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Automatic orienting of visuospatial attention in Parkinson's disease

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Abstract

The basal ganglia are involved in not only motor behavior, but also other more cognitive processes, such as attention. We tested Parkinson's disease (PD) patients in a task that measures reflexive orienting of spatial attention. Seven patients with idiopathic PD and eight control subjects performed a covert orienting task where spatial attention was directed by means of exogenous cues (luminance increments) with no predictive validity for target position. The subjects' task was to make a speeded saccade to a visual target, which appeared a variable time after onset of the cue either in the cued or an uncued spatial position. There was no overall difference between PD patients and control subjects in terms of the initial facilitation following reflexive cues, and later inhibition of return (IOR). However, PD patients differed from control subjects in two important respects. First, they were significantly faster than were control subjects on this reflexive visual-orienting task. Second, disease severity correlated with attentional performance; more advanced patients showed less initial facilitation but greater IOR. Thus PD patients show better performance on a reflexive saccade task and, for more advanced patients, greater IOR than control subjects. These findings are consistent with the possibility that reflexive attentional processes in PD patients may be more active.

1. Automatic orienting of visuospatial attention in Parkinson's disease

Although the basal ganglia (BG) are commonly assumed to be involved in motor control or programming, more recently they have been implicated in higher cognitive behavior as well [10,11,20,39]. Parkinson's disease (PD) is believed to be caused by a loss of dopaminergic innervation of the BG, and PD patients have been observed to show deficits in a number of cognitive paradigms [9,15,23,51]. More generally, their specific deficit has been postulated to be due to a problem with internal, as opposed to an external, control over attention [5].

The present study examines the performance of PD patients on a task of spatial attention. Spatial attention (or spatial orienting) refers to the act of selectively processing information from one location or region in visual space. Specifically, we addressed whether the postulated deficit that PD patients have with internal but not external control over attention, also applies to spatial orienting.

At the outset, one can distinguish between two distinct modes of spatial orienting. "Overt" orienting involves making an eye movement to a particular location of interest, whereas "covert" orienting requires attention to be shifted to this location while the eyes remain fixated elsewhere. Several studies have examined overt orienting in PD, and there is a general consensus that internal control of eye movements through voluntary saccades (remembered, delayed, predictive, and antisaccades) are deficient in PD patients populations

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[4,7,8,31]. At the same time there appears to be no deficit in PD for purely reflexive or visually guided saccades [4,6,7,27]. Thus, studies of overt orienting in PD suggest deficits in voluntary (internal) control, but no deficit in reflexive (external) control.

In comparison with the relatively large number of studies investigating overt orienting in PD, there have been fewer studies of covert orienting in this population. Many of these have reported inconsistent and/or conflicting results, with some finding smaller covert orienting effects in PD [53,54] and others finding no difference [2,37,46]. A critical weakness of these studies is a failure to independently manipulate *voluntary* vs. *reflexive* control of covert orienting. This is particularly important since, as indicated above, it is well documented that PD patients have deficits in voluntary control of *overt* orienting (eye movements), but show no deficit for externally controlled reflexive eye movements. It is critical to know whether an analogous pattern occurs for *covert* orienting as well.

Voluntary covert attention is normally controlled by using symbolic cues such as arrows to direct the subject to shift attention to the indicated spatial location, whereas reflexive covert attention is controlled by presenting a brief cue stimulus in the visual periphery that automatically draws attention to the location of the cue. Only two studies have compared the effects of spatial cues requiring voluntary and reflexive shifts of covert spatial attention in PD patients, Filoteo et al. [12] and Yamaguchi et al. [55]. Furthermore, both of these studies used several different time intervals between cue and target, permitting an examination of changes in covert orienting across time for the two types of cues.[1]

Both studies reported that PD patients showed relatively normal cueing effects with voluntary (i.e., internally controlled) cues at short or intermediate stimulus onset asynchronies (SOAs) between cue and target. That is, PD patients were facilitated when targets appeared as late as 250 ms [12] or 500 ms [55] following valid cues. However, these facilitatory voluntary cueing effects were eliminated at longer SOAs (1000 and 800 ms for Filoteo et al. and Yamaguchi et al., respectively) in PD patients but not controls. Thus, the ability to sustain voluntarily oriented covert attention seemed to be deficient in PD, a finding directly analogous to the pattern observed with voluntarily controlled overt orienting.

When Filoteo et al. [12] and Yamaguchi et al. [55] looked at externally controlled, or reflexive attention in PD, they found that PD patients did not differ from controls at short cue-target SOAs. However, both studies reported altered cueing effects in PD at long cue-target intervals. Filoteo et al. [12] reported a decrease in *inhibition* following valid cues. This inhibitory effect following valid exogenous cues is referred to as inhibition of return (IOR) [26] and is believed to reflect an automatically generated bias against returning attention to previously attended spatial locations. In contrast, in Yamaguchi et al.'s study [55] this altered cueing effect in PD took the form of a more persistent *facilitation* for PD subjects following valid cues. The facilitation effect for control subjects was eliminated at the longer SOA, presumably because of a buildup of IOR. The continued observation of facilitation in the PD subjects was consistent with the possibility that their IOR was somehow deficient. Both of these findings suggest that PD patients have problems in reflexive attention, and are in contrast to the findings of normal or better performance in reflexive *overt* orienting (i.e., eye movements).

Thus the literature on *covert* orienting in PD is somewhat discrepant compared to the *overt* orienting literature in PD. Whereas there is clear evidence for a deficit in voluntary but not reflexive control of eye movements in PD [4], the two most definitive investigations of covert spatial attention in PD suggest deficits of both voluntary and reflexive attentional processes [12,55]. We carried out the present study in order to control for possible design flaws in those studies in hopes of resolving this discrepancy. Specifically, neither of these studies used an optimal procedure to control reflexive spatial attention. Both Yamaguchi et al. [55] and Filoteo et al. [12] used exogenous cues that were predictive of target location, thus conflating reflexive and voluntary attentional effects. That is, targets appeared more often at cued than at uncued spatial locations. Failure to prevent the involvement of voluntary attentional processes (that are already thought to be deficient in PD) may have contributed to the differences in the results of the two studies, as well as to the apparent conclusion that reflexive *covert* orienting is deficient in PD.

The present study compared PD and control subjects in a covert spatial orienting task using exogenous cues (luminance increments) to direct attention. We explicitly varied cue-target SOA in a manner which elicited both the early facilitation and later IOR [33–35], and most importantly, used cues which had no predictive validity whatsoever vis a vis target location. Under these conditions, we were able to test whether purely reflexive covert orienting is normal, less efficient, or more efficient in PD than in control subjects.

[1] A study by Rafal et al. [36] compared covert spatial orienting in PD and progressive supranuclear palsy (PSP) patients. That study used both voluntary and reflexive cues, and also manipulated the timecourse, with cue-target intervals ranging from 50 to 550 ms. While the RT timecourse data for their PSP subjects were presented in some detail, the corresponding data from the PD patients were not shown. Thus it is difficult to discern the relative performance of their PD patients on the voluntary and reflexive covert attention tasks, or how the cueing effects might have changed over time.

Table 1
Background data for Parkinson's patients and control subjects

Patients	Age	Hoehn & Yahr stage	UPDRS (motor)	Disease duration (yr)	MMSE	Medications[a]	Education	Gender
	75	2	30	23	30	L, T, R, O	14	M
	59	3	38	5	27	L, L-SR, S	16	M
	67	2.5	41.5	12	24	L, A, O	9	M
	78	3	28.5	11	25		16	M
	79	3	16.5	4	28	L, S, A	12	F
	72	1.5	19.5	2	27	L, Bz	13	F
	77	2.5	33	7	26	T, S, P, Lx, M, C, B	12	M
Average	72.4		29.6	9.1	26.7		13.1	
Control	66				28		14	M
	74				28		20	M
	67				26		12	M
	66				28		11	M
	74				26		12	M
	79				25		12	M
	73				27		12	M
	82				28		12	M
Average	72.6				27.0		13.1	

[a] L – L-dopa, L-SR – sustained release L-dopa, T – trihexyphenidyl, S – selegine, A – amantidine, R – ropinerole, Bz – benztropine, P – pergolide, O – oxybutynin, Lx – levothyroxine, M – maprotiline, C – clozapine, B – buspirone.

2. Method

2.1. Subjects

Seven patients with mild to moderate idiopathic PD were tested along with eight normal controls; all subjects were non-demented and non-depressed. Background statistics on the patients and controls are given in Table 1. All patients had clinically typical PD, as reviewed by at least one movement disorder specialist and their motor disabilities were responsive to anti-Parkinsonian medications.[2] Any potential subjects suspected at all of showing additional deficits in other neural systems (''Parkinson plus'' patients) were excluded. Other than PD, none of the patients or control subjects tested had any known neurological disorder. These subjects were also part of another study of eye movements in PD [4]. One PD patient who was included in this other study was unable to complete the present experiment (due to fatigue). All subjects were assessed using the Mini Mental State Examination (MMSE) [14] and PD patients were also given the motor section of the UPDRS [16]. None of the subjects showed any signs of dementia or abnormal cognitive functioning on the MMSE (score $>22/30$). With one exception, the Parkinson's patients were tested in the morning after having been off medication for at least 12 h. One patient had an early morning dosage 5 h prior to testing since he depended upon regular frequent dosing and 'froze' in the morning without this initial dose. One potential control subject was excluded from analyses because his MMSE score was below the criterion for normal performance as stated above.

2.2. Apparatus and Stimuli

The IOR paradigm was similar to one used previously [3]. The subject's task involved localization of a visual target stimulus by making a speeded saccade to the target as soon as it appeared. Eye movements were recorded using an ISCAN RK-426 eye-tracking system, interfaced with an infrared sensitive camera. Spatial resolution was $\approx 0.5°$ of visual angle, while temporal resolution was set at 6 ms. Subjects placed their head on a chin rest positioned 72 cm from a computer monitor used to display the stimuli (Sony Trinitron Multiscan sf II). The monitor screen covered a visual area of $25 \times 18°$ from this viewing distance. The stimulus display consisted of a grey fixation spot ($0.2 \times 0.2°$) on a black background, flanked by two grey boxes ($1.0 \times 1.0°$) positioned such that their centers were 5.8° to the left and right of fixation. The target stimulus was a green square measuring $0.6 \times 0.6°$ which appeared in the center of one of the two flanking boxes.

[2] One patient who was not on medication at the time of the study had been on medication during earlier visits (amantidine). He had responded to medication, but ran out of his prescription and elected to manage without medication for a period. On a subsequent visit, he was taking medication (carbidopa/levodopa) with response.

2.3. Procedure

Fig. 1 shows examples of the stimulus display and sequence. Each subject was tested in a single block of 96 trials, or 16 trials for each combination of SOA (67, 133 or 1000 ms) and Cue Position (cued or uncued). Trial type was determined randomly. A practice block of 16 trials was given to subjects prior to the main session to familiarize them with the task. Further practice trials were allowed until the experimenter was confident the subject understood and could complete the task.

Subjects looked at the central fixation spot to initiate the trial sequence. If they successfully maintained fixation for 800 ms, the sequence of cue and target events was initiated. However, if their estimated point-of-gaze shifted more than 2.4° from the center of the fixation point the trial was cancelled and placed back in the pool of uncompleted trials.

After the fixation period expired, there was a 27 ms brightening of one of the two peripheral boxes, which acted as a cue. After an additional 13 ms period elapsed, the fixation point itself then brightened for 27 ms.[3] The entire duration of the cue sequence, from initial brightening of the box to termination of the fixation brightening, was 67 ms. Following this cue sequence, the fixation screen was displayed for either 0, 66 or 933 ms before target onset, resulting in effective SOAs between the initial cue and the target of 67, 133 and 1000 ms. Subjects had to make a speeded saccade to the target following its appearance, and the target remained in view until subjects had completed a saccade to one of the two boxes, or until 1.6 s had elapsed.

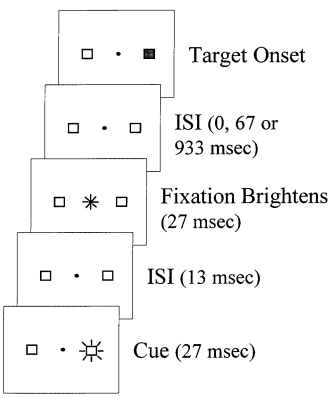

Fig. 1. Example of the stimulus sequence used This example illustrates a cued trials.

[3] Brightening the fixation point allows us to achieve optimal control over the reflexive allocation of spatial attention. By automatically reorienting attention away from the peripherally cued location, we hope to obtain a cleaner measure of IOR that is not contaminated by possible differences in voluntary control of spatial attention that may well exist between PD and control subjects (see also Briand et al. [3]).

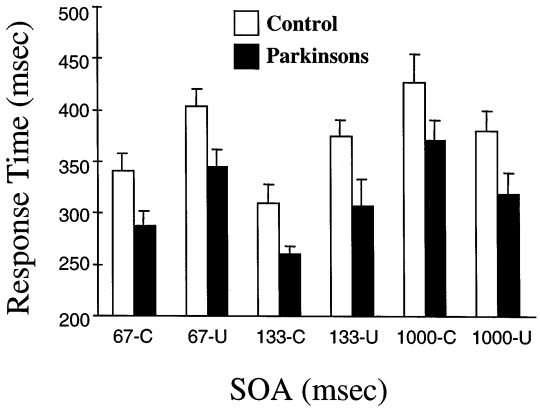

Fig. 2. Average response times for Parkinson's and control groups as a function of SOA and Cue Type. C – cued trials; U – uncued trials.

Brightening of the cue displays was accomplished by switching the color of the box and fixation point from grey to white.

There were two types of trials, defined by what preceded target onset. On cued trials, the target was shown within the peripheral box that had brightened. On uncued trials, the target was shown within the box that had not brightened. The probability of the target appearing within the brightened box was 50:50; hence, cues were unpredictive of target location.

Saccade latency was calculated using a velocity criterion. The start of a saccade was indicated as soon as the change in eye position went above a velocity of 120°/s. The end of the saccade was indicated when eye velocity fell below 12°/s. When the end of the saccade occurred, the saccade was determined to be correct or incorrect. Correct responses were saccades that terminated within a 4.4° window centered on the position where the target appeared. Saccades terminating in any other position on the screen were coded as errors. Feedback following errors consisted of a brief 27 ms tone. If a saccade was not completed within 1600 ms of target onset, that trial was replaced in the pool of unfinished trials to be completed later and a running count of such non-responses was maintained. Trials were also replaced in the pool of uncompleted trials if a subject made an anticipatory response; i.e., initiated a saccade during the period between the onset of the cue and the onset of the target. A running count of such anticipations was kept for later analysis.

3. Results

Slow (RT > 900 ms) and fast responses (RT < 90 ms) were excluded from all subsequent analyses. These accounted for only 1.0% of all trials. Mean correct response latency and error rate for each combination of cue validity and SOA were calculated.

Response time: Mean correct RTs were included in an Analysis of Variance with Group (PD vs. Control), SOA, and Cue Type as factors. The PD patients were significantly faster in their saccadic RTs than the controls (315 vs. 373 ms, respectively), $F_{1,13} = 10.92$, $P < 0.006$ (Fig. 2).

SOA was also significant, $F_{2,26} = 10.91$, $P < 0.001$, as was Cue Type, $F_{1,13} = 7.81$, $P < 0.02$, with cued trials being faster than uncued overall (334 vs 357 ms, respectively). The only significant interaction was between SOA and Cue Type, $F_{2,26} = 18.66$, $P < 0.001$, which indicated significant facilitation in responses on cued trials at short SOAs (facilitation of 60 and 57 ms at SOAs of 67 and 133 ms), but IOR at the 1000 ms SOA (inhibition of -50 ms). The interaction between Group, SOA, and Cue Type was not significant ($F < 1$). Fig. 3 displays this interaction, with the data plotted as RT difference scores (uncued − cued RT). As can be seen, there appears to be little evidence for reflexive orienting differences between the PD and control subjects.

Errors: The error data showed no effect of Group ($F < 1$, 5.1% and 6.5% for control and PD, respectively). The other two main effects were significant; SOA, $F_{2,26} = 6.46$, $P < 0.006$, and Cue Type, $F_{1,13} = 18.34$, $P < 0.001$. The latter effect was in the same direction as the Cue Type effect in RT, with better performance (i.e., fewer errors) on cued trials. None of the interactions were significant.

Effects of disease stage: Follow-up analyses were conducted on the data from the PD subjects, to determine whether the cueing effects (early facilitation and later IOR) were affected by disease stage. The Hoehn and Yahr stage categorization, as well as the UPDRS motor subscale score, are provided in Table 1. Overall correlation between these two measures for the seven patients tested was very low, $r = 0$. However, the UPDRS motor subscale has six distinct factors, as reported by Stebbins and Goetz [47]. When these six factors for the UPDRS motor scale were separately correlated with the Hoehn and Yahr scores, only Factor 1 (Axial Function/Balance/Gait) correlated significantly with Hoehn and Yahr score ($r = 0.727$, $P < 0.05$). We then created a correlation matrix in which the three disease stage scores (Hoehn and Yahr, combined UPDRS, and UPDRS Factor 1) were correlated with the RT cueing effects ($RT_{uncued} - RT_{cued}$) for the three different SOAs tested. These correlations are shown in Table 2, and in Fig. 4.

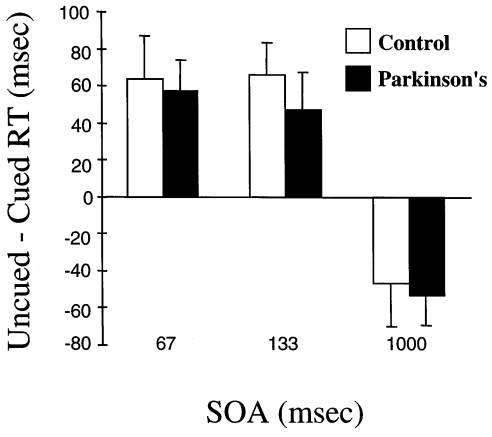

Fig. 3. Size of Cueing effects ($RT_{uncued} - RT_{cued}$) for Parkinson's and control subjects as a function of SOA.

Table 2
Correlations between measures of disease stage and cueing effects ($RT_{uncued} - RT_{cued}$)

	Stimulus onset asynchrony		
	67 ms	133 ms	1000 ms
Hoehn & Yahr	−0.729[a]	0.374	−0.729[a]
UPDRS	−0.507	−0.301	−0.249
UPDRS Factor 1	−0.875[b]	−0.036	−0.639

[a] $P < 0.05$.
[b] $P < 0.01$.

As can be seen from Table 2, both the Hoehn and Yahr score and Factor 1 from the UPDRS showed significant correlations with cueing effects in the PD patients despite the small sample size. The overall pattern was such that more advanced PD patients showed *smaller* cueing effects at the shortest SOA (UPDRS Factor 1, $P < 0.01$; Hoehn and Yahr, $P < 0.05$), but *greater* IOR at the longest SOA (Hoehn and Yahr, $P < 0.05$; UPDRS Factor 1, $P < 0.10$). Overall UPDRS score (which is multifactorial) failed to significantly correlate with any cueing effect, perhaps because of its multifactorial nature.

Anticipations: The mean number of anticipations (responses after the cue but before the target) did not differ significantly between PD and control subjects (36.4 and 27.5, respectively, $t(13) = 0.74$, $P > 0.46$).

4. Discussion

We found significant differences in baseline RT between our PD and normal control subjects, and a correlation between cueing effects (uncued − cued RT) and disease stage in our Parkinson's subjects. Both aspects suggest that automatic spatial attention processes were more active in our PD group.

4.1. Cueing effects

Two previous studies examining exogenous covert orienting in PD claimed to find reduced reflexive attention mechanisms in PD in the form of weaker IOR

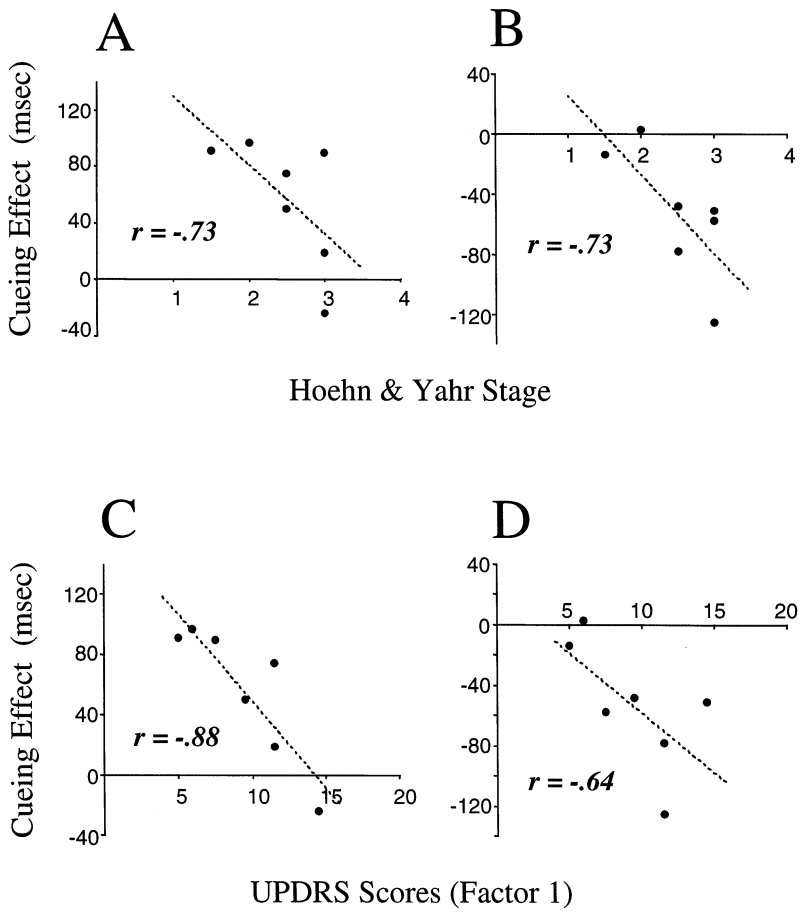

Fig. 4. Scatterplots showing relationship between RT cueing effects and disease stage for the Parkinson's patients. In panels (a) and (b), disease stage is defined by Hoehn and Yahr stage. In panels (c) and (d), Factor 1 of the UPDRS motor subscale score is used. The SOA is 67 ms in panels (a) and (c), and 1000 ms in panels (b) and (d).

effects at long cue-target SOAs [12,55]. The present findings contrast with this. Firstly, overall cueing effects did not differ between our PD and control subjects. Thus, minimally, our data suggest that there is no deficiency of reflexive covert orienting in PD, which would be analogous to the general pattern (described earlier) found in studies of reflexive eye movements in PD.

In addition, we found evidence that reflexive covert orienting in PD may actually be more robust, in the form of correlations between disease stage and cueing effects. Most importantly, the amount of IOR was significantly correlated with disease stage; more advanced PD patients showed more, not less IOR. Since IOR has been found to reflect automatic but not voluntary attentional mechanisms (e.g. not being observed when voluntary cues are used to shift spatial attention; [34,38]) this suggests that reflexive spatial orienting was more active, not less so, in our patients.

At the shortest SOA, we also obtained evidence for reduced cueing effects for more advanced PD patients. This might seem to suggest poorer reflexive attention in PD. However, it is plausible that the decreased cueing effects obtained at the 67 ms SOA for more advanced PD patients are caused by improved performance on uncued trials. Thus advanced PD patients show smaller costs when cued to the incorrect spatial position, because their hyper-reflexive automatic attention quickly disengages them from the cued position and shifts to the actual target position.[4] This possibility is compatible with claims by others [24] that covert attentional dysfunctions in PD are characterized by reduced response times following invalid cues.

A second alternative explanation for this reduced facilitation in more advanced patients is also possible. Recent studies have suggested that reflexive spatial cues such as those used here actually lead to separate facilitatory and inhibitory effects, which each have a different time course [48,49]. These studies have argued that

[4] To test such a hypothesis requires the presence of some trials with neutral cues to allow us to unequivocally attribute the decreased cueing effect to either smaller benefits on cued trials, or reduced costs on uncued trials. Unfortunately, we did not include such trials in our procedure due to consideration of the need to limit the length of tasks while subjects delayed medication.

what is observed empirically as the onset of IOR is the result of the combined effect of a decaying facilitatory component and a slower rising but more persistent inhibitory component. If this is true, then our data would suggest that either the initial facilitatory process is weaker in PD patients, or that the inhibitory component is stronger and develops more quickly in PD. This latter possibility would be consistent with the finding (reported above) that IOR effects are greater in more advanced PD patients.

The relatively small sample size suggests that these correlations should be interpreted with caution. Nevertheless, it is worth noting that the correlations for the early facilitation and later IOR effects each went in the same direction (i.e., shifting towards less facilitation and more inhibition in advanced patients), and were found with two different measures of disease stage. While this suggests that the pattern is at least somewhat reliable, further verification of these effects in future studies is obviously called for, perhaps using a between-group manipulation including samples with either a weak or strong motor impairment.[5]

Whether the present data are best characterized as showing more active reflexive spatial attention in PD, or more conservatively as reflecting no difference between PD and controls, they must be contrasted with the earlier findings of Filoteo et al. [12] and Yamaguchi et al. [55], each of whom claimed that reflexive orienting was weaker in PD. We believe that our results differ from these previous findings primarily due to our use of exogenous cues that were totally nonpredictive of target location. These cues reduced the chances that task performance was influenced by the involvement of voluntary attentional mechanisms, thought to be deficient in PD.

4.2. Baseline RT effects

In addition to the correlation between disease stage and cueing effects, we also obtained a significant overall RT *advantage* for the PD compared to control subjects (315 and 373 ms, respectively). The present task involved reflexive, visually guided saccades. These same PD subjects were significantly *slower* than the controls in a separate study looking at voluntary eye movements, antisaccades [4]. More importantly, in our previous study these same PD subjects were not significantly faster than these control subjects in a reflexive saccade task (251 vs 257 ms, respectively). We believe the failure to find a RT difference between our PD and control subjects in the previous study (as opposed to the robust difference obtained in the present study) is due to the fact that our earlier study included a "gap" manipulation. A gap or offset of the fixation point prior to target onset has been shown to speed or disinhibit reflexive saccades [13] and thus would act to reduce any group differences that might exist. In contrast, the procedure used in the present experiment was analogous to an overlap paradigm, which would make reflexive saccades more sluggish and difficult to execute. This task condition would be more likely to reveal any putative hyper-reflexive saccade performance in the PD patients.

The gist of this argument is that if PD patients do have hyper-reflexive orienting, using a gap procedure would tend to eliminate any advantage they might normally show. The overlap procedure we used in the present study presumably makes hyper-reflexive orienting easier to observe. One study by Roll et al. [40] has directly compared the magnitude of gap effects in PD and control subjects, but reported no difference. This would seem to run counter to our proposal. However, Roll et al. may not have used an optimal procedure for comparison of the gap and no-gap conditions. In their study [40], a gap condition, where the fixation point was removed 200-ms before target onset, was compared to a "step" condition. In this step condition, the fixation point is removed simultaneous with target onset. In effect, this corresponds to a gap condition with a 0-ms delay. In contrast, we used an overlap condition in the present experiment, in which the fixation point remained on. It has been previously reported that a 0-ms gap can result in reductions in the magnitude of the gap effect [50,52]. Thus, comparing 0 and 200 ms gap conditions probably underestimates the true magnitude of overall RT differences between PD and control subjects. Indeed, data from Roll et al. [40] do go in the direction that we might have predicted. That is, the overall RT difference between PD and control subjects in the gap condition was 13.5 ms and it doubled to 25.2 ms in the step (0-ms gap) condition. We would hypothesize that if they had included an overlap condition, this RT advantage for PD subjects would have grown even larger still, perhaps more closely approximating the significant advantage shown by PD subjects in the present study.

Brown and Marsden [5] have characterized the evidence for cognitive deficits in PD as reflecting poor internal, as opposed to external control over attention.

[5] A reviewer has suggested the possibility that our observed correlations between performance and Hoehn and Yahr and UPDRS (Factor 1) might be due to involvement of neurological structures related to axial symptoms and balance, rather than a general worsening of PD. The small sample size and limited number of Hoehn and Yahr stages precludes any definitive answer to this question. However, our results do raise the intriguing possibility that the correlation may be due more to deficits in brain stem structures (for example, the pedunculopontine nucleus, [32]) whose output pathways could mediate both axial control and balance, and reflexive eye movements (see also Leigh and Riley [28]). Since it is known that axial/balance symptoms tend not to respond to L-Dopa [29], it is possible that the dopamine system may not be a major contributing factor to the differences in the cueing effects within the PD group. Future studies will be necessary to explore these questions.

Accordingly, it is now well documented that PD patients have problems with "internal" or voluntary control of both overt [4] and covert spatial attention [12,55]. However, their performance on tasks involving "external" or reflexive spatial attention might be hyper-reflexive in nature. In the case of overt attention, visually guided saccades, rather than being unaffected as implied by Brown and Marsden's scheme [5], may actually be faster and more easily generated. The present demonstration of a robust RT advantage for PD patients in a visually guided eye movement task certainly supports this possibility, as does the correlation between disease stage and magnitude of cueing effects. Thus PD could well follow a pattern of (a) deficient voluntary attention performance and (b) more active reflexive attention mechanisms. As already stated, there is empirical support for the first claim. However the second will require confirmation in further studies with careful control over voluntary influences.

Other empirical evidence suggesting the possibility of hyper-reflexive orienting in PD comes from studies examining overt orienting (i.e., eye movements). Much of the evidence for poor voluntary saccadic performance in PD reflects the fact that reflexive eye movements often intrude on voluntary performance. For example, PD patients make more errors on antisaccade tasks, often erroneously making a saccade to the stimulus instead of in the opposite direction, as the task requires [4]. In addition, they show an inability to prevent saccadic responses during the delay period in remembered [8] and cued saccade paradigms [19]. Furthermore at least one study [26] has reported that PD patients have hyper-reflexive responses in a task requiring *overt* orienting, but only when the eye movement is summoned by an exogenous peripheral cue, and not when it is induced by a purely voluntary cue. Thus, overt orienting does seem to follow the proposed pattern; PD patients have difficulty with voluntary saccades but generate reflexive or visually guided saccades more easily.

As we have suggested elsewhere [4] a dual pattern of decreased voluntary and increased reflexive attentional processing in PD is consistent with a model that has been proposed by Sereno [42,43]. That model was intended to account for patterns of voluntary and reflexive attention and eye movements in schizophrenia, but may also apply to voluntary saccade deficits in PD. Sereno and Holzman [44,45] found that whereas schizophrenic patients had problems on a voluntary antisaccade task, they showed hyper-reflexive (i.e. faster than normal) reflexive (visually guided) saccades. Sereno's model [43] explained this pattern by proposing that two separate attentional systems control eye movements. One is a voluntary system which controls voluntary eye movements (e.g., remembered, predictive, volitional or antisaccades). Under normal circumstances, this system tonically inhibits a second, reflexive attention system that controls visually guided (reflexive) saccades. Sereno proposed that if the voluntary attention system were hypoactive or not functioning properly, this would cause voluntary saccades to become less efficient. However, reflexive saccades might actually become more efficient, as the neural system controlling these would no longer be subject to tonic inhibition from the voluntary attention system. Although the similarities in the overall patterns of saccadic and attentional performance in schizophrenia and PD are striking, the specific mechanisms causing the relative performance deficits or enhancements in the two populations no doubt differ significantly. Nevertheless, this simple framework positing dual, interacting attention systems may have great heuristic value across disorders in analyzing outcomes from a variety of attentional and eye movement paradigms.

An abnormality in brain functioning in PD could account for the proposed pattern of attention and eye movement performance in the following manner. A disruption of corticostriatal loops caused by BG dysfunction could lead to reduced facilitatory outputs from the BG to frontal or prefrontal areas controlling voluntary processes [1,10]. Deficits in voluntary attentional processes exhibited in PD could also arise from frontal lobe disruption via a reduced dopaminergic projection from the ventral tegmental area, as has been reported in PD [25,41]. Either of these mechanisms would lead to deficits in the control of both overt and covert voluntary orienting. Increased activation of reflexive orienting mechanisms could also arise in two ways. BG deficiencies could exert a direct influence on subcortical areas controlling eye movements and covert attention. Decreased inhibitory outputs from the BG would thus tend to disinhibit these reflexive orienting systems [20–22,30]. In addition, frontal areas themselves have an inhibitory influence on subcortical structures controlling orienting [17,18]. Thus any frontal dysfunction could also lead to reduced inhibition of reflexive orienting.

In summary, we studied the timecourse of purely reflexive covert spatial attention in PD, using a procedure that should have eliminated any undue influences from voluntary attentional processes believed to be deficient in this population. Patients suffering from PD made visually guided saccades that were faster than those of control subjects, and more advanced patients showed more IOR. These results suggest that automatic orienting processes are not deficient, and perhaps operate more quickly or are more active in PD.

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