall	0–41	20.1 (12.4)	20.9 (11.2)	23.0 (9.1)	0.21	.811
Stroop Test (45-s version)	Stroop, 1935	H,T	Color Section	0–100+	58.5 (17.8)	63.2 (23.4)	68.0 (23.3)	0.37	.697
			Interference Section	0–100+	32.5 (11.7)	30.8 (12.1)	39.6 (14.4)	0.86	.438
Facial Emotion	Borod, Martin, Alpert, Brozgold, & Welkowitz, 1993		Identification Task	0–21	16.7 (3.4)	18.7 (2.1)	15.9 (2.7)	2.99	.065
Lexical Emotion	Borod, Andelman, Obler, Tweedy, & Welkowitz, 1992		Identification Task	0–21	18.8 (3.0)	19.1 (2.0)	19.7 (1.8)	0.50	.614
Visual Form	Benton, Hamsher, Varney, & Spreen, 1983		Discrimination Task	0–16	13.0 (3.9)	14.3 (2.1)	15.5 (1.2)	2.37	.111
Odd Man Out	Richards, Cote, & Stern, 1993		Total (Trials 1-4)	0–40	36.8 (2.9)	35.8 (6.0)	35.7 (3.6)	0.19	.830

Table 1 continues.

Table 1. continued.

Test	Reference	LPD vs. RPD Source	Individual Measure	Possible Score Range	LPD *M* (*SD*)	RPD *M* (*SD*)	HC *M* (*SD*)	ANOVA for all 3 groups *F*	*p*
Left-Hemisphere Tasks (7 tests, 13 measures)									
WAIS-R Vocabulary	Wechsler, 1981	B,G,G,S,H	Vocabulary Subtest	0–70	52.9 (9.8)	48.2 (8.2)	50.9 (7.8)	0.86	.435
WAIS-R Digit Span	Wechsler, 1981	S,R,L	Digit Span Forwards	0–14	9.4 (2.6)	11.4 (3.3)	10.2 (3.3)	1.17	.324
			Digit Span Backwards	0–14	7.8 (3.2)	9.1 (3.1)	8.5 (3.1)	0.53	.593
BDAE	Goodglass & Kaplan, 1983	B,G,G,S,H	Animal Naming Subtest	0–	17.8 (5.1)	18.1 (6.5)	22.4 (6.0)	2.12	.137
Auditory Verbal Learning	Rey, 1964	S,L,G,B	Total Recall (Trials 1-5)	0–75	38.4 (11.0)	40.4 (10.9)	48.2 (9.3)	2.78	.080
			Interference (Trial 6)	0–15	4.0 (2.3)	4.1 (2.2)	5.2 (1.7)	1.09	.348
			Immediate Recall	0–15	7.1 (3.2)	8.8 (3.6)	9.8 (2.7)	2.19	.130
			Delayed Recall (30 min.)	0–15	6.0 (4.2)	7.8 (3.9)	10.3 (2.8)	3.81	.033
Oral Word Association	Benton & Hamsher, 1976	S,R,L	‘‘F’’ (1 minute)	0–	14.7 (3.9)	15.1 (6.1)	18.8 (4.7)	2.40	.108
			‘‘C’’ (1 minute)	0–	14.2 (5.5)	14.6 (6.0)	17.6 (5.8)	1.20	.314
			‘‘L’’ (1 minute)	0–	14.1 (4.5)	14.2 (5.6)	15.9 (5.1)	0.46	.634
Oral Word Association	Raskin, Borod, & Tweedy, 1992		Alternating ‘‘A-S’’	0–	13.2 (5.3)	13.5 (6.6)	14.8 (5.9)	0.25	.780
Depression	Zung, 1965		Self-Rating Scale	20–80	47.3 (7.0)	51.8 (5.3)	41.2 (5.9)	8.22	.001

Note. LPD = patients with PD and left-sided signs; RPD = patients with PD and right-sided signs; HC = healthy control participants; WAIS-R = Wechsler Adult Intelligence Scale-Revised; Vis. Rep. = Visual Reproductions; BDAE = Boston Diagnostic Aphasia Examination; H,T = Hietanen & Teravainen, 1989; V,S,Z = Villardita, Smirni, & Zappala, 1983; B,G,G,S,H = Blonder, Gur, Gur, Saykin, & Hurtig, 1989; S,R,L = Spicer, Roberts, & Lewitt, 1988; S,L,G,B = Starkstein, Mayberg, Leiguarda, Gershanik, Barthier, 1987.

eral HPD group most likely has from 50% to 80% substantia nigra/basal ganglia damage on the ''unaffected'' side. Further, it is known that a 50% loss of the substantia nigra/basal ganglia fibers is a normal, age-related event. Therefore, when assessing lateralization of function in either exclusively or predominantly unilateral PD, one is almost assuredly assessing, to some extent, bilateral brain damage.

On the other hand, from a methodological perspective, there are several reasons why there could have been no differences in neuropsychological functioning between RPD and LPD groups. In terms of power, although a small sample does diminish the statistical power to detect group differences, it does not necessarily bias effect size. Examination of the effect sizes from ANOVAs that were conducted indicates that, in general, effect sizes were quite low, especially for comparisons between the LPD and the RPD groups. In terms of sampling, as described above, we were rigorous in selecting participants and careful in matching the two PD groups for clinical factors (i.e., illness duration, motor severity, and degree of lateralized motor signs) and in matching all three groups for demographic variables (i.e., gender, age, and education) and global cognitive status. Finally, it may be the case that the lack of cognitive and affective differences between the RPD and the LPD groups is a real phenomenon.

When combining the patients with LPD and the patients with RPD into one group and comparing them to the healthy control group, depression scores were higher in the patient group, consistent with earlier findings comparing patients with PD to controls and to other neurological populations (e.g., Cummings, 1992; Dakof & Mendelsohn, 1986; Levin, Llabre, & Weiner, 1988).

In summary, the strengths of the current study involve the use of a sensitive battery of tests and well-matched, carefully screened participant groups. This study supports the view that patients with left-sided and right-sided Parkinson's disease do not present different neuropsychological profiles.

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