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Processing Efficiency of the Orienting and the Focusing of Covert Attention in Relation to the level of Disability in Parkinson's Disease

MORENA MARI†, KERRY M.B. BENNETT‡, MARINA SCARPA§, GIANNI BRIGHETTI† AND UMBERTO CASTIELLO‡

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This study assessed covert visuo-spatial attentional mechanisms in Parkinson's disease (PD). Reaction times (RTs) of subjects at early and late disease stages, and of matched control subjects, were compared. The task was to respond to a stimulus in a square positioned in either the left or right hemifield. To assess the orienting of attention, the stimulus was preceded by an arrow which gave a valid (stimulus appeared in the indicated square) or an invalid (stimulus appeared in the square which had not been indicated) cue. Both hemifields were indicated in the case of neutral trials. To assess the focusing of attention, the square could be small (1 × 1°), medium-sized (2 × 2°) or large (4 × 4°). To compare voluntary and reflexive mechanisms, the cue(s) could be central or peripheral, respectively. For the orienting of attention, controls and "early" PD subjects showed greater RTs for centrally cued invalid than for neutral trials. "Late" PD subjects showed no such difference. In contrast, the pattern of results for peripherally cued stimuli was similar across all groups. With respect to focusing, "late" PD subjects showed the normal pattern of an increase of reaction time with square size, both for centrally and peripherally cued trials; however, this increase was greater than that of the control and "early" PD subjects. "Late" PD subjects showed greater reaction times for centrally than for peripherally cued trials; however, unlike controls and "early" PDs, this difference was reduced for invalid trials, and absent for trials to the small and medium-sized squares. It is concluded that Parkinson's disease compromises both endogenous and exogenous visuo-spatial functions. However, it is particularly processes which have a more endogenous component which show the greatest deterioration at later disease stages. © **1997 Elsevier Science Ltd. All rights reserved.**

Parkinson's disease Attention Orienting Focusing Voluntary Involuntary Cognition Basal ganglia

INTRODUCTION

Accumulating evidence suggests that visuo-spatial attentional functions, particularly those under internal control [1,2], are disrupted in Parkinson's disease, and that the level of this disruption increases with disease severity. The purpose of the current study is to investigate selective aspects of these cognitive processes at different disease stages. In particular, the mechanisms of focusing and of orienting attention under voluntary and reflexive conditions are addressed.

The procedures employed are modified from those which are well established in experimental psychology. The basic structure is provided by the reaction time paradigm of Posner [3] for the evaluation of the orienting of attention. In this paradigm the subject maintains gaze upon a fixed stimulus, but directs covert attention to another stimulus which is presented later in an expected (valid) or an unexpected (invalid) position of the visual field. The reaction time of non-PD subjects for detection of the imperative stimulus is usually quicker for the validly than for the invalidly cued stimulus [3,4]. These so-called "benefits" of the valid trials are attributed to the prior activation of sensory–perceptual pathways that will subsequently be used to process the target stimulus [5]. The slower responses, or "costs", of the invalid trials are interpreted as reflecting the time taken for the disengagement and re-engagement of the attentional focus [3,4,6]. Mixed results have been obtained when using this paradigm with PD subjects. For example, in

†Department of Psychology, University of Bologna, Bologna, Italy.
‡Faculty of Health Sciences, Latrobe University, Melbourne, Australia.
§Department of Neurology, University of Modena, Modena, Italy.
Address correspondence to: Umberto Castiello, Psychology Department, Monash University, Churchill, Victoria 3842, Australia. Tel: (61) 051-226767; Fax: (61) 051-226590; E-mail: umberto.castiello@sci.monash.edu.au

some studies, PD subjects have shown no dysfunction with shifting attention; that is a normal difference between "valid" and "invalid" trials [1,7]. In other studies, PD subjects showed reduced costs, and this was attributed to poor maintenance of attention in the cued location [8,9]. Further research has indicated that dysfunction with the covert orienting of attention differs according to the level of disease progression [6,10–12].

One of the modifications applied to Posner's paradigm [3] in the current study enabled the assessment of the focusing of attention [1]. Trial by trial, the size of the area to be focused upon was varied; that is the imperative stimulus could appear in either a small, medium-sized or large area. Previous studies with non-PD subjects have shown that processing efficiency decreases (as indicated by an increase of reaction times) as the area upon which covert attention is focused increases [13–18]. Parkinson's disease subjects at early stages of the disease also show this direct relationship. However, with respect to control subjects, they show a greater increase of reaction time with focus area [1]. To explain the increased reaction times with an increase of attentional focus, Bennett *et al.* [1] proposed that PD subjects take a longer time to process a given temporal, spatial or functional cognitive "unit". Thus, as the number of units increases, if this assumption can be made for a greater focus area, this would result in a progressively greater difference between the processing times of Parkinson's disease and control subjects. To date, the function of focusing attention has not been investigated in subjects at later stages of Parkinson's disease. Combining the assessment of both the orienting and the focusing of attention is thought to sufficiently stress the cognitive processing resources of the PD subjects for the emergence of effects upon response times [1,8].

A further modification to the basic Posner paradigm [3] was performed in order to evaluate whether or not voluntary mechanisms of covert visuo-spatial attention are more affected than reflexive mechanisms. The reason for this evaluation stems from the wealth of research on PD subjects which suggests that exogenous functions are less compromised than endogenous functions, and that this finding applies both to the motor and to the cognitive domains. Looking, for example at eye movements, PD subjects show normal reflex saccades to peripheral targets, but impairment with tasks which require the voluntary overt orienting of attention [19,20]. Within the cognitive domain, it has been proposed that greater deficits to voluntary function may also apply to covert attentional mechanisms, that is, when selective visuo-spatial tasks are performed in the absence of eye movements [2,21,22]. In Posner's basic paradigm [3], the pre-stimulus cue is typically presented in the centre of the visual field. Because the symbolic cue must be decoded before the spatial location that it designates can be determined, and because it is subject to specific interference effects, it is proposed to promote the accessing and utilizing of internally stored information and strategies. That is, a central cue is thought to activate a voluntary attentional system [23,24]. The further modification adopted in the current experiment consisted of an additional session whereby the cue was presented in the peripheral visual field. Because the cue is directly above the spatial location within which the subsequent stimulus may appear, it has been proposed that less emphasis is placed upon decoding the cue and that attention is captured in a more automatic manner [25,26]. The prompting of a reflexive attentional system by a peripheral cue is further supported by studies which have found that these automatic mechanisms neither require limited-capacity resources nor are subject to intentional control [16,23,25–28]. Theoretically, the results of the current study should indicate greater dysfunction to voluntary than to reflexive processes, and that this dysfunction is more evident at later disease stages.

By combining the tasks of orienting and focusing, demands upon attentional resources are increased, attentional executive pathways (for review see Brown and Marsden [21]) of PD subjects demonstrating a lower limit on how much mental work or how many cognitive operations can be dealt with than control subjects [1]. Wright *et al.* [8] have proposed that the level of difficulty during an orienting task is insufficient to compromise attentional resources of PD subjects, thus the current study employs the strategy of "loading" attentional resources to maximize chances of revealing exogenous/endogenous differences between the different subject groups.

In summary, the aim of the current study was to assess the voluntary and reflexive performance of the orienting and focusing of covert attention at different stages of Parkinson's disease. In this way, it was hoped not only to contribute to a more complete description of the PD dysfunction, but also to address more general neuropsychological questions related to the voluntary and reflexive mechanisms which underlie visuo-spatial attentional tasks.

METHODS AND MATERIALS

Subjects

Details of the subjects who were assessed are shown in Table 1. The 20 PD subjects, 10 males and 10 females, had a diagnosis of idiopathic Parkinson's disease. There were five PD subjects at each of the first four stages (I–IV) of the Hoehn and Yahr (H and Y) scale [29]. All PD subjects were taking dopaminergic medication (Madopar or Sinemet), and were tested during a period of least signs and symptoms, 1–2 h after medication. None showed motor complications

TABLE 1. Details of the Parkinson's disease and control subjects

Age	Gender	Medication	MMSE score	H and Y score	Years of diagnosis	Age	Gender	MMSE score
Mildly affected PD subjects						Control subjects		
56	F	Sinemet	30	I	2	56	F	30
57	F	Sinemet	30	I	3	56	F	30
58	F	Sinemet	27	I	3	56	F	30
58	F	Madopar	30	I	2	57	F	30
70	M	Sinemet	28	I	1	64	M	30
51	M	Sinemet	30	II	2	52	M	30
56	M	Sinemet	30	II	1	53	M	29
57	F	Madopar	28	II	3	55	F	30
65	M	Sinemet	30	II	3	57	M	30
66	F	Madopar	28	II	2	64	F	30
Severely affected PD subjects								
55	F	Madopar	30	III	7	55	F	30
57	M	Madopar	30	III	6	59	M	30
60	M	Madopar	30	III	7	60	M	30
69	F	Madopar	30	III	8	60	F	30
71	M	Madopar	30	III	10	65	M	29
54	F	Sinemet	30	IV	9	50	F	30
55	M	Sinemet	30	IV	9	54	M	30
57	M	Sinemet	29	IV	12	56	M	30
58	F	Madopar	29	IV	10	56	F	28
65	M	Sinemet	28	IV	10	58	M	28

due to therapy. The 20 age- and gender-matched control subjects did not show neurological dysfunction, and none were taking drugs known to affect the central nervous system. The mean age of the PD subjects (59.8 yr, SD = 5.7) was not significantly different from that of the control subjects [57.2 yr, SD = 4; $F(1,38) = 2.76$, $p = 0.11$]. There were no significant differences when comparing the mean age of the PD subjects across H and Y stages [$F(3,16) = 0.53$, $p = 0.67$]. With visual acuity testing, PD subjects scored, on average, 9/10, and control subjects 10/10. All PD and control subjects showed right handed dominance (19/19 for both groups; Edinburgh inventory [30]), and were naive as to the purpose of the experiment.

The Mini-Mental State Examination (MMSE; [31]) was used to provide an index of the global cognitive state. The mean MMSE score for PD subjects (29.4, SD = 1.0; range = 27–30) was not significantly different from that for control subjects [29.7, SD = 0.7; range = 28–30; $F(1,38) = 1.74$, $p = 0.2$]. There were no significant differences when comparing the mean MMSE scores of the PD subjects across H and Y stages [$F(3,16) = 1.0$, $p = 0.42$]. (Note that, of some cause for concern, two control subjects showed MMSE scores of only 28. However separate analysis of the reaction data for these two subjects revealed no obvious differences when compared to the data from the other eight control subjects.)

The number of years from initial diagnosis of Parkinson's disease ranged from 1 to 12, and a comparison of the mean number of years across H and Y stages revealed a significant effect [$F(3,16) = 59.54$, $p < 0.0001$]. The mean for stage IV PD subjects (10, SD = 1.2) was greater than the mean for stage III PD subjects (7.6, SD = 1.5), which, in turn, was greater than the means for stage II and stage I PD subjects (2.2, SD = 0.84 and 2.2, SD = 0.84, respectively; $p_s < 0.05$).

Apparatus and procedure

The experiment was conducted in a dimly illuminated, acoustically attenuated room. The subject sat in front of a video screen which was driven by a personal computer (IBM compatible, 486), with his/her head resting in a chin-and-head rest frame, so that the distance between the eyes and the screen was approximately 50 cm. Observing through a mirror, one experimenter discarded trials where eye movements were detected. Horizontal eye movements were also recorded with two Ag/AgCl electrodes (Ver Med; diameter 6 mm) positioned on the inner and outer canthi of the right orbit. The recorded signals were subjected to high gain amplification (10^4), filtered using a Butterworth filter (cut-off frequency = 30 Hz) and digitized using a sampling frequency of 100 Hz. Prior to commencement of the experiment, the mean signal amplitude was determined for a 10 s period of static gaze fixation upon the fixation stimulus. During the experiment, an algorithm determined the number of sample points whereby the electro-oculogram (EOG) signal exceeded a voltage which was greater than 2 SE above this mean. If this number exceeded 20, eye movement was assumed to have occurred and the trial was rejected. Accuracy of reaction time measurements (approximately 55/65536 ms) was ensured by performing suitable software adaptations.

The experiment consisted of two main experimental

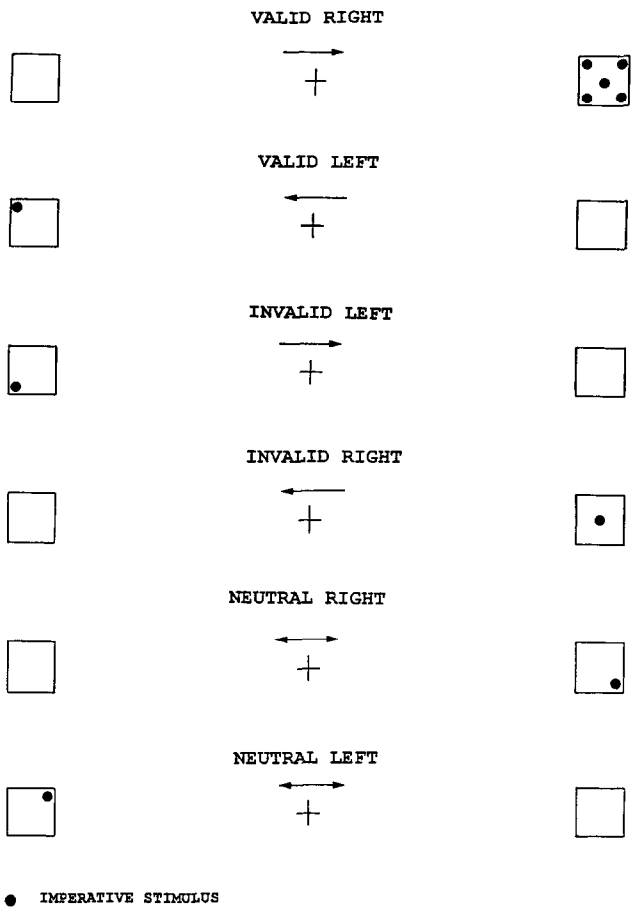

FIGURE 1. Examples of the screen presentations for central cue trials. The central arrow cue preceded appearance of the red imperative stimulus. For the purposes of illustration, the cue and imperative stimulus are shown together, and the first row gives an example of the five possible imperative stimulus positions within the square. This example shows only the medium-sized square, but the same trial types applied to the small and large squares.

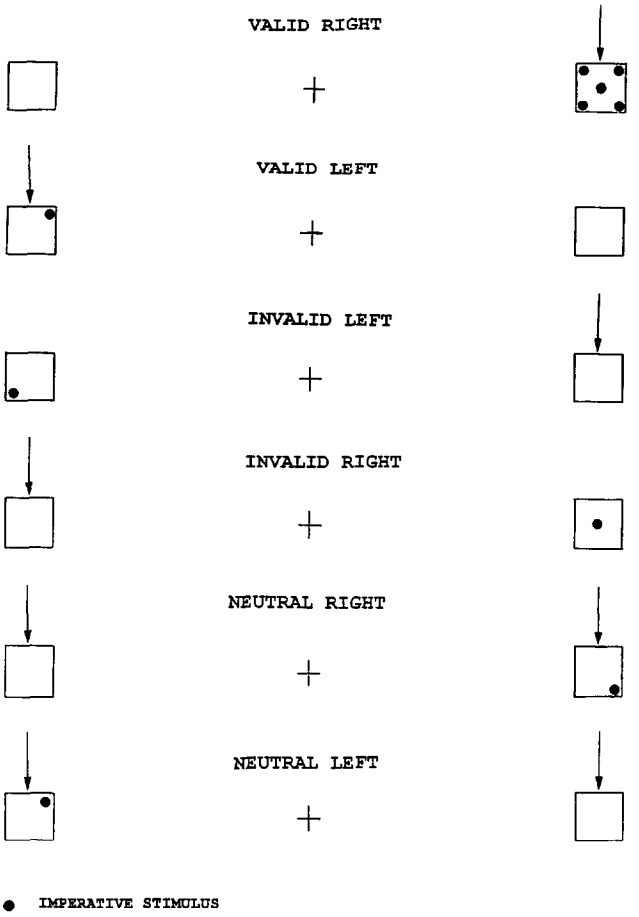

FIGURE 2. Examples of the screen presentations for peripheral cue trials. Please refer to the legend of Fig. 1 for an explanation of this diagram.

sessions (Central Cue and Peripheral Cue) which were conducted on different days but at the same time of day. Practice of each session was conducted one day prior to actual testing. The order of session performance was counterbalanced across subjects. Each session consisted of four blocks of 100 experimental trials with adequate rest periods between each block. Reaction time (RT) was measured to the nearest millisecond and if less than 150 ms or greater than 2000 ms, the trial was discarded. These "error" trials, plus those rejected due to eye movement, those where no response was given and those where a response to a catch trial (see later) was given, were later analysed. If trials were rejected, additional trials were presented at the end of each block to ensure that 100 error-free trials were performed.

At the beginning of each trial, a white fixation cross (0.5 × 0.5°) was shown in the centre of the screen together with two squares (hollow with white line borders), one to the horizontal left and one to the horizontal right of the cross. The distance from the centre of the fixation cross to the centre of each square was 10 degrees. The squares could be small (1 × 1°), medium-sized (2 × 2°) or large (4 × 4°). The square on the left was always the same size as the square on the right. After an interval of 600 ms, a white cue appeared. Of importance is that the position of this cue differed for the Central Cue and the Peripheral Cue sessions. In the Central Cue session (see Fig. 1), the cue was central and horizontal, and appeared 0.5° directly above the cross. This central cue was either a double-arrow (< — > , 2° in length) or a single arrow (2° in length) which pointed to the left or to the right square. In the Peripheral Cue session (see Fig. 2), the cue was not central. It consisted either of two vertical arrows, each 2° in length and pointing downwards, with one arrow directly over (0.5°) the left square and the other directly over (0.5°) the right square, or of one vertical arrow over either the left or the right square.

After a further interval of 600 ms, the imperative stimulus, a red dot with a diameter of 0.4°, was shown in one of the squares for 100 ms. (Results from previous studies have confirmed that PD subjects can orient attention to the most probable position with an interval of 600 ms between a central precue and the

imperative stimulus [1].) Results from the current study confirmed that both control and PD subjects show lower reaction times for peripheral than for central cues, suggesting that the 600 ms interval between the peripheral cue and imperative stimulus elicited an orienting which was more based upon involuntary than voluntary mechanisms). The imperative stimulus could appear either in the centre of the square or in one of the corners of the square.

The subject was instructed to maintain his/her gaze on the fixation point and, upon appearance of the imperative stimulus, to press the space bar of the computer keyboard with the right index finger as quickly as possible. The fixation cross, cue and squares remained on the screen for two seconds after appearance of the imperative stimulus, or until the subject pressed the space bar. No performance feedback was given.

In order to reduce anticipatory responses to the target stimuli, "catch" trials (n = 10 for every 100 experimental trials) were randomly presented amongst trials with directional and non-directional cueing. In these trials no imperative stimulus was presented after the cue, thus the subject was expected not to emit a response. Experimental trials were of two forms: (a) those with directional cueing (75%); and (b) those with directional cueing (25%). For 68% of the trials with directional cueing, the single arrow cue pointed to the box within which the imperative stimulus subsequently appeared. For 27% of the trials with non-directional cueing, the cue pointed to the box contralateral to the box within which the stimulus appeared. In non-directional trials, the cue was a central double arrow in the Central Cue session, or two peripheral arrows in the Peripheral Cue session, and the probability of imperative stimulus appearance was the same for each square. The different trial types were presented in random order. The stimulus could appear with equal probability in either the left or the right square and with equal probability in each of the five positions within the square.

RESULTS

Statistical analysis

Mean reaction time of each subject for the trials which were not rejected was determined and the values were entered into repeated measures analyses of variance (ANOVAs). Analysis was divided into two main parts according to the between-subjects factor: (1) for a comparison of results between the PD (n = 20) and control subjects, the between subjects factor was Group (PD, control); and (2) for a comparison of results between PD subjects at stages I and II and PD subjects at stages III and IV, the between subjects factor was PD Group (I and II, III and IV). In further ANOVAs, each of these PD subject groups was compared to a group of 10 matched control subjects [between-subjects factor = Group (PD, control)].

The within-subjects factors for all sets of ANOVAs were Cue Session (central, peripheral), Condition (valid, neutral, invalid), Visual Field (left, right), Square Size (small, medium, large) and Stimulus Position (central, non-central). Since there were no effects for Visual Field [$F(1,38) = 2.11$, $p > 0.05$] or for Stimulus Position [$F(1,38) = 1.00$, $p > 0.05$], and no significant interactions between these two variables and any of the other independent variables, subsequent analysis used data that was collapsed across Visual Field and Stimulus Position. *Post-hoc* comparisons between means of interest were performed using the Newman–Keuls procedure (α level = 0.05). The transform method of O'Brien [32] was used to test trial-by-trial variability of the different groups for each within-subject factor.

For all of the above mentioned comparisons, the number of misses (i.e. when no response was given), responses to catch trials, trials rejected due to eye movements and "error" trials (with RTs less than 150 ms or greater than 2000 ms) were determined. The means were not analysed as the numbers of these trials were very low: (a) misses — none; (b) catch trial responses — 2% of total number of trials for PD subjects; 1% for controls; (c) errors — 1% and 0, for PD and controls, respectively; and (d) eye movements — 3 and 1% for PD and controls, respectively. The effect of fatigue was examined by performing an ANOVA on the mean RT values with Block (1, 2, 3 and 4) as a within-subject factor. There was no effect of Block [$F(3,38) = 1.07$, $p > 0.05$] and no significant interactions between Block and the other within-subjects factors.

Comparison between Parkinson's disease and control subjects

The results of this comparison are shown in Table 2. Not surprisingly, PD subjects showed longer reaction times (695 ms) than control subjects [304 ms; Group effect: $F(1,38) = 135.6$, $p < 0.0001$]. The PD subjects also showed greater variability than control subjects ($p < 0.05$). However, a significant effect for Cue Session [$F(1,38) = 26$, $p < 0.0001$] but no interaction between Group and Cue Session [$F(1,38) = 1.4$, $p = 0.24$], indicated that the pattern of performance with respect to Cue Session was the same for both groups; that is, mean RT for Central Cue (voluntary) trials (506 ms) was greater than mean RT for Peripheral Cue (reflexive) trials (494 ms).

Both groups also showed a similar pattern of results when considering the reaction times from the Conditions of each Cue Session. This was indicated by a significant interaction between Cue Session and Condition [$F(2,76) = 22.8$, $p < 0.0001$], but no interaction between Group, Cue Session and Condition [$F(2,76) = 1.2$, $p = 0.31$]. In the Central Cue session, and

TABLE 2. Mean reaction times (with standard deviations in parentheses) of Parkinson's disease and control subjects

	PD subjects			Control subjects		
	Valid	Neutral	Invalid	Valid	Neutral	Invalid
Central cue						
Small	640	670	674	280	293	312
	(111)	(120)	(115)	(31)	(30)	(30)
Medium	682	707	717	295	306	324
	(98)	(112)	(120)	(35)	(33)	(35)
Large	724	747	765	308	319	338
	(121)	(136)	(120)	(40)	(38)	(33)
Peripheral cue						
Small	639	663	658	278	297	292
	(110)	(115)	(180)	(29)	(28)	(30)
Medium	672	696	695	290	306	302
	(118)	(90)	(176)	(30)	(32)	(31)
Large	707	733	730	301	315	312
	(132)	(135)	(192)	(32)	(33)	(31)

in accordance with previous results [1,3,4,7] mean RT for the valid trials (488 ms) was less than that for the neutral trials (507 ms), which, in turn, was less than that for the invalid trials (522 ms). In the Peripheral Cue session, again in accordance with previous results [23,33] mean RT for neutral trials (502 ms) was not significantly different from that for invalid trials (498 ms). Mean RT for valid trials (481 ms) was, however, less than that for both neutral and invalid trials ($p_s < 0.05$). Of note, and of relevance when considering the results presented later for Square Size, is that the difference of RTs between Conditions was not greater for PD subjects. As an example, the mean RTs for the PD subjects were 682 and 719 ms for the valid and invalid trials of the Central Cue session — a difference of 33 ms. For the control subjects, this difference was 31 ms. Note that these values are comparable to the 38 ms reported by Sharpe [12].

Performance disparity between the two groups became evident when considering the mean RTs to stimuli presented in squares of different sizes. [Interaction between Group and Square Size, $F(2,76) = 141.2$, $p < 0.0001$.] Although both groups showed an increase of RT with square size, the difference of RT between a pair of square sizes was much greater for the PD than for the control subjects. As an example, the RTs for the valid trials in Session A for PD subjects were 640, 682 and 724 ms for the small, medium and large squares, respectively — a response time increase of 84 ms with a four-fold increase of square size. In contrast, the response time increase for control subjects was only 28 ms. This value was comparable to the Condition differences noted in the previous paragraph, indicating that the exaggerated response time increase with square size was not simply a product of the longer PD subject reaction times.

Comparison between Parkinson's disease subjects at stages I and II and Parkinson's disease subjects at stages III and IV of the Hoehn and Yahr scale

This section will focus on the results obtained with the comparison between the two PD groups. It will also report differences found with the comparison of PD I and II subjects to the matched control subjects.

Overall, the results demonstrated a clear deterioration of performance with disease progression (see

TABLE 3. Mean reaction times (with standard deviations in parentheses) of Parkinson's disease subjects

	I and II			III and IV		
	Valid	Neutral	Invalid	Valid	Neutral	Invalid
Central cue						
Small	504	535	556	776	804	791
	(90)	(88)	(85)	(140)	(142)	(146)
Medium	539	574	596	826	840	838
	(86)	(84)	(88)	(129)	(133)	(138)
Large	572	599	630	877	894	900
	(84)	(85)	(94)	(138)	(140)	(150)
Peripheral cue						
Small	502	526	524	776	801	792
	(102)	(100)	(106)	(160)	(162)	(184)
Medium	529	553	552	816	839	838
	(90)	(95)	(98)	(159)	(158)	(168)
Large	558	586	585	856	879	874
	(120)	(118)	(136)	(174)	(178)	(190)

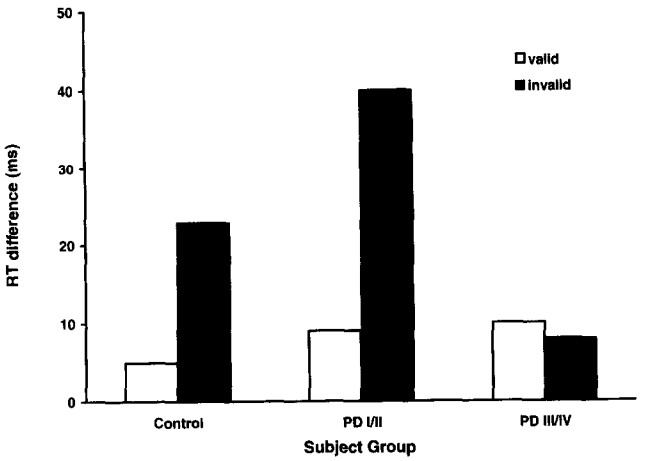

FIGURE 3. Reaction time differences between the centrally cued and peripherally cued sessions for control; PD I and II, and PD III and IV subjects. Unfilled bars = valid trials, filled bars = invalid trials. Note that control and PD I and II subjects show greater RT differences between the centrally and peripherally cued sessions for the invalid than for the valid trials. In contrast, the PD III and IV subjects show a reduction in the central/peripheral difference for the invalid trials.

Table 3). Mean RT of III and IV subjects (834 ms) was greater than that of I and II subjects [556 ms; $F(1,18) = 199.3$, $p < 0.0001$], which, in turn, was greater than that of control subjects [306 ms; $F(1,18) = 405.8$, $p < 0.0001$]. Variability was also greater for III and IV subjects than for I and II subjects ($p < 0.05$). Note, however, that both PD groups showed lower variability for the Central Cue than for the Peripheral Cue session ($p < 0.05$); this difference was not found for control subjects.

In accordance with the comparison between the control subjects and all PD subjects, there was a significant effect for Cue Session (PD I and II vs. PD III and IV comparison: $F(1,18) = 12.2$, $p < 0.01$; PD I and II vs. control comparison: $F(1,18) = 12.4$, $p < 0.01$) but no interactions between Group and Cue Session [$F(1,18) = 2.1$, $p = 0.16$ and $F(1,18) = 3.7$, $p = 0.07$, respectively]. These results indicated that all subject groups showed greater reaction times for the Central Cue than for the Peripheral Cue session. However, the finding of a significant interaction between Group, Cue Session and Condition for only the PD I and II vs. PD III and IV comparison [$F(2,36) = 7.0$, $p < 0.01$], and not for the PD I and II vs. control comparison [$F(2,36) = 0.9$, $p = 0.4$] indicated that the PD III and IV subjects showed differences in the pattern of performance. In particular, these PD III and IV subjects showed no difference of RT between neutral (843 ms) and invalid trials (846 ms) of the Central Cue session. This contrasted to the results for the PD I and II subjects (569 and 594 ms, respectively; $p < 0.05$), and for the control subjects. As illustrated in Fig. 3, a further difference was that PD III and IV subjects showed a significant reduction in the RT difference between centrally and peripherally cued tasks for the invalid trials (8 ms) when compared to the RT results for the PD I and II subjects (40 ms, $p <$

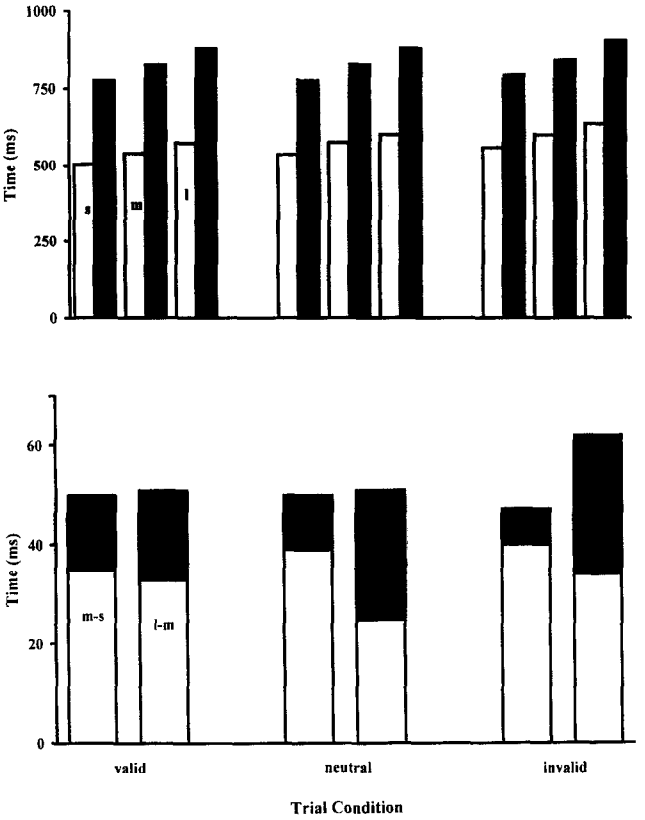

FIGURE 4. Upper panel: mean reaction times for the small (s), medium-sized (m) and large (l) squares of the valid, neutral and invalid trials which were centrally cued. Unfilled bars = PD I and II subjects, filled bars = PD III and IV subjects. For both groups and for all trial types, reaction time increased with square size. Reaction times of the III and IV PD subjects were greater than those of the I and II PD subjects. Lower panel: stacked bar-graph showing the differences of reaction times between the small and medium-sized squares (m – s) and between the medium-sized and large squares (l – m) of the trials described for the upper panel. The total height of each bar represents the time differences for the III and IV PD subjects; the height of the white section, that of the I and II PD subjects.

0.01) and control subjects (23 ms; for PD I and II vs. control comparison, $p < 0.01$).

Both PD groups and the control subjects showed an increase of RT with Square Size [Size Effect: $F(2,36) = 573.4$, $p < 0.0001$ and $F(2,36) = 204.3$, $p < 0.0001$, respectively]. This is demonstrated in the upper panel of Fig. 4 for the centrally cued trials of the PD subjects; a similar result pattern was found for the peripherally cued trials. However, further analyses of the significant interactions between Group and Square Size [PD III and IV vs. PD I and II $F(2,36) = 16.4$, $p < 0.0001$; PD I and II vs. controls: $F(2,36) = 41.9$, $p < 0.0001$], indicated that the RT difference between a pair of square sizes was greater for the III and IV than for the I and II subjects. In turn, these RT differences were greater for the PD I and II than for the control subjects. For example, the difference of RT between the small and the large square (Central Cue session, valid trials) was 100 ms for the PD III and IV subjects but 68 ms for the PD I and II subjects ($p < 0.01$). The lower panel of Fig. 4

shows these differences for central cued trials. Looking, for example, at the first pair of bars (valid trials), the reaction time difference between the small and the medium-sized square (first bar) and that between the medium-sized and the large square (second bar) is clearly greater for the III and IV subjects (total height of bars) than for the I and II subjects (white section).

There were significant third order interactions between Group, Cue Session and Square Size for both the PD III and IV vs. PD I and II comparison [$F(2,36) = 3.6$, $p < 0.05$] and the PD I and II vs. controls comparison [$F(2,36) = 4.3$, $p < 0.05$]. *Post-hoc* analyses indicated that the PD III and IV subjects showed no statistical differences of RT between centrally and peripherally cued trials for the small and medium-sized squares. This was in contrast to the results for the PD I and II subjects (15 and 25 ms, respectively, $p_s < 0.05$). Both the PD I and II and control subjects showed greater RTs for the centrally than for the peripherally cued tasks, but this difference was greatest for the large square trials for control subjects (26 ms) in contrast to the medium-sized square trials for the PD I and II subjects (25 ms).

DISCUSSION

Using different cueing conditions, this study investigated the orienting and focusing of attention by Parkinson's disease subjects. Several lines of evidence point to a progressive deterioration of visuo-spatial attentional function, particularly that of a more endogenous component, with severity of disease process. Not unexpectedly, reaction time, is greater for Parkinson's disease than for control subjects [34], with PD subjects classified at stages III and IV on the Hoehn and Yahr scale [29] showing the greatest general reaction times.

Such a clear progression of dysfunction is also apparent for the task of orienting/reorienting attention to different sizes of focus area. Previous studies of non-brain-damaged subjects have demonstrated increases of reaction time with the size of attentional focus [13–18]. Such results are reproduced by all subject groups of the current study; however, PD III and IV subjects show greater step-wise increases in reaction time for each increment in focus area, than PD I and II subjects, who in turn show greater stepwise increases than control subjects. It has been proposed that a greater number of cognitive processing units is involved when narrowing down the attentional focus from a large area to the imperative stimulus, than when narrowing down from a small area [1]. The current results indicate that despite a retained ability to suitably modulate the attentional focus, there is a progressive increase with disease severity in the time taken to process these units.

A further indication of a progressive dysfunction is found when looking at the results for the "invalid" trials. PD subjects at later disease stages (III and IV) show different results for tasks requiring the reorienting of attention from an expected location which has been signalled by a cue in central vision, to an unexpected location source of stimulation. This is revealed by a lack of "costs" when comparing the "invalid" to the "neutral" trials. This finding of a quicker release of attention to an alternative stimulus is in line with previous results, and has been interpreted as reflecting a deficit in the function of maintaining attention upon the cued area [8]. Because attention is not "anchored" appropriately, it is more readily released for alternative sites. However, the results for the PD subjects at stages I and II of the Hoehn and Yahr scale challenge this interpretation. If Parkinson's disease subjects, in general, can be said to have a dysfunction in the maintenance of attention, it would be expected that PD I and II subjects should also show reduced or no costs. Contrary to this expectation, and in line with previous studies of Parkinson's disease subjects at similar disease stages [1,10], this group show a clear difference (mean 25 ms) between centrally cued "neutral" and "invalid" trials. Such a result leads itself open to a variety of interpretations. Because the "costs" were greater for PD I and II subjects than controls, it could be proposed, for example, that the functions of disengaging maintained voluntary attention from a cued location and reorienting attention to an unexpected location show signs of time inefficiency in the early stages of Parkinson's disease. At later disease stages, the reduced costs can be interpreted either as a breakdown of these functions, or as a compensatory suppression of the maintenance of voluntary attention because of time inefficiency problems.

Like the other subject groups (control and PD I and II), the PD III and IV subjects show generally greater reaction time values for centrally cued trials than for peripherally cued trials. This difference (RT central cue trial *minus* RT peripheral cue trial) can be referred to loosely as the "*voluntary component*" of the task. The reason for using the word "loosely" in this context, is that there is no guarantee that the processing for peripherally cued trials is entirely involuntary or that the processing for centrally cued trials is entirely voluntary. For example, in most peripherally cued experiments the proportion of the different trial types (valid, invalid, neutral) is equal. Because of experimental design purposes, and to conform with previous studies which have investigated both centrally and peripherally cued mechanisms (see [33]), the current study varies the proportions of trial types. However, it could be proposed that any benefits of the valid over the invalid cue could be attributed to endogenously initiated shifts of attention because the proportions of trial types are not equal. Because of such arguments it is important to clarify that the

current study assumes that the centrally cued trials induce more of a voluntary processing component than the peripherally cued trials. All other features of the experimental design being equal, this would mean that subtracting reaction time values of the peripherally cued trials from those of the centrally cued trials gives a measure of the degree to which voluntary mechanisms are more employed in centrally cued trials.

Of interest for the "invalid" trial results of the PD III and IV subjects was the comparatively low reaction time difference between centrally cued and peripherally cued trials. Both control and PD I and II subjects showed greater differences between centrally cued and peripherally cued trials for invalid than for valid trials (see Fig. 3). The results for the controls and PD I and II subjects could be interpreted as indicating that the voluntary component of the centrally cued trials was greater for the invalid than for the valid condition. The PD III and IV subjects show a different pattern for the processing of this *voluntary component*, and, in fact, could be described as performing in a more time efficient manner, employing only slightly greater time commitments for the centrally cued task than for a task (peripherally cued) which is thought to induce a greater degree of involuntary processing. Again, it is difficult to know whether this signifies a breakdown in voluntary mechanisms or a compensatory strategy which, in order to avoid the risk of excessive time inefficiency, minimises the use of internal processing mechanisms, placing greater emphasis on exogenous processing mechanisms. Indeed, the latter interpretation is more supported by the results obtained from the PD I and II subjects, where the processing time of the voluntary component is greater for this PD group than for the control subjects.

Reinforcing the idea that the later stages of the disease are associated with greater dysfunction to the *voluntary components* of visuo-spatial attentional functions, is the lack of RT difference between the centrally cued and peripherally cued conditions for the small and medium-sized squares, again for only the PD III and IV subjects. However, in this case, rather than the PD I and II subjects showing consistently greater processing times for the *voluntary component*, they show a performance pattern which differs from that of the control subjects, indicating signs of a breakdown.

The results also indicated a progressive increase of variability with disease severity — standard deviations of the mean reaction times are greater for the PD III and IV than for the PD I and II subjects. This is in line with the expectation of Fimm *et al.* [22] of greater performance variability between PD subjects because of intersubject variability in caudate dopamine depletion. A finding which is difficult to explain is the lower variability for the centrally cued than for the peripherally cued tasks (only for PD subjects). One explanation is that this relates to a differential effect of dopaminergic medication according to cognitive load, or endogenous processing level, of the task [22,35–39] — dopaminergic medication exerting a normalizing effect more upon voluntary than upon reflexive covert attentional mechanisms. However, given this explanation, PD subjects who had been taking dopaminergic medication for extended periods (III and IV) might be expected to show lower variability than those (I and II) who had been taking such medication for shorter periods. This was not the case. For the same reason, an explanation of normalizing effects resulting from pathology could be dismissed. In addition, no obvious positive medication effects appeared to have been exerted upon the pattern of endogenous processing, although it must be noted that the results for untreated subjects, as found by Zimmermann *et al.* [39], may have demonstrated a more rapid progression of deterioration than that of treated subjects.

Throughout this discussion we have alluded to the difficulty in interpreting these results according to whether they reflect a breakdown in endogenous processing mechanisms, or the utilization of compensatory strategies to reduce the risks of time inefficiency. For the former supposition, the idea of a progressive decrease in the capacity of endogenous attentional resources [2] with disease progression could be used as an explanation. The PD subjects at early disease stages could be said to show a lower resource capacity limit (if the term "capacity" is defined in terms of quantity; see [1]) because of compromises to time efficiency of visuo-spatial attentional tasks. The PD subjects at later disease stages may be demonstrating an even lower threshold, which if exceeded by the demands of the attentional task, results in signs of performance breakdown. The alternative explanation of compensatory mechanisms, however, could also be used to explain this change in performance pattern in later stages of the disease. Rather than invest large amounts of time upon more demanding endogenous processes, the nervous system may resort to a more time-efficient system. Although not proposed for cognitive mechanisms, the idea of re-routing compensatory strategies has been suggested previously by researchers who have studied voluntary eye and arm movements [40,41].

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