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Frontostriatal circuits are necessary for visuomotor transformation: Mental rotation in Parkinson's disease

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Abstract

The mental rotation of objects requires visuospatial functions mediated by the parietal lobes, whereas the mental rotation of hands also engages frontal motor-system processes. Nondemented patients with Parkinson's disease (PD), a frontostriatal disorder, were predicted to be impaired on mentally rotating hands. Side of PD motor symptom onset was investigated because the left motor cortices likely have a causal role in hand mental rotation. The prediction was that patients with right-side onset (RPD, greater left-hemisphere dysfunction) would commit more errors rotating hands than patients with left-side onset (LPD). Fifteen LPD, 12 RPD, and 13 normal control adults (NC) made same/different judgments about pairs of rotated objects or hands. There were no group differences with objects. When rotating hands, RPD, but not LPD, made more errors than the NC group. A control experiment evaluated whether visual field of presentation explained differences between PD subgroups. In the first experiment (1A), the hand to be mentally rotated was presented in the right visual field, but here (1B) it was presented in the left visual field. Only the LPD group made more errors than the NC group. The evidence suggests a double dissociation for the RPD and LPD groups between tasks differing in visual-field presentation. The findings indicate that hemifield location of a to-be-rotated hand stimulus can cause the hemispheric frontoparietal networks to be differentially engaged. Moreover, frontostriatal motor systems and the parietal lobes play a necessary role during the mental rotation of hands, which requires integrating visuospatial cognition with motor imagery.

Keywords: Visual spatial; Parietal cortex; Motor imagery; Visual object; Hemispheric laterality; Basal ganglia

1. Introduction

Diverse visuospatial functions are impaired in Parkinson's disease (PD), including route walking, angle size estimation, left–right decisions, and visuospatial closure (reviewed in Cronin-Golomb and Amick (2001)). There is currently no consensus, however, as to whether or not PD patients are impaired on mental rotation tasks. Some studies have reported spared mental rotation abilities in PD patients (Boller et al., 1984; Duncombe, Bradshaw, Iansek, & Phillips, 1994; Raskin et al., 1990). Other studies that instead documented impaired performance considered whether different stimulus types may engage different cognitive operations on mental rotation tasks (Dominey, Decety, Broussolle, Chazot, & Jeannerod, 1995; Lee, Harris, & Atkinson, 1998). In particular, mental rotation of objects invokes object-centered transformations, whereas mental rotation of hands invokes viewer-centered transformations. Each mode of mental transformation is associated with a distinct network of brain regions. These networks are likely affected differentially by the neuropathology of PD.

During the mental rotation of objects, the coordinate system is object-centered; objects are rotated in space irrespective of the viewer's position in the environment (Cronin-Golomb & Amick, 2001; Ogden, 1990). In the

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typical experimental design, two objects appear in different orientations and are either identical to each other ("same" objects) or left–right mirror images of each other ("different" objects). Response time to make "same" or "different" judgments has been found to increase linearly as the difference in orientation between the two objects increases. The linear relation between angular disparity and response time and error rate is interpreted as evidence that observers imagine the object moving through space along the same continuous trajectory as if they were physically rotating the object into the upright position (Cooper & Shepard, 1975).

Behavioral and neuroimaging studies have shown that posterior parietal cortices, especially in the right hemisphere, are engaged during the successful execution of the mental rotation of objects. Behavioral studies of object mental rotation support a unique role for the right parietal lobe (reviewed in Corballis (1997)). Neuroimaging studies with a parametric design reveal a linear increase in activation of the intraparietal sulcus (IPS) as the degree of rotation is increased. The IPS may be responsible for the scaling of mental rotation task performance with angular disparity (Carpenter, Just, Keller, Eddy, & Thulborn, 1999; Harris et al., 2000; Podzebenko, Egan, & Watson, 2002). Neuroimaging findings of lateralization are more mixed but similar to behavioral studies in favoring right-hemisphere dominance. Specifically, some neuroimaging studies reveal lateralized activity in the superior and inferior parts of the right parietal lobe (Harris et al., 2000; Vingerhoets et al., 2001), whereas others report instead bilateral posterior parietal activation (Carpenter et al., 1999; Cohen et al., 1996; Kosslyn, DiGirolamo, Thompson, & Alpert, 1998; Podzebenko et al., 2002; Richter et al., 2000; Richter, Ugurbil, Georgopoulos, & Kim, 1997). Some studies reporting bilateral parietal activation, however, do support a right-hemisphere advantage for this task, finding more extensive activation in the right than left hemisphere (Carpenter et al., 1999; Podzebenko et al., 2002).

By contrast, the mental rotation of hands may be performed using a different strategy of viewer-centered transformation, wherein viewers consider their own spatial coordinates with respect to other objects in the environment (Cronin-Golomb & Amick, 2001; Ogden, 1990). During this cognitive operation, viewers are thought to access and then manipulate a mental representation of their body in space (Kosslyn et al., 1998).

In contrast to the right-hemisphere advantage for object-centered transformations, regions in the left hemisphere appear to be necessary for viewer-centered transformations, as shown in studies of patients with lateralized brain damage or artificially induced transient dysfunction. For example, autotopagnosia, the disorientation of personal space, and right–left disorientation are two neuropsychological disorders that occur in patients with left posterior parietal-lobe lesions (De Renzi, 1982; Semmes, Weinstein, Ghent, & Teuber, 1963; Sirigu, Grafman, Bressler, & Sunderland, 1991). Parsons, Gabrieli, Phelps, and Gazzaniga (1998) examined the mental rotation of left and right hands projected to either the left or right hemisphere in two callosotomy patients and a control group, and observed a left hemisphere advantage. The patients were accurate only when mentally rotating the hand processed routinely by that hemisphere, demonstrating a double dissociation, but all participants tended to be more accurate when targets were presented to the left relative to the right hemisphere. These findings were taken as evidence that the left hemisphere has representations of both hands, whereas the right hemisphere has representations only of the contralateral left hand. Ganis, Keenan, Kosslyn, and Pascual-Leone (2000) found that applying transcranial magnetic stimulation to the hand region of the left primary motor cortex impairs performance for the mental rotation of images of hands, and more so than for the mental rotation of images of feet. Critically for the present study, these findings also indicate that the mental rotation of hands draws upon the same cortical regions necessary for overt movement.

In studies comparing object-centered and viewer-centered transformations directly, differences have been found in behavioral hemispheric dominance and in neural activity within hemispheres. Specifically, Tomasino, Toraldo, and Rumiati (2003) found a double dissociation of performance on object and hand mental rotation in patients with left- versus right-hemisphere lesions. Patients with left-hemisphere lesions are impaired at mentally rotating hands but not objects, whereas patients with right-hemisphere lesions show the opposite pattern. In a neuroimaging study, Kosslyn et al. (1998) had participants perform a mental rotation task with Shepard and Metzler (1971) objects or hands. Mental rotation of objects elicited bilateral activation in superior and inferior parietal areas, whereas the mental rotation of hands elicited activation in left parietal and left frontal regions centered on primary motor, premotor, and supplementary motor areas. Taken altogether, convergent findings indicate that object-centered transformations require primarily the IPS of the right hemisphere, whereas viewer-centered transformations require primarily the motor cortex of the left hemisphere.

These two main cortical regions for mental rotation of objects and hands are likely disrupted by the neuropathology of PD. Consider that the loss of dopamine-producing cells in the substantia nigra results in dysregulation of the striatum and consequently in dysfunction of multiple circuits connecting the basal ganglia with motor and cognitive cortical regions (Middleton & Strick, 2000a, 2000b). Neurons of the substantia nigra and the globus pallidus, the basal ganglia output nucleus, terminate in non-overlapping prefrontal regions (Middleton & Strick, 2000a). This connectivity pattern suggests that the prefrontal cortex may be functionally deafferented in PD due to reduced dopamine availability in the basal ganglia. Critically for mental rotation, the prefrontal and posterior parietal cortices are densely interconnected and share zones of termination within the striatum. Further, both regions are part of a large neural circuit that is specialized for spatially guided behavior, and this circuit includes the head of the caudate nucleus (Selemon & Goldman-Rakic, 1988) which is depleted of dopamine even at the earliest stages of PD (Kish, Shannak, & Hornykiewicz, 1988).

An important aspect of the neuropathology of PD to consider in studies of mental rotation is hemispheric asymmetry, for two reasons. First, as already noted, differences in hemispheric dominance have been found on mental rotation tasks requiring either viewer- or object-centered transformations. Second, in PD, the onset of motor symptoms is typically unilateral, and asymmetric motor symptoms have been associated with asymmetrical dopamine depletion in the basal ganglia across the range of disease severity (Antonini et al., 1995; Innis et al., 1993; Laulumaa et al., 1993; Leenders et al., 1990; Tissingh et al., 1998). Asymmetrical metabolism likely has consequences for the function of areas receiving inputs from or projecting to the basal ganglia, including parietal and motor regions supporting mental rotation. Body side of motor symptom onset may therefore be an important factor to consider when assessing PD patients' performance on mental rotation tasks.

Consistent with this idea of hemisphere effects, several reports suggest that patients with RPD (right-side onset, greater left-hemisphere dysfunction) and LPD (left-side onset, greater right-hemisphere dysfunction) show different mental rotation deficits. RPD but not LPD patients make more errors on a personal orientation task (viewer-centered transformation) than a control group (Bowen, Burns, Brady, & Yahr, 1976). Further, RPD patients are slower at mentally rotating hands (viewer-centered transformation) than a control group, whereas groups do not differ when mentally rotating alphanumeric stimuli (object-centered transformation) (Dominey et al., 1995); note, LPD patients were not tested. In a study by Lee et al. (1998), LPD patients were impaired relative to a control group on the mental rotation of objects (object-centered transformation) in three dimensions (3D) but not two dimensions (2D); note, RPD patients were not tested. To our knowledge, no study has directly compared RPD to LPD patients on tasks requiring object- versus viewer-centered transformations, as in the present research.

The present study aimed to determine if RPD and LPD patients differ in their performance on mental rotation tasks with objects, requiring object-centered transformations, or with hands, requiring viewer-centered transformations. PD patients were expected to perform more poorly on the mental rotation of hands than objects because mentally rotating hands would engage a more extensive region of dysfunctional cortex (primary and association motor and parietal cortices) than rotating objects (parietal). In addition, we hypothesized that side of motor-symptom onset would influence the severity of impairment on mental rotation. Specifically, because object mental rotation is associated with more extensive right-hemisphere processing, LPD patients were hypothesized to be the more impaired group. By contrast, because hand mental rotation engages largely left parietal and frontal areas, RPD patients were hypothesized to be more impaired.

As a contrast to the mental rotation of objects, the hands task was designed to elicit maximal involvement of the left hemisphere. To do so, the hand to be mentally rotated always appeared in the right visual field. This design (Experiment 1A) is used widely in the hand mental rotation literature, and serves to facilitate comparison with prior studies. Its limitation is that visual field of presentation, instead of stimulus type, could account for poorer performance by the RPD than the LPD group on mental rotation of hands. Specifically, while the evidence reviewed so far suggests that the left hemisphere has a dominant role in performing egocentric transformations, visual-field presentation may have been a factor. As information from one visual field is processed first in the contralateral hemisphere, the side of presentation and not the stimulus type may explain lateralized brain activity. In prior studies of hand mental rotation, the hand to be rotated was shown in the right visual field, and left hemisphere engagement was observed (Ganis et al., 2000; Kosslyn et al., 1998). To examine this, a control study (Experiment 1B) assessed a subsample of participants performing mental rotation of hands with the hand to be rotated appearing instead in the left visual field. If visual field of presentation determines the hemisphere recruited for hand mental rotation, then, in this case, the LPD group would be the more impaired group. If so, then together Experiment 1A and 1B results may also indicate a double dissociation of RPD and LPD groups on hand mental rotation, depending upon the visual field of presentation.

2. Method

2.1. Experiment 1A

2.1.1. Participants

Fifteen individuals with LPD (8 women), 12 with RPD (5 women), and 13 healthy normal control (NC) individuals (5 women) who were community volunteers took part in this study. LPD, RPD, and NC groups were matched closely for age, education, male:female ratio, and general cognitive status (mini mental state examination (Folstein, Folstein, & McHugh, 1975); dementia rating scale (Mattis, 1988). Table 1 summarizes group characteristics. Methods conformed to the ethical standards described in the 1964 Declaration of Helsinki and were approved by the Boston University Institutional Review Board (IRB), Charles River Campus, and the Boston Medical Center IRB. Participants gave informed consent prior to inclusion.

Individuals with PD were recruited from the Parkinson's Disease Clinic at the Boston Medical Center and local support groups. Review of PD participants' medical records confirmed diagnosis of idiopathic PD, side of disease onset, and disease duration, which did not differ significantly between PD subgroups (LPD $M = 7.5$ years, S.D. = 3.4; RPD $M = 6.2$ years, S.D. = 3.8; $t[26] = .5$, ns). None had undergone any brain surgery. A Hoehn and Yahr (H–Y) score for stage of motor disability was provided by each PD participant's neurologist. Groups did not differ in the frequency of LPD and

Table 1
Group characteristics

	Group	Mean	S.D.	*F*	*p*
Age	LPD	66.0	11.0	1.46	n.s.
	RPD	59.9	6.9		
	NC	62.7	9.9		
	Range	46–80			
Education	LPD	16.8	2.9	.84	n.s.
	RPD	17.8	2.8		
	NC	17.6	2.7		
	Range	12–21			
MMSE	LPD	29.3	.9	.72	n.s.
	RPD	29.1	.9		
	NC	29.5	1.0		
	Range	27–30			
DRS	LPD	140.8	4.2	.59	n.s.
	RPD	140.6	4.5		
	NC	142.2	3.0		
	Range	135–144			
BDI-II	LPD	9.0	4.9	7.18	.002
	RPD	10.3	4.9		
	NC	2.5	2.0		
	Range	0–27			

LPD: left body side of motor symptom onset, RPD: right body side of motor symptom onset, NC: normal control, MMSE: mini mental state examination, DRS: dementia rating scale, BDI-II: Beck depression inventory.

RPD ($\chi^2[2, N = 27] = .9$, ns) at each H&Y stage (1.5 = 1 LPD, 1 RPD; 2 = 11 LPD, 8 RPD; 3 = 3 LPD, 3 RPD).

All PD participants were taking medication for their parkinsonian symptoms. At the time of testing, the motor response was at its optimum (“on” period). Among LPD participants, seven followed a medication regimen that included levodopa/carbidopa therapy alone ($n = 1$), or in combination with another dopamine agonist ($n = 3$), or a dopamine agonist plus dopaminergic medication (amantadine, $n = 2$ or selegiline, $n = 1$). Three were treated with levodopa/carbidopa therapy and amantadine ($n = 1$), or a monoamine oxidase inhibitor type B (MAO B) ($n = 1$), or an MAO B plus an anticholinergic ($n = 1$). The remaining five did not receive levodopa/carbidopa pharmacotherapy but instead followed a medication regimen of a dopamine agonist ($n = 1$), or a dopamine agonist plus either an MAO B ($n = 1$), a catechol-*O*-methyltransferase inhibitor (COMT) ($n = 1$), or an anticholinergic ($n = 2$). Three LPD participants were on antidepressants, and two were treated also with a benzodiazapine.

Of RPD participants, seven received levodopa/carbidopa therapy alone ($n = 1$), in combination with one other dopamine agonist ($n = 3$), or a dopamine agonist plus a dopaminergic medication (amantadine, $n = 1$ or COMT, $n = 2$). Four were treated with levodopa/carbidopa therapy and amantadine ($n = 1$), an MAO B ($n = 1$), a COMT ($n = 1$), or an MAO B inhibitor plus a COMT ($n = 1$). One was treated with only a dopamine agonist plus amantadine. Two RPD participants were being treated with an antidepressant.

Participants were interviewed about their medical history, and their medical records were examined to rule out confounding diagnoses, such as stroke, head injury, and serious medical illness. They also answered questions about ophthalmologic health to ensure that they did not have ocular/optical abnormalities. All participants, except for one from each group (LPD, RPD, NC), underwent a detailed neuro-ophthalmological examination within a year of the study. Examinations were conducted by the same neuro-ophthalmologist of the Boston University Eye Associates for all participants, except one control participant whose exam was completed by his own ophthalmologist according to our criteria for determining intact visual functioning. No participant had any ocular illnesses or abnormalities that could have influenced their performance on the visuospatial measures. All participants had binocular central acuity equal to or better than 20/40. There was no group difference in the distribution of participants at the five acuity levels (20/16, 20/20, 20/25, 20/32, 20/40), $\chi^2(8, N = 40) = 7.1$, ns. The Functional Acuity Contrast Test (Stereo Optical Co. Inc., Chicago, IL) was used to assess near and far static spatial contrast sensitivity. There were no group differences on the measures of contrast sensitivity, all $p > .2$. The three participants who did not receive an eye exam had binocular acuity and contrast sensitivity within the same range as the other participants.

2.1.2. Materials

Stimuli were shown on a 17 in. Studio Display color monitor controlled by a Power Mac G3 computer with microphone (Sony ECM-MS907). The mean luminance of the testing room (sampled from six different locations) was 17.1 cd/m^2.

Four sets of line drawings of objects (Shepard & Metzler figures) and four sets of right and left hands were created. Four objects and four finger configurations (two front and two back of the hand) were used to minimize practice effects (as in Ganis et al. (2000)). For each of the hand and object blocks, 144 pictures were created: eight unique stimuli for each type of mental rotation (four same and four mirror images) at each mental rotation increment (nine different angles, from 0° to 180° in 20° increments) for two axes of rotation (2D; 3D). There were 144 trials in one block of objects and 144 trials in another block of hands.

Stimulus pairs were formed by placing one object or left hand (oriented upright) in a circle, subtending ∼5° visual angle, on the left side of the computer screen and placing a rotated hand or object in a circle on the right side of the screen (Fig. 1). For hands, in the right visual field, half of the stimuli were a right hand and the other half a left hand. The left visual-field stimulus was always an upright left hand. To minimize the potential for left–right confusion, the fixed hand was presented on their natural side only. Specifically, presenting a fixed left hand in the left visual field, consistent with its natural side, was designed to encourage participants to visualize manipulating their right hands to evaluate the rotated figure in the right visual field. This presentation was expected to recruit mainly the left hemisphere, providing a contrasting condition for the mental rotation of objects.

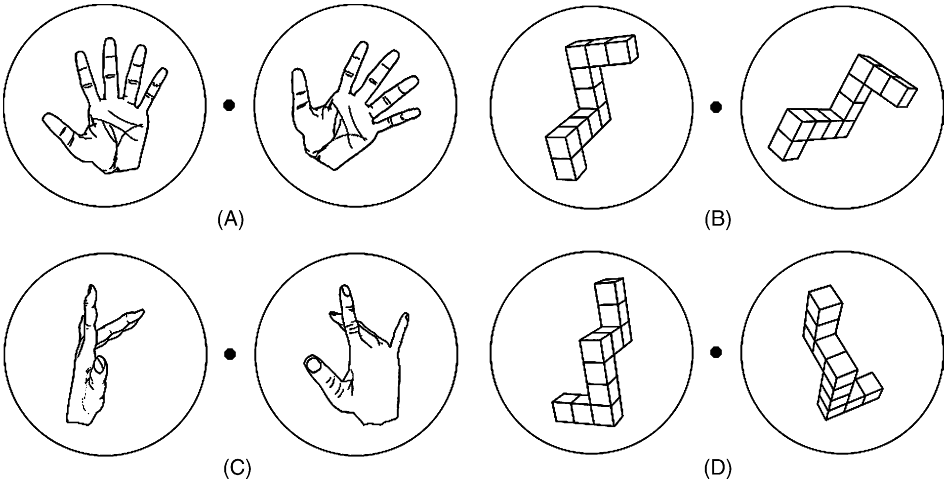

Fig. 1. Mental rotation stimuli. (A and B) Examples of pairs of hands and objects rotated in 2D space when the correct response is “same”. (C and D) Examples of pairs of hands and objects rotated in 3D space when the correct response is “different”.

2.1.3. Procedures

Participants sat in a chair with a chin rest supporting the head. The eye-to-monitor distance was ∼72 cm. After fixating a central black spot for 500 ms, a stimulus pair was shown until a response was verbalized. There was unlimited time to respond. Participants both read and heard instructions asking them to say “same” if the hand (or object) on the right side of the screen was identical to the hand (or object) on the left side. They were asked to say “different” if the hand (or object) on the right side of the screen appeared to be mirror-reversed images from the hand (or object) on the left-side (Fig. 1). Instructions encouraged participants to be as fast and as accurate as possible, stressing that accuracy was more important than speed to further minimize motor demands.

To explain the strategy to solve both mental rotation tasks, participants were given a task demonstration using real models of pairs of objects and hands that they held and manipulated. Here, one hand (or object) was presented in the upright position on the participant’s right side and the other hand (or object) was presented on the participant’s left side. The stimulus on the right side was then rotated into an upright position. Critically, participants were not allowed to physically move their hands while solving each mental rotation trial. Rather, this demonstration aided participants in developing a mental representation of how to solve the task. After this, they were given separate practice blocks (hands or objects) of 18 trials with 10° rotation increments (10–170°) using the methods of the experimental blocks, except only one nonexperimental object or hand configuration was practiced.

Methods of measuring response time (RT) in individuals with PD are problematic because of the motor symptoms of the disease (e.g., slow response initiation, low voice volume), and for this reason, number of errors was our primary dependent measure. A voice onset time was used instead of a finger press because the brain regions controlling hand movements overlap with brain regions recruited to process the mental rotation of hands (Ganis et al., 2000). This RT was a secondary dependent measure.

Object and hand stimuli were presented in separate blocks counterbalanced across participants. Each block consisted of equal numbers of identical- and mirror-imaged stimuli, configurations, and rotation angles. Trials occurred pseudorandomly with the following constraints. No more than three of the same response (“same” or “different”) could occur in a row; the same angular disparity could not be shown a second time until all other angular disparities had been shown once (and so forth), and the same hand/object configuration could not be shown a second time until all other configurations were shown once (and so forth), as in Kosslyn et al. (1998). The plane of rotation was switched after every trial. This presentation was used to maintain a high level of mental rotation throughout the experiment because factors such as order of presentation and training can alter task demands. Specifically, given enough trials or a predictable format (i.e., increments of 20°), mental rotation tasks may be facilitated by memory (Tarr & Pinker, 1989). To control for order effects, two separate orders of presentation were created. Both orders were administered, one for hands and one for objects, and this presentation was counterbalanced across participants. For example, one participant would be given hands following Order 1 and objects following Order 2, then the next participant would be given objects following Order 1 and hands following Order 2.

2.2. Experiment 1B

2.2.1. Participants

A subset of participants from Experiment 1A was tested: seven LPD (three men, four women, age $M = 61.7$ years, S.D. = 9.3; education $M = 18.1$ years, S.D. = 3.2; disease duration $M = 5.6$ years, S.D. = 3.0; H–Y score Mdn = 2), six RPD (two men, four women, age $M = 60.8$ years, S.D. = 10.5; education $M = 16.0$ years, S.D. = 2.5; duration $M = 8.2$, S.D. = 5.7; H–Y score Mdn = 2), and six NC (two men, four women, age $M = 62.3$ years, S.D. = 6.5; education $M = 17.0$ years, S.D. = 2.5). Groups did not differ significantly on any of these participant characteristics.

2.2.2. *Materials and procedures*

Methods were identical to Experiment 1A with two exceptions. First, participants performed only the mental rotation of hands task. Second, the hand to be mentally rotated was presented in the *left* visual field, and the right visual-field stimulus was always an upright right hand.

3. Results and discussion

3.1. *Experiment 1A*

The primary dependent measure was total number of errors, but mean RTs for correct responses were also analyzed separately. To increase power, errors and RTs were collapsed across the three levels of rotation: low (20–60°), medium (80–120°), and high (140–180°). To remove outliers, an RT cut-off of the mean ± 2 S.D.s was applied to each of the three rotation levels, removing less than 4% of the data for all participants and conditions. Data were analyzed separately for mental rotation of objects and hands in two-way repeated measures ANOVAs with a within-subjects factor of Rotation (low, medium, high) and between-subjects factor of Group (LPD, RPD, NC).

In addition, the slopes and y-intercepts of the best fitting line (in the least squares sense) of the mental rotation functions for errors and RTs were analyzed using one-way ANOVAs with the Group factor. The slope provides the rotation rate (number of errors/degree and ms/degree for errors and RTs, respectively) and is a key measure of the actual mental rotation process, whereas the y-intercept is thought to be affected primarily by more general processes occurring before (e.g., stimulus encoding) or after (e.g., response preparation) mental rotation proper (Shepard & Cooper, 1982).

3.1.1. *Depth*

For errors, we assessed a factor of Depth and found no significant interaction of Group on mental rotation in 2D versus 3D (all $p > .2$). Further analyses collapsed across depth.

3.1.2. *Order*

Separate ANOVAs on errors and RTs with an added between-subjects factor of Order of picture presentation revealed no significant effect of order on the hand and object tasks (all $p > .2$). Further analyses collapsed across order.

3.1.3. *Gender*

Because women as a group have been noted to have a relative disadvantage on tasks of mental rotation (reviewed in Cronin-Golomb and Amick (2001)), Gender was considered as a between-subjects factor in separate ANOVAs on errors and RTs. No effect of Gender was significant (all $p > .2$). Further analyses collapsed across gender.

3.1.4. *Other demographics*

The PD groups differed significantly from the NC group on the Beck depression inventory-II (BDI-II; Table 1). Five PD participants attained scores above 14 on the BDI-II (consistent with at least mild symptoms of depression) but their mental rotation data did not differ from the rest of the PD group. Correlations between scores on the BDI-II and errors or RTs for each mental rotation task were not statistically significant (all $r < .1$). The possible effect of various medications on mental rotation performance was examined. There was no significant difference between PD participants who were taking levodopa/carbidopa and those who were not for each mental rotation task (all $p > .2$). Likewise, for each of the mental rotation tasks, there was no significant difference between PD participants who were taking a dopamine agonist and those who were not (all $p > .2$). To examine the contribution of disease severity and performance on the experimental measures, correlations were conducted between errors, RTs, and H&Y motor disability scores. None were statistically significant (Spearman's all $\rho < .2$). Similarly, the correlation between disease duration (in years) and errors and RTs for each mental rotation task was not significant (all $r < .2$). Further analyses did not consider these factors.

3.1.5. *Objects*

One RPD participant who was unable to complete this task was excluded.

Main Rotation effects were significant for errors (Fig. 2A; $F[2, 72] = 125.20$, $p < .0001$) and RTs (Fig. 2B; $F[2, 72] = 42.94$, $p < .0001$) but not for Group effects (both Fs[2, 36] < .3, ns) or Group × Rotation interactions (errors $F[4, 72] = 2.20$, $p = .08$; RTs $F[4, 72] = .18$, ns). For RTs, a Huynh–Feldt correction for violation of the sphericity assumption applied ($\varepsilon = .68$; $p < .0001$).

3.1.5.1. *Slopes and intercepts.* The slopes and y-intercepts of the best fitting lines of the mental rotation functions did not differ between groups for errors and RTs, all $F < 1.6$ and $p > .2$.

3.1.6. *Hand errors*

Main effects of Group ($F[2, 37] = 3.47$, $p = .04$) and Rotation ($F[2, 74] = 52.89$, $p < .0001$) and the interaction of Group × Rotation ($F[4, 74] = 2.94$, $p = .03$) were significant (Fig. 3a); a Huynh–Feldt correction for violation of the sphericity assumption was applied ($\varepsilon = .90$; $p = .01$).

The significant Group effect was assessed further in planned comparisons using Fisher's least significant difference (LSD) test. The hypothesis that the RPD group would make significantly more errors on the mental rotation of hands than the NC group was supported ($p = .01$). The LPD

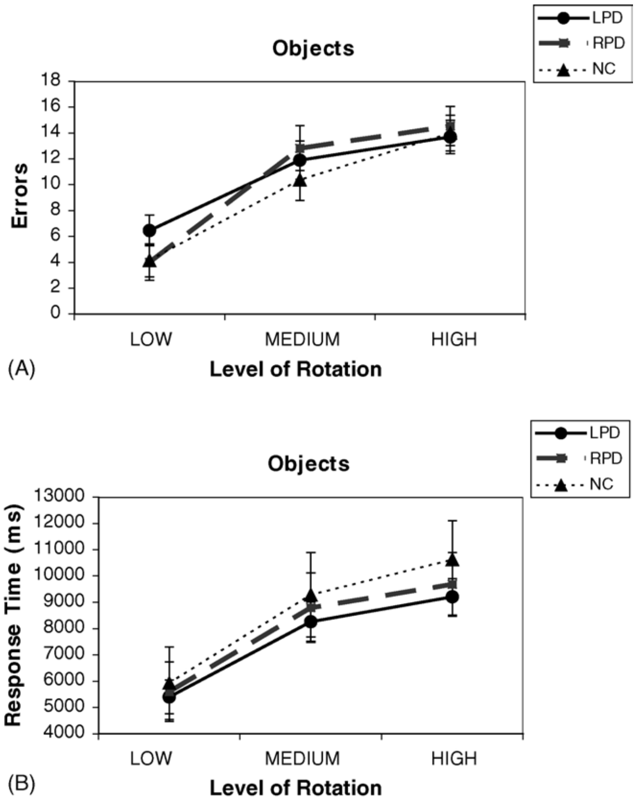

Fig. 2. Mean number of errors (A) and mean RTs (B) for the LPD, RPD, and NC groups on the mental rotation of objects collapsed across rotation axis (2D, 3D) in Experiment 1A. Nine rotation angles were collapsed into three levels of rotation: low (20°, 40°, 60°), medium (80°, 100°, 120°), and high (140°, 160°, 180°).

group did not differ significantly from RPD ($p = .33$) and NC ($p = .09$) groups.

3.1.6.1. *Slopes and intercepts.*

Critically, the slopes, but not *y*-intercepts, of the best fitting lines of the mental rotation functions differed significantly between groups (main Group effect, $F[2, 37] = 4.03$, $p = .03$) (Fig. 3a). Planned comparisons using the LSD test indicated that the slopes differed significantly between RPD and NC groups ($p = .008$), but not between LPD and RPD groups ($p = .26$) and the LPD and NC groups ($p = .08$).

3.1.7. *Hand RTs*

Data from one RPD participant were excluded due to disproportionately slower RTs (>2 S.D.s above the mean) than other participants; removal of these data did not change the results. The ANOVA showed that the main effect of Rotation was significant ($F[2, 72] = 40.3$, $p < .0001$) but not the main effect of Group ($F[2, 36] = .06$, ns) or the Group × Rotation interaction ($F[4, 72] = .81$, ns) (Fig. 3b).

3.1.7.1. *Slopes and intercepts.*

These did not differ between groups, all $F < 1.4$ and $p > .3$.

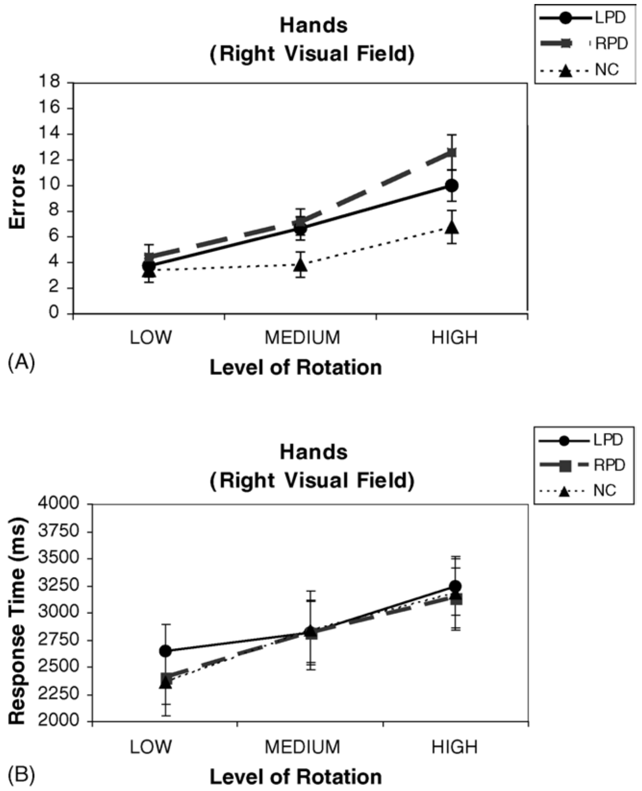

Fig. 3. Mean number of errors (A) and mean RTs (B) for the LPD, RPD, and NC groups on the mental rotation of hands collapsed across rotation axis (2D, 3D) in Experiment 1A. The hand to be mentally rotated was presented in the right visual field. Nine rotation angles were collapsed into three levels of rotation: low (20°, 40°, 60°), medium (80°, 100°, 120°), and high (140°, 160°, 180°).

3.1.8. *Summary*

Altogether, the error results demonstrate a single dissociation of RPD patients on mental rotation tasks with objects versus hands. Moreover, the slope findings indicate that the impairment with hands shown in the *right* visual field affects the mental rotation process itself rather than some non-specific process preceding or following mental rotation.

3.2. *Experiment 1B*

Errors and RTs on hand mental rotation were analyzed as in Experiment 1A.

3.2.1. *Hand errors*

Main effects of Group ($F[2, 16] = 5.24$, $p = .018$) and Rotation ($F[2, 32] = 15.62$, $p < .0001$) were significant but not the Group × Rotation interaction ($F[4, 32] = 1.18$, ns). The significant Group effect (Fig. 4) was assessed further in planned comparisons using the LSD test. Here, with left visual-field presentation, the LPD group, made significantly more errors than both the NC ($p = .01$) and RPD groups ($p = .02$). As these results contrast with the normal LPD performance with right visual-field presentation (Experiment 1A), results from

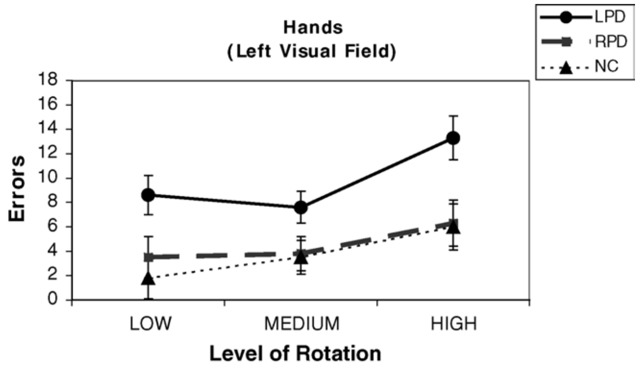

Fig. 4. Mean number of errors for the LPD ($n=7$), RPD ($n=6$), and NC ($n=6$) subgroups on the mental rotation of hands when the hand to be mentally rotated was presented in the left visual field (Experiment 1B). Results are collapsed across rotation axis (2D, 3D). Nine rotation angles were collapsed into three levels of rotation: low (20°, 40°, 60°), medium (80°, 100°, 120°), and high (140°, 160°, 180°).

the two experiments indicate a single dissociation of LPD patients on mental rotation of hands, depending upon visual-field presentation.

3.2.1.1. Slopes and intercepts. A one-way ANOVA showed that *y*-intercepts (but not slopes) differed significantly between groups ($F[2, 16] = 3.53$, $p = .05$). Planned comparisons with the LSD test indicated that the *y*-intercepts differed significantly between LPD and NC groups ($p = .02$) but not between the LPD and RPD groups ($p = .13$) or the RPD and NC groups ($p = .34$). Experiment 1B data thus support a single dissociation whereby RPD patients show steeper slopes with right but not left visual-field presentation and suggest further evidence for an LPD impairment with left but not right visual-field presentation.

3.2.2. Hand RTs

Main effects of Group and Rotation and their interaction were not significant (all $F < 2.2$ and $p > .1$).

3.2.2.1. Slopes and intercepts. These did not differ between groups (all $F < 2.8$ and $p > .09$).

3.2.3. Summary

Across Experiments 1A and 1B, the observed pattern of error results suggests a double dissociation. Specifically, RPD patients show impairment relative to NC with right but not left visual-field presentation, whereas LPD patients show impairment relative to NC with left but not right visual-field presentation. Moreover, the slope results indicate a single dissociation of RPD patients on mental rotation of hands shown in the right but not left visual field and that the core deficit affects the mental rotation process. In contrast, the *y*-intercept results suggest a single dissociation with LPD patients on mental rotation of hands shown in the left but not right visual field; this deficit perhaps affects the mental rotation process, but more likely a process preceding mental rotation that is differentially recruited depending on visual-field presentation.

4. General discussion

Findings support the first hypothesis that individuals with PD are more impaired on the mental rotation of hands than objects. Specifically, PD patients make more errors than the control group while mentally rotating hands but show no impairments with objects, revealing a single dissociation. Findings also support the second hypothesis that side of motor symptom onset predicts impairments on mental rotation tasks. Specifically, regarding errors on hand mental rotation, relative to the control group, RPD patients are impaired with right (Experiment 1A) but not left (Experiment 1B) visual-field presentation, showing a single dissociation. In contrast, LPD patients show the opposite single dissociation, being impaired with left but not right visual-field presentation. Together, these findings suggest a double dissociation between RPD and LPD groups on the hand mental rotation task, depending upon whether the hand to be mentally rotated appears in the visual field that is ipsilateral to their side of onset.

Evidence was also obtained that dysfunction of the core mental rotation process, as opposed to other processes recruited by the task, is the cause of impaired hand rotation. The evidence was clear for RPD but only suggestive for LPD. In particular, relative to the NC group, a steeper mental rotation slope characterizes the performance accuracy of the RPD group with right but not left visual-field presentation. As slope results are thought to probe the mental rotation process per se (Shepard & Cooper, 1982), this constitutes strong evidence for a single dissociation of RPD patients on the mental rotation process itself when hands are shown in the right but not left visual field.

LPD patients, by contrast, show only a higher *y*-intercept of the mental rotation curve with left but not right visual-field presentation. Effects on *y*-intercepts are thought to reflect pre- or post-rotation processes, as opposed to a mental rotation function itself (Shepard & Cooper, 1982). Given visual-field dependence, the LPD deficit may be related more to an input process preceding mental rotation, instead of a post-rotation process. For example, the problem for LPD when the hand to be mentally rotated was presented in the left visual field (Experiment 1B) may be related to the lack of a right hand representation in the right hemisphere (Parsons et al., 1998). Even so, we note that slope effects are very sensitive to noise (especially when the linear fit is performed on a small number of data points) (e.g., Ganis et al., 2000; Kosslyn et al., 1998); the apparent (Fig. 4), but null, slope difference in Experiment 1B leaves open the possibility that the hand mental rotation function itself may also have been affected in LPD, but we did not detect it.

We conclude that the LPD and RPD groups show a double dissociation regarding errors on hand mental rotation, depending upon the side of visual-field presentation. The source of the impairment in RPD is clearly the mental rotation process itself but in LPD it may mainly be a prior process recruited for the task. Taken together, these findings provide evidence that the visuospatial and motor-related neural networks supporting mental rotation of body parts within each hemisphere can be differentially recruited depending upon the visual-field location of the to-be-rotated limb.

4.1. Hemisphere effects

In the present study, the relation between side of motor symptom onset and errors on hand mental rotation is driven by visual-field presentation. Likewise visual-field presentation may have influenced findings in earlier studies reporting hemispheric dominance during hand mental rotation. Reports of a unique involvement of the left hemisphere during mental rotation of hands also confounded visual-field presentation (Ganis et al., 2000; Kosslyn et al., 1998). By design, the hand to be mentally rotated was shown only in the right visual field, as also in our Experiment 1A. Our data suggest that visual-field presentation partially accounts for prior findings of left-hemisphere advantage in the mental rotation of hands. Though the mental rotation of hands may require some specialized processes mediated by only the left hemisphere (Ganis et al., 2000), the current findings emphasize the importance of considering hemifield presentation when studying patients with lateralized deficits.

4.2. Viewer-centered transformation

The specificity of our findings for viewer-centered transformations is highlighted by our observation of no significant group difference on the mental rotation of objects, even though this was a more difficult task than the same one with hands. All groups produced more errors and slower RTs when the task required mentally rotating objects compared to hands; the interaction of Rotation (low, medium, high) by Task (objects versus hands) was significant for both errors ($F[2, 35] = 20.5$, $p < .0001$) and RTs ($F[2, 35] = 19.4$, $p < .0001$). The neuropathology of PD appears to disrupt the distinct neural network required for accurate mental rotation of hands.

On mental rotation of objects, groups did not differ in the number of errors made. This null result contrasts with that of Lee et al. (1998), who found LPD patients to be more impaired than a control group on this task with 3D rotations. Participant differences may explain these apparently contrary findings. Participants in the current study were matched for education and were nondemented with normal cognitive status, whereas these factors were not reported by Lee et al. (1998). Differences in education level, which is used widely to estimate general intelligence, and in overall mental status may have resulted in differences between the LPD and control groups on this challenging task.

Dominey et al. (1995) also found viewer-centered transformation is disrupted in PD. Specifically, RPD patients were slower than an NC group when mentally rotating hands but not alphanumeric characters. Further, PD patients showed RT correlations between hand mental rotation and imagined and overt finger movements. Deficient motor, rather than visuospatial, processing was the proposed explanation, but the core mental rotation process may not have been strongly recruited in this study. A single hand posture and few rotation angles were used, and so repetition priming (e.g., reduced RTs for repeated relative to new items) could have reduced the magnitude of mental rotation effects (Schendan & Kutas, 2003; Tarr & Pinker, 1989). In contrast, the design of the present study aimed to minimize repetition effects, using four postures at nine angles, and so maximize mental rotation effects and the opportunity to observe a PD deficit, as found for errors.

More important, our results do not support a simple relation between motor functioning and hand mental rotation in PD. Specifically, a measure of motor disability, Hoehn and Yahr stage, did not correlate with errors for the mental rotation of hands. Perhaps more important, the PD and NC groups did not show RT differences during hand mental rotation. The absence of a relation between motor impairment and the mental rotation of hands indicates that brain regions other than the basal ganglia may be predominantly involved in viewer-centered transformations.

4.3. Visuomotor neural systems

There is an alternative explanation for deficient performance on the mental rotation of hands, other than dysfunction of processes necessary for overt movement. Goodale and Milner (1992) have proposed that the primary function of the dorsal visual pathway, and particularly the posterior parietal lobe, is to mediate the visuomotor transformations necessary for visually guided actions directed at the environment. Studies of rhesus monkeys have found that the main output of the anterior intraparietal sulcus (AIP) is F5 (part of the ventral premotor cortex) (Luppino, Murata, Govoni, & Matelli, 1999), and single cell recordings reveal that neurons in F5 (Rizzolatti, Fogassi, & Gallese, 1997) and AIP (Sakata & Taira, 1994) respond to both 3D stimuli and goal-related hand movements. The finding that visual and motoric information activate the same neurons suggests that these processes are relatively integrated under certain conditions, such as viewer-centered transformations. Because neurons in AIP and F5 are responsive to both visual and motor information, impaired reaching and grasping behaviors, which require viewer-centered transformations, are not indicative of motoric dysfunction alone.

Evidence from the animal literature (Selemon & Goldman-Rakic, 1988; Yeterian & Pandya, 1993) supports the hypothesis that the IPS, which is critical for performing mental rotation, may be disrupted in PD. In rhesus monkeys, the IPS sends direct projections to the basal ganglia. Specifically, the upper bank of the IPS projects to the rostral and intermediate zones of the putamen, and the lower bank of the IPS projects predominantly to the head of the caudate nucleus (Yeterian & Pandya, 1993). Further, the dorsolateral prefrontal cortex projects also to the caudate head as part of a reciprocal striatal-thalamo-cortical circuit (Middleton & Stick, 2000a). Consider that the frontal and parietal lobes are densely interconnected. The loss of dopamine in the caudate and putamen in PD may therefore disrupt both unidirectional projections from the posterior parietal lobes and reciprocal connections between posterior parietal and dorsolateral prefrontal cortex.

4.4. Neural dysfunction in PD

The neuropathology of PD is consistent with disruption of the frontal–parietal circuits and their subcortical connections. An autopsy study found that the dorsal and intermediate zones of the putamen and caudate head are affected earliest in PD and show the most profound loss of dopamine as the disease progresses (Kish et al., 1988). Based on the neuropathological and animal findings, the functions of both the frontal and parietal lobes (i.e., regions critical for mental rotation) are likely to be disrupted due to reduced dopamine availability in the striatum.

5. Conclusions

In the present study, a single dissociation was found between hand and object mental rotation in PD. Individuals with PD have an impaired ability to mentally rotate hands but not objects. General motoric dysfunction does not account for this deficient performance because errors on hand mental rotation do not correlate with motor impairment, and RTs do not differ between groups. More important, a double dissociation was found for two PD groups on two hand mental rotation tasks. Specifically, body side of PD motor symptom onset predicts impairment on the mental rotation of hands, with the relation between side of motor symptoms and errors driven by visual-field presentation. The hemifield of the to-be-rotated stimulus causes the two hemispheres to be differentially recruited for a hand mental rotation task. Further, the impairment in RPD affects the slope of the rotation function, indicating an underlying dysfunction specific to hand mental rotation. Deficient performance on the mental rotation of hands therefore points to abnormal functioning of cortical regions, such as fronto-parietal circuits, not only the basal ganglia.

Taken together, these findings indicate that PD patients can be substantially impaired on a spatial task that requires visuomotor transformation. Because visual and motoric functions are highly integrated, limiting research to tasks of spatial cognition that are independent of motoric processes will yield a limited and inaccurate description of the visuospatial impairments associated with PD. The present neuropsychological findings indicate that frontal motor and posterior parietal cortices are necessary for the visuomotor transformations supporting hand mental rotation, which requires integration of visuospatial information with motor imagery.

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