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The reach-to-grasp movement in Parkinson's disease: response to a simultaneous perturbation of object position and object size

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Abstract This study assessed the adaptive response of the reach-to-grasp movement of 12 Parkinson's disease (PD) and 12 control subjects to a simultaneous perturbation of target object location and size. The main aim was to test further the reported dysfunction of PD subjects in the simultaneous activation of movement components. Participants were required to reach 30 cm to grasp a central illuminated cylinder of either small (0.7 cm) or large (8 cm) diameter. For a small percentage of trials (20/100) a visual perturbation was introduced unexpectedly at the onset of the reaching action. This consisted of a shift of illumination from the central cylinder to a cylinder of differing diameter, which was positioned 20° to the left (n=10) or to the right (n=10). The subject was required to grasp the newly illuminated cylinder. For the Parkinson's disease subject group, the earliest response to this 'double' perturbation was in the parameter of peak reaching acceleration, which was on average 50 ms earlier for 'double' perturbed than for non-perturbed trials. The grasp component response followed more than 500 ms after the earliest transport response. For the control subjects initial signs of a response to the 'double' perturbation were seen almost simultaneously in the transport parameter of peak arm deceleration, and in the manipulation parameter of maximum grip aperture, but these changes were not evident until more than 400 ms after movement onset. These results indicate that the basal ganglia can be identified as part of a circuit which is involved in the integration of parallel neutral pathways, and which exercise flexibility in the degree to which these components are 'coupled' functionally. With basal ganglia dysfunction the activation of integration centres that at first gate the flow of information to the parallel channels of reach and grasp seems inefficient.

Key words Reach to grasp · Human · Perturbation · Kinematics · Motor control · Parkinson's disease · Elderly

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Introduction

Apart from the obvious clinical signs of bradykinesia, tremor and rigidity, Parkinson's disease (PD) has been described as manifesting a number of dysfunctions to movement organisation. One such dysfunction is the performance of simultaneous or sequential movements or movement components (Benecke et al. 1986a, 1986b, 1987; Marsden 1987; Johnels et al. 1989; Harrington and Haaland 1991; Bennett et al. 1995; Weiss et al. 1997). For example, the simultaneous performance by PD subjects of the separate motor patterns of elbow flexion and isometric opposition between the index finger and thumb in one limb shows an increase in movement time well above that taken to perform either task in isolation (Benecke et al. 1986a). A similar result is found with performance of these tasks in sequence when the switching from one motor set to another is required (Benecke et al. 1987).

The common everyday action of reaching to grasp an object provides an ideal experimental action for definition of this dysfunction. Under non-perturbed conditions (that is, with the participant simply reaching to grasp an object which maintains stability of its intrinsic and extrinsic form), it is said to consist of two main components, the reach and grasp (hand opening and closing during the reach; Jeannerod 1981). Because the reach-to-grasp action is relatively easy to perturb, it also affords the opportunity to assess the ability to 'shift' motor sets (for a review see Haggard 1994). A typical perturbation

paradigm consists of a large number of non-perturbed trials, where a subject reaches to grasp an object of a certain diameter (e.g. small) or at a certain distance (e.g. nearby), and a very low number of interspersed unexpected perturbed trials where, at movement onset, the target object changes in size (e.g. becomes large) or position (e.g. is further away). Because perturbation requires that the subject recruit quickly a motor output which is different from that executed originally, it can be hypothesised that PD subjects should show dysfunction during the transition phase from the original to the final motor output. Again this is borne out by findings that PD subjects show definable transition periods between the closing of one and the opening of another pattern, in contrast to the smooth change shown by non-PD subjects (Castiello et al. 1993a; Castiello et al. 1994; Scarpa and Castiello 1994; Castiello and Bennett 1994). However, despite this transition, Parkinson's disease subjects are able to activate prompt mechanisms to rearrange the motor output for successful end-task performance (Castiello and Bennett 1994; Scarpa and Castiello 1994).

The present study investigates the ability of PD subjects to respond to a 'double' perturbation, whereby both an intrinsic (size) and extrinsic (location) feature of the target object are changed. This is in contrast to the great majority of previous studies with healthy subjects where perturbation is directed solely at the reach component by perturbing object position or solely at the grasp component by perturbing object size (for a review see Haggard 1994).

In a recent study with non-brain-damaged subjects, perturbation was targeted at both channels by changing both the position and the size of the object at the onset of the reaching movement (Castiello et al. 1998). It was found that movement duration for these 'double' (position and size) perturbed trials was much longer than those of non-perturbed trials to the central cylinder, and that these increased values were much greater than those reported previously in 'single' perturbation studies where either size or location of the object was perturbed. Initial signs of a response to the 'double' perturbation were seen almost simultaneously in the reach parameter of peak arm deceleration, and in the grasp parameter of maximum grip aperture at a time which was much later than found in 'single' perturbation studies. In light of these results, it was proposed that the visual change, resultant from the double perturbation, activates integration centres which first 'gate' the flow of information to the parallel channels of reach and grasp. Following processing of this information, these centres act to instigate a synchronised and coordinated response in both components. Such results add support to the existence of neural centres which are dedicated to the integration of parallel neural pathways, and which exercise flexibility in the degree to which these components are 'coupled' functionally.

In using the 'double' perturbation paradigm in the current study, and given the proposed dysfunction of PD subjects in activating movements (or movement components) simultaneously, it was predicted that PD subjects would show evidence of a sequential rather than a simultaneous response. This prediction was fulfilled, a sequential pattern was found for PD subjects, while the control subjects showed a simultaneous response to the double perturbation.

Materials and methods

Participants

Details of the subjects who were assessed are shown in Table 1. The 12 Parkinson's disease subjects had a diagnosis of idiopathic Parkinson's disease which was of 1–18 years standing. According to the Hoehn and Yahr scale (Hoehn and Yahr 1967), all were at stages I or II. Sign and symptoms were bilateral in all cases, with one side usually being worse than the other (UPDRS). The level of rigidity and tremor was minimal at the time of testing. Medication was mostly commonly Madopar (PD=9), Sinemet and/or Eldepryl. Two Parkinson's disease subjects (6, 10) were not taking dopaminergic medication (the results from these subjects showed no obvious differences when compared with the results from other PD subjects). PD subjects were always tested during a period of least signs and symptoms, 1–2 h after medication. None showed motor complications due to therapy. The 12 sex- and age-matched control subjects reported no neurological or skeletomotor dysfunctions. The mean age for both the Parkinson's disease and the control subjects was 52.5 years (SD=10). All PD and control subjects showed right-handed dominance (Edinburgh inventory, Oldfield 1971), were naive as to the experimental design or purpose, and gave their consent to participate. The Mini-Mental State Examination (MMSE) was used to provide an index of the current global cognitive state (Folstein et al. 1975). The scores for Parkinson's disease subjects ranged from 29 to 30; for the control subjects the average score was 30. A non-parametric (Mann-Whitney U-test) comparison between the Parkinson's disease and control subject ordinal scores was not significant. With visual acuity testing, PD subjects scored on average 19 out of 20, and control subjects 20 of 20 (Smellem Eye Chart).

Apparatus

The working surface was a semicircular table the surface of which was implanted with concentric rows of light-emitting diodes (LEDs). The participant was seated on a height-adjustable chair so that the thorax pressed gently against the front edge of the table and the feet were supported. A pressure-sensitive starting switch was positioned 10 cm anterior to the mid-line of the participant's thorax. With the hypothenar eminence of the right hand placed upon this switch, the starting position was slight shoulder flexion and 70–80° of internal rotation, 90° of elbow flexion, semipronation of the forearm, 5–10° wrist extension and opposition between the pads of the index finger and thumb.

Reflective passive markers (0.25 cm in diameter) were attached to the following points of the reaching limb: (a) wrist-radial aspect of the distal styloid process of the radius; (b) index finger-radial side of the nail; and (c) thumb-ulnar side of the nail. Movements were recorded with the ELITE system (Ferrigno and Pedotti 1985). This consisted of two infrared cameras (sampling rate 100 Hz) inclined at an angle of 30° to the vertical, and placed 3 m in front of the table and 3 m apart. The calibrated working space was a parallelepiped (length 60 cm, breadth 30 cm, height 60 cm) from which the spatial error measured from stationary and moving stimuli was 0.4 mm. Coordinates of the markers were reconstructed with an accuracy of 1/3000 over the field of view and sent to a host computer (PC 486 Pentium). The SD of the reconstruction error was 1/3000 for the vertical (y) axis and 1.4/3000 for the two horizontal (x and z) axes.

Table 1 Characteristics of the Parkinson's disease (PD) subjects ()

Subject	Gender	Age (years)	Medication	UPDRS right limb	UPDRS left limb	Score (Hoehn and Yahr)	MMSE score	Diagnosis (years)
1	F	55	Sinemet CR (200×1) Eldepryl	8	4	II	29	2
2	F	45	Sinemet CR (200×1) Eldepryl	5	4	I	30	3
3	F	44	Sinemet CR (100×1/2) Eldepryl	8.5	8.5	II	29	3
4	M	51	Sinemet CR (200×4)	3	5	II	29	3
5	M	60	Sinemet CR (200×1) Eldepryl	4	3	I	29	6
6	F	39	Eldepryl	3	5	II	29	1
7	M	58	Sinemet CR (200×1) Eldepryl	8	4	I	30	7
8	M	46	Sinemet CR (100×3) Eldepryl	2	4.5	II	30	7
9	F	58	Madopar CR (100×3) Eldepryl	3.5	3	II	30	4
10	F	68	Eldepryl	5	4	II	29	3
11	M	39	Sinemet CR (200×3) Eldepryl	8	3	II	30	8
12	F	67	Sinemet CR (200×3) Eldepryl	5	2	II	30	7

The target stimuli were three translucent Perspex cylinders placed vertically upon the table surface the implanted LEDs. One, the central cylinder, was placed 30 cm directly in front of the starting switch. The other cylinders were placed 20° to the right and left of the mid-sagittal plane, 30 cm from the switch. Each cylinder could be selectively illuminated in pink/red hues by computer activation of the underlying LEDs. Two types of cylinders were employed. The small cylinder had a diameter of 0.7 cm, a height of 10 cm and a weight of 9 g. The large cylinder had a diameter of 8 cm, a height of 8 cm and a weight of 202 g. To ensure an even distribution of lighting for both cylinder sizes, one underlying LED was activated to illuminate the small cylinder, and three underlying LEDs were activated to illuminate the large cylinder.

Two target object configurations were presented (see Fig. 1). In one (session A), a small cylinder was placed centrally and large cylinders were placed laterally to the left and right. In the other (session B), a large cylinder was placed centrally and small cylinders were placed in the two lateral positions. Perceptual perturbation of both object size and position could be achieved by deactivating the LED(s) under the central cylinder, to extinguish illumination, while simultaneously activating the LED(s) under a lateral cylinder so that it became illuminated. For a low percentage of trials (see "Procedure"), release of the starting switch activated computer control of this shift in illumination.

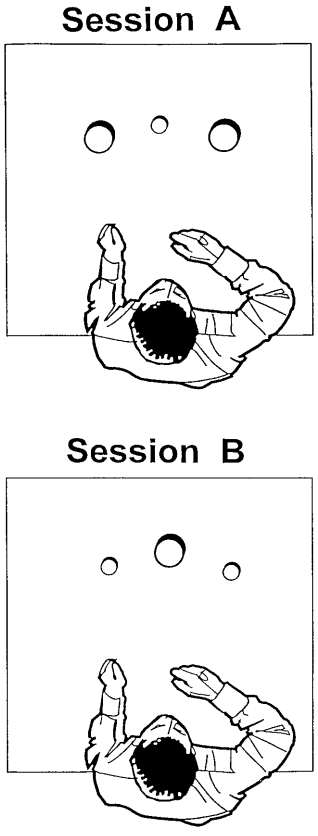

Fig. 1 The experimental setup showing a view of the participant from above and behind the working surface. In session A the stimulus array consisted of a small-diameter cylinder 30 cm directly in front of the participant, and two large-diameter cylinders, one 20° to the left and one 20° to the right of this central cylinder. In session B, the array consisted of a large-diameter cylinder placed centrally, and small-diameter cylinders placed laterally. (Note: this diagram is not drawn to scale)

Procedure

To avoid fatigue and lack of concentration/attention, each participant performed two experimental sessions (A and B) conducted at the same time of day on separate days over a 1-week period. The order of sessions was counterbalanced across participants. The anatomical landmarks for the markers were dotted with indelible ink to ensure that the same points were recorded across sessions.

At the beginning of each session, the experimental requirements were explained. Each participant was informed that shortly after positioning the hand upon the starting switch a tone would be heard to indicate that a cylinder would become illuminated soon afterwards. They were instructed to begin the movement as soon as a cylinder became illuminated, and then reach for, grasp and lift the illuminated cylinder a small distance off the table. Participants were advised to perform the movement without undue emphasis on speed or on the demonstration of accurate performance. No instructions were given as to the type of grasp to adopt for each size of cylinder. Prior to blocked trials participants were informed that only one cylinder would be illuminated for a series of trials, and that no perturbation would be introduced. Prior to non-perturbed/perturbed trials participants were informed that for most trials the central cylinder would be illuminated but that for some trials illumination could change unexpectedly, and that, in this case, they should grasp the cylinder that became illuminated.

One hundred trials were recorded from each of the two sessions, 80 of which were non-perturbed trials to the central cylinder and 20 were perturbed trials, 10 to the left and 10 to the right cylinder. The perturbed trials were randomly interspersed with the non-perturbed trials. In session A the perturbation was thus from a small central cylinder to one of the large lateral cylinders. In session B, the perturbation was from a large central cylinder to one of the small lateral cylinders. At the beginning of each trial the participant placed their hand on the starting switch and the experimenter initiated a computer-generated tone (880 Hz; duration 250 ms). To reduce expectancy and rhythmical effects, the duration between this tone and subsequent illumination of a cylinder was randomly set at 500, 1000, 1500 or 2000 ms. Data acquisition began with illumination of the cylinder and continued until after the cyl-

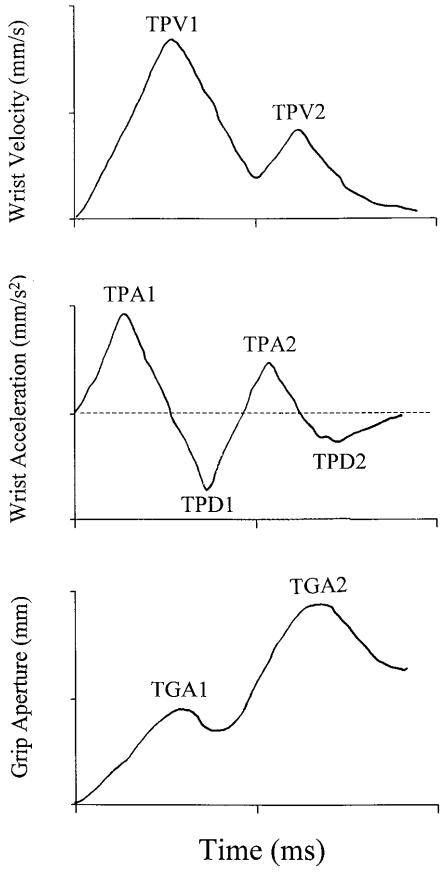

Fig. 2 Example trial illustrating the dependent measures considered in the present study [*TPA1* time to first grip velocity, *TPD1* time to first peak deceleration, *TPV1* time first to peak velocity, *TPA2* time to second grip velocity, *TPD2* time to second peak deceleration, *TPV2* time to second peak velocity, *TGA1* time to the first maximum grip aperture, *TGA2* time to the second maximum grip aperture (only for the session A perturbation)]

inder had been lifted. The experimenter was given computer screen feedback of the three-dimensional position of each marker – if one marker was 'missing' (indicating that the cameras were not detecting the signal) during task performance the trial was manually discarded. Following each trial, the cylinder was replaced in its original position by the experimenter. Experimentation continued until the required number of successful trials was collected.

Prior to each recording session the participants were given ten practice trials, including one example of a perturbation. During this practice session, all participants naturally adopted a precision grip (PG, opposition between the index finger and thumb) to grasp the small cylinder and whole-hand prehension (WHP, all fingers opposing the thumb) to grasp the large cylinder.

Data processing and analysis

The Eligrasp (BTS 1994) software package was used to assess the data. This gave a three-dimensional reconstruction of the marker positions. The data were then filtered using a finite impulse response (FIR) linear filter with a transition band of 1 Hz (sharpening variable=2; cut-off frequency 10 Hz; D'Amico and Ferrigno 1990, 1992). The reach component was assessed by analysing the trajectory, velocity, and acceleration profiles of the wrist marker. The grasp component was assessed by analysing the trajectory of each of the hand markers, and the distance between these two markers.

Movement initiation was taken from the release of the starting switch. The end of the movement was taken as the time when the fingers closed on the cylinder and there was no further change in the distance between the index finger and thumb. The period following this, during which the cylinder was lifted, was not assessed.

The dependent variables were (a) movement duration, (b) reach component parameters: times to peak velocity, peak acceleration, peak deceleration of the wrist marker, and (c) grasp component parameters: time to maximum grip aperture, and amplitude of maximum finger aperture.

Perturbed trials were characterised by a double-step movement, evident for both reach and grasp parameters (see "Results"), whereby the first movement was halted and a secondary movement initiated. For the dependent variables measured from the secondary movements (times and amplitudes of peak wrist velocity, acceleration and deceleration, and of peak grip aperture) a comparison was performed only between perturbed right and perturbed left trials given that non-perturbed trials did not show such a patterning. The onset of the second movement was detrained from the velocity and grip aperture profiles, being taken arbitrarily as the minimal value between the first and second peaks which preceded a clear risk to peak (please refer to Fig. 2 for an example trial illustration of all dependent measures).

Mean values of each measure for each participant were entered into analyses of variance (ANOVAs). Post hoc contrasts were conducted using the Newman-Keuls procedure (α level 0.05). For each session a repeated measures ANOVA was conducted with the between subject factor being 'group' (PD and control) and the within subject factor being 'type of trial'. In this analysis (three levels) the comparison was between central non-perturbed (10 trials randomly selected from 80), perturbed right and perturbed left trials. Thus in the case of session A trials to the small central cylinder were compared with perturbed trials to the left and right large lateral cylinders. In the case of session B, trials to the large central cylinder were compared with perturbed trials to each of the small lateral cylinders.

Results

Effects of perturbation

Preliminary analysis showed that results for perturbation to the right did not differ from those obtained for the left perturbation. For this reason subsequent analyses were performed, collapsing the data with respect to side of perturbation.

As expected, Parkinson's disease patients showed longer, slower movements. Furthermore, PD subjects appeared to structure the response to the double perturbation in a different way than control subjects.

As illustrated in Fig. 3, movement duration was longer for perturbed than for non-perturbed trials. For both groups, it was longer for perturbed trials from small central to large lateral cylinder than for the small non-perturbed trials (session A, $F_{(1,11)}$=44.32, P<0.0001; see Table 2). Similarly, movement duration was longer for perturbed trials from large central to small lateral cylinder than for the large non-perturbed trials (session B, $F_{(1,11)}$=76.01, P<0.0001; see Table 3).

This increase in movement duration was primarily achieved via increases to the decelerative rather than to the accelerative phase of the movement. Deceleration time, the time from peak arm velocity to the end of the movement, was longer for perturbed than for non-per-

Table 2 Means of kinematic parameters for session A, perturbed and non-perturbed trials (SD *in parentheses*)

	Parkinson's disease subjects		Control subjects	
	Non-perturbed Central small	Perturbed To large	Non-perturbed Central small	Perturbed To large
Movement duration (ms)	1187 (200)	1512 (212)	800 (97)	1032 (180)
Transport component				
Reach				
Time to peak acceleration (ms)	321 (38)	287 (42)	171 (21)	178 (19)
Time to peak velocity (ms)	535 (62)	436 (58)	346 (31)	334 (32)
Time to peak deceleration (ms)	761 (73)	600 (82)	496 (53)	463 (45)
Deceleration time (ms)	652 (73)	1076 (100)	454 (39)	698 (82)
Secondary movement				
Time to 2nd peak acceleration (ms)		783 (131)		641 (80)
Time to 2nd peak velocity (ms)		914 (92)		756 (81)
Time to 2nd peak deceleration (ms)		1121 (152)		871 (92)
Manipulation component				
Grasp				
Time to peak grip aperture (ms)	758 (91)	933 (92)	438 (52)	532 (62)
Amplitude of peak grip aperture (mm)	50 (6)	92 (18)	64 (7)	91 (10)
Secondary movement				
Time to 2nd peak grip aperture (ms)		1171 (118)		872 (91)
Amplitude of 2nd peak grip aperture (mm)		114 (10)		112 (11)

Table 3 Means of kinematic parameters for session B, perturbed and non-perturbed trials (SD *in parenthesis*)

	Parkinson's disease subjects		Control subjects	
	Non-perturbed Central large	Perturbed To small	Non-perturbed Central large	Perturbed To small
Movement duration (ms)	1254 (133)	1465 (132)	794 (91)	1032 (97)
Transport component				
Reach				
Time to peak acceleration (ms)	338 (41)	276 (35)	173 (18)	169 (17)
Time to peak velocity (ms)	551 (67)	446 (53)	332 (42)	321 (32)
Time to peak deceleration (ms)	761 (91)	595 (77)	500 (71)	440 (67)
Deceleration time (ms)	703 (84)	1019 (183)	462 (53)	711 (82)
Secondary movement				
Time to 2nd peak acceleration (ms)		810 (98)		581 (68)
Time to 2nd peak velocity (ms)		900 (112)		662 (75)
Time to 2nd peak deceleration (ms)		1083 (21)		757 (86)
Manipulation component				
Grasp				
Time to peak grip aperture (ms)	863 (100)	712 (85)	507 (65)	456 (51)
Amplitude of peak grip aperture (mm)	109 (10)	53 (6)	115 (9)	87 (8)
Secondary movement				
Time to 2nd peak grip aperture (ms)		1037 (111)		752 (81)
Amplitude of 2nd peak grip aperture (mm)		51 (6)		49 (4)

turbed trials (session A, $F_{(1,11)}$=45.03, P<0.0001; session B, $F_{(1,11)}$=38.54, P<0.0001; see Tables 2, 3).

The significant interaction between group and type of trial for a few of the dependent measures indicates that for the PD subjects, but not for the control subjects, the earliest indication of a response to the perturbation was during the accelerative part of the movement. For the reach component certain parameters were anticipated. For control subjects the first sign of response to the perturbation was during the decelerative phase (see Fig. 4). For PD subjects in both sessions A and B the peak of arm-reaching acceleration was earlier for the perturbed than for the non-perturbed trials, yet control subjects did not show the same trends (session A, $F_{(1,11)}$=21.05, P<0.0001; session B, $F_{(1,11)}$=31.05, P<0.0001; see Tables 2, 3). Peak velocity was also earlier for perturbed than for non-perturbed trials only by PD subjects (session A, $F_{(1,11)}$=41.04, P<0.0001; session B, $F_{(1,11)}$=38.32,

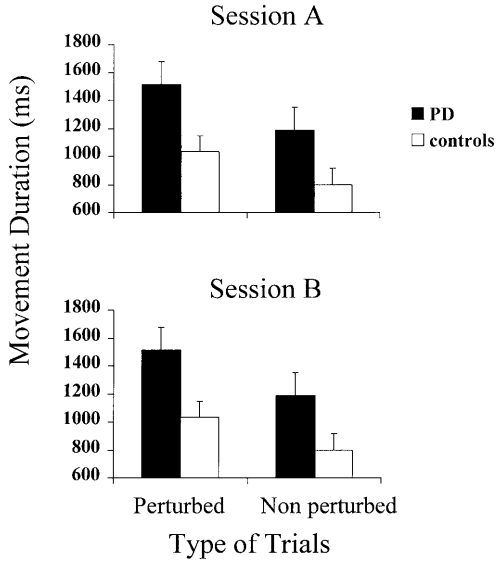

Fig. 3 Average values for the parameter of movement duration for perturbed and non-perturbed trials in session A and session B for PD and control subjects. Note the significantly longer movement durations for perturbed trials

P<0.0001; see Tables 2, 3). In contrast to the differences found for the two groups for time to peak acceleration and time to peak velocity, both groups showed the same level of anticipation for perturbed as for non-perturbed trials for time to peak deceleration (session A, $F_{(1,11)}$=23.07, *P*<0.0001; session B, $F_{(1,11)}$=11.06, *P*<0.001; Tables 2, 3). For the grasp component, the earliest indication of a response to the perturbation was evident at the time of maximum grip aperture. It occurred earlier for non-perturbed than for perturbed trials in session A ($F_{(1,11)}$=5.54, *P*<0.001) and earlier for perturbed than for non-perturbed trials in session B ($F_{(1,11)}$=28.11, *P*<0.0001). The result that aperture response to perturbation occurs earlier in session A for non-perturbed trials and vice versa for session B depends on the degree the initial pattern has been expressed. For session A, where the initial movement is directed to a small object, the participants seem unable to break the execution for the small cylinder when the perturbation occurs. Thus the almost complete development of the first grip pattern delays the grip reorganisation for the second larger grip pattern. For session B the passage from the larger to the

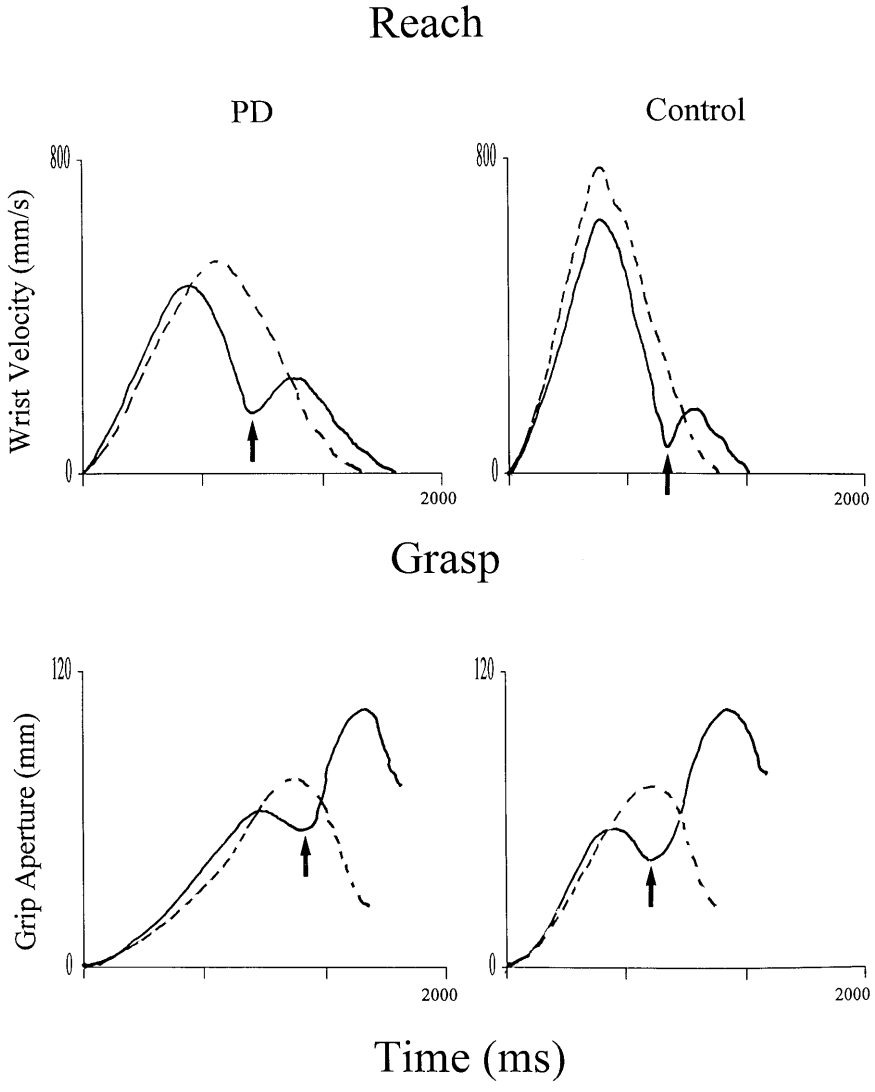

Fig. 4 Example trial for one PD (*3*) and one control subject (*3*) showing bimodal pattern for perturbed trials for session A. *Arrows* indicate that for PD subjects the response is first observed in the reach component and then in the grasp component while for the control subjects the response is observed near simultaneously in the reach and the grasp components (*solid line* perturbed trials, *dotted line* non-perturbed trials)

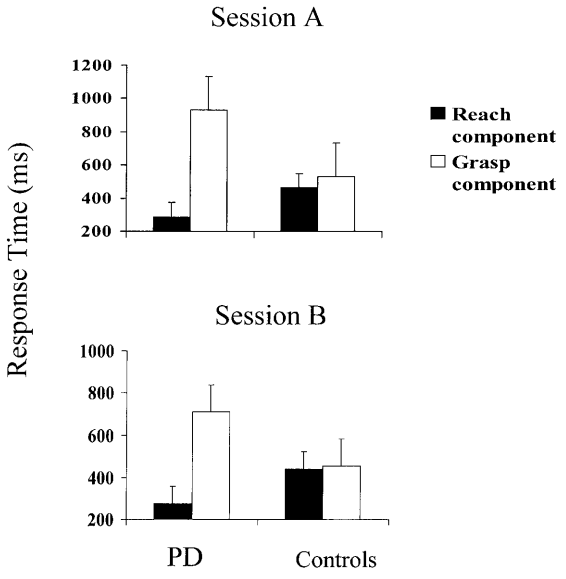

Fig. 5 Average times at which a response to perturbation was first observed for the reach-and-grasp components for the PD and control subjects. For PD subjects the response is first observed in the reach component (time to peak velocity) and then in the grasp component (time to maximum grip aperture). For the control subjects the response is observed near simultaneously in the reach and the grasp components

smaller object is more easily managed and the time of maximum grip aperture anticipated in response to the perturbation. The means of implementing the second pattern were thus in operation well before the first pattern showed signs of closing. Several factors may have contributed to the differences between the 'grasp' response to a perturbation. One of these is that biochemically there may be more advantage for closure than for opening (for a detailed account of this issue please refer to Castiello et al. 1993).

Figures 4 and 5 show the average times at which response to perturbation was first observed in the reach (time to peak velocity) and subsequently in the grasp components (time to maximum grip aperture) for the PD subjects. For the control group the response to perturbation was nearly simultaneous for the same parameters for the reach and the grasp components. One-way ANOVAs were conducted to compare this difference between PD and control subjects. For both sessions, this difference was significant (session A, $F_{(1,11)}$=72.12, P<0.0001; session B, $F_{(1,11)}$=88.05, P<0.0001), with PD subjects showing a much greater time span between the first transport response to perturbation and the first manipulation response than control subjects (session A, 437 vs 69 ms; session B, 436 vs 16 ms, for PD and control subjects, respectively).

All participants showed a double movement pattern response to perturbation for at least six of the ten perturbed trials that were analysed. For the reach component, this was evidenced by second peaks of acceleration, velocity and deceleration. For the grasp component, the peak of the second hand opening and closing sequence generally reflected the size of the target to grasp (session A, PD 114 mm, controls 112 mm; session B, PD 51 mm, controls 49 mm). The earliest responses to perturbation in either the reach or the grasp components were well before the onset of these secondary movements. For PD subjects, secondary movements began first in the reach and then in the grasp component. In session A, onset of the secondary transport movement was at 750 ms while onset of the manipulation secondary movement was at 1080 ms. A similar pattern was found for session B, with onset in the reach component being at an average of 734 ms and onset in the grasp component being at 816 ms. This sequential patterning was in contrast to the near synchronous onset of secondary movements for the control subjects (session A 631 ms transport, 629 ms manipulation; session B 558 ms transport, 560 ms manipulation; see Fig. 4).

Coordination between the reach and grasp components

Motivated by Jeannerod's (1984) suggestion that grasp closure is synchronised with peak deceleration, the relationship between the time of peak deceleration and the time to peak hand opening aperture was explored with correlation analysis (Pearson product-moment correlation). There appeared to be no group differences in the degree to which the two components were correlated in time for both perturbed and non-perturbed trials. Table 4 shows the results for session A and B perturbed trials (collapsed according to direction of perturbation). All bar two PD subjects (PD2 and PD12) in session A show significant correlations between the reach and the grasp components at some point in the first and/or second parts of the movement.

In session A, four control and six PD subjects showed significant correlations between the time of the first peak of reaching arm deceleration (transport) and the time of the first peak in grip aperture (manipulation). For session B, correlations between these two parameters were found for three control and two PD subjects. Interestingly, when correlating the same parameters for the second movement, a greater number of control (nine in session A, nine in session B) and PD subjects (eight in session A, eight in session B) showed significant correlations. The mean timings of these two parameters were quite similar (session A controls: time to second peak deceleration=871 ms, time to second grip aperture=872 ms, PD subjects: time to second peak deceleration=1121 ms, time to second grip aperture=1171 ms; session B controls: time to second peak deceleration=757, TGA2=752 ms; PD: time to second peak deceleration=1083 ms, time to second grip aperture=1037). The earlier sequencing by PD subjects is no longer evident at this late stage of the action. For the majority of the control subjects, yet very few of the PD subjects, the onset of the second transport movement was correlated with the onset of the secondary manipulation movement (session A PD 3, controls 11; session B PD 0, controls 9).

Table 4 Results of correlational analysis of perturbed trials. Values are the standardised Pearson-product moment correlation coefficients (*P* participant number, *TPD* time to peak arm deceleration, *TGA* time to peak grip aperture, *1* first movement, *2* submovement, *OV* onset of 2nd velocity peak, *OG* onset of 2nd hand opening)

P	Session A						Session B					
	TPD1-TGA1		OV-OG		TPD2-TGA2		TPD1-TGA1		OV-OG		TPD2-TGA2	
	PD	Control	PD	Control	PD	Control	PD	Control	PD	Control	PD	Control
1	–	–	–	0.58	0.71	0.84	0.64	–	–	0.90	0.73	0.63
2	–	–	–	0.63	–	0.74	–	–	–	0.88	0.92	0.73
3	0.74	0.67	0.71	0.74	0.82	0.67	0.59	–	–	0.75	0.88	0.84
4	0.82	–	–	0.58	0.60	–	–	–	–	–	0.68	0.65
5	–	–	–	–	–	0.90	–	0.74	–	0.77	–	0.75
6	–	0.81	–	0.92	0.77	–	–	–	–	0.68	0.88	–
7	0.91	0.71	0.55	0.81	–	0.59	–	–	–	0.65	0.73	0.61
8	–	–	–	0.81	0.85	0.63	–	–	–	0.58	–	0.92
9	0.67	–	–	0.67	0.82	0.72	–	0.90	–	0.79	0.97	0.77
10	0.58	0.62	–	0.73	0.93	0.88	–	–	–	–	0.88	0.76
11	0.71	–	0.88	0.91	0.78	0.85	–	–	–	–	–	–
12	–	–	–	0.73	–	–	–	0.62	–	0.58	–	–

Discussion

The current study utilised what has been termed a 'double' perturbation paradigm to assess the adaptive responses of Parkinson's disease (PD) subjects to an unexpected change of object size and the location. Given the proposed dysfunction in the simultaneous activation of movement components, it was predicted that PD subjects would show particular movement disorganisation at correction stages of the perturbed movement because both components needed to be altered either simultaneously or in sequence. Furthermore, it is predicted that this 'double' perturbation would reveal dysfunctions in the ability of PD subjects to emit a near synchronous response in both components.

The results did support these predictions. The PD subjects in the current study did not respond to the 'double' perturbation in the same manner as the control subjects or the younger subjects tested in a previous study (Castiello et al. 1998). PD subjects anticipated and showed sequential movement parameterisation when unexpectedly confronted with the simultaneous perturbation of object position and size. Conversely, control subjects showed a simultaneous response to the perturbation which was much later.

For both subject groups the most obvious perturbation response is a large increase in the duration of the reach-to-grasp movement. For the perturbation from a small central to a large lateral target, movement duration is around 300 ms longer than a non-perturbed movement to the small central cylinder. For the perturbation from a large central to a small lateral target, movement duration is around 200 ms longer than the non-perturbed action to the large central cylinder. These increases in movement duration are comparable to those found in a study of young subjects who performed the same experiment where it was proposed that a 'double' perturbation elicits an additive function (Castiello et al. 1998). To explain this more clearly, consideration must be given to the results from single perturbation studies of non-brain-damaged subjects. With perturbation of object location alone, movement duration increases by around 100 ms (Paulignan et al. 1991a; Castiello et al. 1991; Gentilucci et al. 1992; Scarpa and Castiello 1994). With perturbations of object size alone, movement duration increases by around 85 ms when the perturbation is from a large to a small object, and by around 170 ms when the perturbation is from a small to a large object (Paulignan et al. 1991b; Castiello and Jeannerod 1991; Castiello et al. 1992, 1993b; Castiello and Bennett 1994). Simply by adding the 'location perturbation' movement duration value to the appropriate 'size perturbation', movement duration values gives results which are remarkably similar to those found in the current study.

The pattern of the perturbation response by the PD subjects of this study differs from the response found in non-brain-damaged subjects in that it is not synchronous; first the reach and then the grasp component shows a change following perturbation. For the PD subjects of this study, the first measurable response to the perturbation is in the reach component in the parameter of peak acceleration. For PD subjects this is around 280 ms after movement onset of perturbed trials. Responses in the grasp component (in the parameter of peak grip aperture) are more than 400 ms later. This tendency for sequentialisation is particularly evident in PD subjects with perturbation responses requiring a shift from a small central to a large lateral cylinder (the difference between manipulation and transport onsets being >600 ms). To a degree this latter result concurs with those from 'single' size perturbation experiments with PD subjects where the transition from precision grip to whole hand prehension appears to demand more of the system than the opposite perturbation from whole hand prehension to precision grip (Castiello and Bennett 1994).

Furthermore, PD subjects continue to display this sequential organisation at slightly later stages of the movement. For example, the onset of the transport secondary

movement is well before the onset of the manipulation secondary movement. In contrast, for control subjects, the onset of the transport secondary movement is almost synchronous with that of the grasp component. In other words, the breakdown from parallel to serial organisation occurs in responses to perturbations as well as the preplanned voluntary movements in other studies (Weiss et al. 1997; Castiello et al. 1993).

The interpretation given for the younger subjects (Castiello et al. 1998) to explain the lateness of the response in both reach and grasp components was that a 'gating' mechanism operated to prevent the very early responses that are often observed in 'single' perturbation experiments. For example, the young subjects did *not* show changes as early as 100 ms in the acceleration profile, a result that would be expected if the perturbation response was simply 'run-off', or automatically executed, with unexpected changes to object location (Paulignan et al. 1991a; Castiello et al. 1991). Because such early responses were absent, it was proposed that this 'gating' function occurred at a very early stage of visuomotor processing. The control but not the PD subjects of the present study showed the same pattern of response to perturbation. Such results suggest that the proposed 'gating' function is disrupted in Parkinson's disease. Further, they add support to the contention that such a function operates at a visuomotor processing stage to which basal ganglia contributes.

A certain degree of consistency is apparent in the degree to which the components are 'coupled' in time. All bar 10 PD subjects and 11 control subjects from this study show significant correlations between components during perturbed trials. This is of particular interest when considering that the first overt transport response to perturbation could be so disparate in time with respect to the first manipulation response for PD subjects. Further, both PD and control subjects show near synchronous timing of parameters from the reach and the grasp components near the conclusion of the secondary movements. Hence, in terms of defining Parkinson's disease, there does not appear to be any dysfunction in the ability to adopt certain perturbation response strategies to achieve the required temporal arrangement for the final required output, not in the ability to coordinate the two components in time (see also Castiello and Bennett 1994).

Above all these results add further support to the contention that PD subjects demonstrate difficulties in performing coordinated actions (Marsden 1982, 1984), under conditions which place severe demands upon the system of parallel visuomotor processing. In particular, there are indications that the basal ganglia may act as part of a circuit that modulates the degree to which the components are coordinated according to output requirements. In this view, basal ganglia might be seen in the context of the neural networks that actively control the passage of information to and between the channels. Brain imaging studies of reach-to-grasp action suggest that subcortical regions are suitable candidates for integrating different object's attributes such as size and location (Decety et al. 1994; Grafton et al. 1991, 1992, 1996). Further, a degree of caution is necessary before assigning to basal ganglia a role for specific functions given that the testing of patients in a medicated state may lead to conclusions which are partially generalizable. Nevertheless, all PD participants of the present study did not show deficits due to medication and the reported effects were evident in all of them.

As a final point, because the organisation of the movement is different to that of control subjects, any dysfunction in the simultaneous activation of movements is clearly compensated for at a more global level. Hence, if this problem in activation can be explained in terms of less responsiveness within higher cortical regions such as the SMA (Goldberg 1985; Albin et al. 1989; Marsden 1989; Chevalier and Deniau 1990; DeLong 1990; Parent 1990; Brotchie et al. 1991a, 1991b; Rascol et al. 1992), central nervous system mechanisms ensure that this does not disrupt the proportional organisation of movement.

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