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Research Article

Dopaminergic effects on the implicit processing of distracter objects in Parkinson's disease

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Abstract. The aim of the present study was to assess the effects of dopaminergic medication on the selection-for-action mechanisms in Parkinson's disease (PD). PD subjects were tested after not having taken medication for at least 12 h ("Off" state) and then retested 1-2 h after medication ("On" state). A three-dimensional kinematic system (ELITE, BTS, Italy) was used to record reach-to-grasp movements to a target object placed at a reaching distance of 30 cm. The target was presented alone or in the presence of distracter objects, which could be of either the same size (compatible distracter) or a different size (incompatible distracter). PD subjects in the Off state were significantly more affected by the presence of the incompatible distracter than in the On state. These results indicate that dopaminergic medication is of benefit in reducing interference effects when distracter objects evoke motor programs that differ from the motor program elicited by the target. Results are discussed in light of the role played by the striatal and mesocortical dopaminergic systems for response selection in basal ganglia disorders.

Key words. Reach to grasp - Motor control - Basal ganglia - Selection for action - Human

Introduction

Important insights into how the attentional selection of action may operate can be drawn usefully from the study of brain-injured patients. For example, several papers have investigated how hand-path curvature is/is not increased in neglect patients (Chieffi et al. *1993*; Jackson et al. *2000*; Karnath et al.

1997) and how the presence of a distracter object affects the reaching-to-grasp action towards a target in patients with frontal lobe damage (Riddoch et al. *in press*).

Chieffi et al. (*1993*) have investigated the effect of attentional impairments on the planning and control of hand movements in a patient with unilateral neglect. The patient reached and grasped targets in the presence of distracters placed either to the right or left side of the target. Both the target and the distracter were presented ipsilaterally to the right hand. The patient did not show misreaching, although her hand trajectory deviated abnormally towards the distracter position when the distracter was ipsilateral to the target.

Riddoch and colleagues (*in press*) have studied reaching-for-grasp responses to a cup in a patient with frontal lobe damage. In one task, the patient had to respond with the hand congruent with the location of the cup irrespective of the position of the handle. They found that the patient had difficulty in suppressing a response to the "affordance" of the object, determined by the position of the handle. In a second task, distracter effects were examined. The task now was to respond to the affordance of a central target cup, and a distracter cup (differing in colour) was placed in the reach trajectory. The position of the handle of the distracter cup could be congruent or incongruent with the handle of the target. Interestingly the patient made errors by sometimes actually reaching to the distracter rather than the target, but the hand used was always based on the affordance of the target and not of the distracter. This was the case even though sometimes the patient used a hand incongruent with the affordance of the distracter (e.g., reaching with his right hand to pick up a distracter with a left-side handle, when the target's handle was on the right). Riddoch et al. (*in press*) propose that the patient attends to the target and that the grasp response is programmed to that object. However, a distracter in the reach trajectory could also be attended as the action was initiated; thus there was transference of the grasp activated by the target to the distracter. Under conditions of disinhibition, as can occur with frontal lobe dysfunction, if a distracter is attended it is very difficult to resist the strong motor response elicited by the distracter object.

Deficits in the frontal-subcortical circuits prove useful in the explanation of a wide range of human behavioural disorders (Cummings *1993*). A few deficits that form the basis of a number of descriptions of frontal lobe functions have been reported in Parkinson's disease (PD; Brown and Marsden *1990*). For example, Stam et al. (*1993*) proposed that cognitive dysfunction in PD can be understood as a disturbance in the frontal regulation of attentional processes. Further, these frontal attentional disturbances could depend on the degeneration of the mesocortical innervation of the frontal cortex. Along these lines, it may be advanced that PD subjects might experience similar problems to frontal subjects in sensorimotor selection under conditions of visual clutter, for example, when required to direct attention to one among several objects, and generate the limb movements necessary to grasp and manipulate the selected object.

Recently, Jackson and Houghton (*1994*) have suggested that basal ganglia perform a computational function concerned with sensorimotor selection. In these terms, basal ganglia are proposed to provide an important means by which cortical neural networks exert control over subcortical structures involved in visuospatial cognition (Jackson and Houghton *1994*). Jackson and colleagues (Jackson et al. *1995*) have investigated the effects of PD upon the sensorimotor mechanisms used to control reaching-to-grasp movements. Subjects were required to grasp a red block presented in isolation or flanked by a yellow block (distracter). Their results suggest that PD patients are not particularly susceptible to distraction by non-relevant objects when vision is allowed. However, without visual guidance, the reach-to-grasp movement is affected in the presence of non-relevant distracter objects. Further, these effects are confined to the reaching component of the movement (Jackson et al. *1995*).

The interference effects reported by Jackson et al. (*1995*) can be interpreted as a conflict between the motor program relative to the intended-but-not-executed action towards the distracter and the intended-and-executed action towards the target. Neuronal populations, kinematic planning and functional properties for the irrelevant distracter object are alerted and interfere with neuronal populations, kinematic planning and functional properties activated and executed for the target object. In other words, as happens to frontal patients (Riddoch et al. *in press*), distracters automatically activate their responses without the participant's intention to act (Lhermitte *1983*).

In order to address the notion that inhibition of motor programs for the irrelevant information is dysfunctional in PD subjects, in the present study the target and the distracter size were manipulated in such a manner that distracter and target required different kinematic patterning to be grasped (whole-hand prehension and precision grip). Thus, the first aim of this research was to investigate whether PD subjects are affected by distracting information during the reach-to-grasp movement when this information enhances the activation of an implicit and different motor program.

In addition the present study also examined whether the selection-for-action phenomena could be associated with a dopaminergic mechanism by studying patients in "Off" and "On" medication states. PD participants in the reach-to-grasp experiments of Jackson et al. (*1995*) were tested after having taken their morning dose of carbidopa/levodopa. Thus, it is not known whether the lack of distracter effects in the visual condition is masked by dopamine assumption. For example, the normal patterning of the reach-to-grasp movement seen in unmedicated PD participants varies according to object size and distance (Castiello et al. *1999*). Consistent with previous findings (Brown and Robbins *1989*; Robbins and Brown *1990*), we predicted that for PD subjects in the Off state the selection from the range of possible responses will be altered and interference will be more pronounced than for the same subjects in the On state.

Materials and methods

Participants

The characteristics of the 12 PD participants are shown in Table 1. Each PD participant was initially tested before the first morning dose of carbidopa-levodopa, after not having taken medication for at least 12 h (Off state), and then retested 1-2 h after medication. Objective evidence that the patients were having an optimum response to their levodopa was given by the administration of the Unified Parkinson's Disease Rating Scale (UPDRS; Fahn et al. *1987*) both in Off and On states. Dopaminergic medication was most commonly Sinemet or Madopar, with other medications including Artane, Eldepryl and Parlodel. Disease duration for the PD participants ranged from 1.5 to 10 years at the time of testing, and no participant showed motor complications due to therapy that interfered with the task (please refer to the dyskinesia ratings on the UPDRS presented in Table 1). The 12 sex- and age-matched control participants reported no neurological or skeletomotor dysfunctions. All participants showed right-handed dominance (Oldfield *1971*), were naive as to the experimental design or purpose and gave informed 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 of the PD participants ranged from 28-30 years, and those of the control participants from 29-30 years. With visual acuity testing, PD participants scored, on average, 18 out of 20 and control participants 20 out of 20. All subjects signed informed consent before participating in the study.

Table 1. Characteristics of the Parkinson's disease subjects (*UPDR* unified Parkinson's disease rating, *MMSE* mini-mental state examination)

Subject	Age (years)	Gender	UPDR			Hoehn and Yahr scale[a]	MMSE	Length of diagnosis	Medication dosage (levodopa)
			Limb-right	Limb-left	Alt. Mov.[a]				
1	38	F	4.0	4.0	1.0	1	30.0	6.0	Sinemet CR 200 × 3
2	66	F	4.0	3.0	1.0	1	29.0	1.5	Sinemet CR 200 × 1
3	72	M	8.0	8.0	2.0	2	28.5	6.0	Sinemet CR 200 × 3
4	58	M	5.0	5.0	1.0	2	28.0	8.0	Sinemet CR 100 × 3
5	66	M	5.0	4.0	1.0	2	30.0	1.5	Sinemet CR 200 × 1
6	65	M	5.0	6.0	2.0	3	28.0	3.5	Sinemet CR 100 × 3
7	68	M	4.0	10.0	2.0	1	30.0	3.0	Sinemet CR 200 × 1
8	64	M	4.0	3.5	1.0	2	29.0	7.0	Sinemet CR 200 × 3
9	73	M	3.0	2.5	1.0	2	29.0	4.0	Madopar CR 100 × 3
10	69	M	3.0	4.5	2.0	1	28.0	2.0	Sinemet CR 100 × 0.5
11	73	F	5.0	1.5	0.5	1	29.0	10.0	Madopar CR 100 × 3

Subject	Age (years)	Gender	UPDR			Hoehn and Yahr scale[a]	MMSE	Length of diagnosis	Medication dosage (levodopa)
			Limb-right	Limb-left	Alt. Mov.[a]				
12	79	M	3.5	3.5	1.0	2	29.0	7.0	Sinemet 100 × 2

[a] Rapid alternating movements

Apparatus

The experiment was conducted under normal room lighting. Details of the experimental setup are shown in Fig. 1. The participant was seated in front of the table working surface (1 m × 1 m). Before each trial, the subject's hand was positioned on the table in the mid-sagittal plane, 15 cm from the thorax. In this position the shoulder was flexed (5-10°), the elbow was flexed, the forearm was semipronated and the wrist was in 10-15° of extension. The index finger and the thumb were held gently opposed, and the ulnar border of the hand rested on a pressure-sensitive starting switch. The target was a red plastic apple (diameter 70 mm; mass 538.853 cm^3) presented so that it was 30 cm from the starting position. The position of the target was central to the mid-sagittal plane. A second plastic apple, either identical to the target or smaller (30 mm diameter; mass 42.417 cm^3), was individually presented 30° to the right or 30° to the left of the central apple (see Fig. 1). The size of the larger apple was such to elicit a type of prehension that could be defined as whole-hand prehension (opposition of the thumb with the other fingers). The size of the smaller apple was such to elicit a type of prehension that could be defined as precision grip (index finger thumb opposition with the exclusion of the other fingers). In summary, the central target apple was presented alone (no distracter), or in the presence of an apple similar to the target (compatible distracter) or with an apple of a smaller diameter (incompatible distracter). The order of presentation was randomised. The objects were not visible prior to trial onset. In order to minimise the time of stimuli processing, visual availability of the stimuli was controlled with Plato spectacles (Plato Technologies). These were lightweight, and were fitted with liquid crystal lenses; the opacity of the lenses was controlled by the computer. The release of the circular starting switch (diameter 10 cm, height 1 cm) on which the hand rested signalled movement initiation to the computer. Participants were asked to perform the movement with their dominant hand.

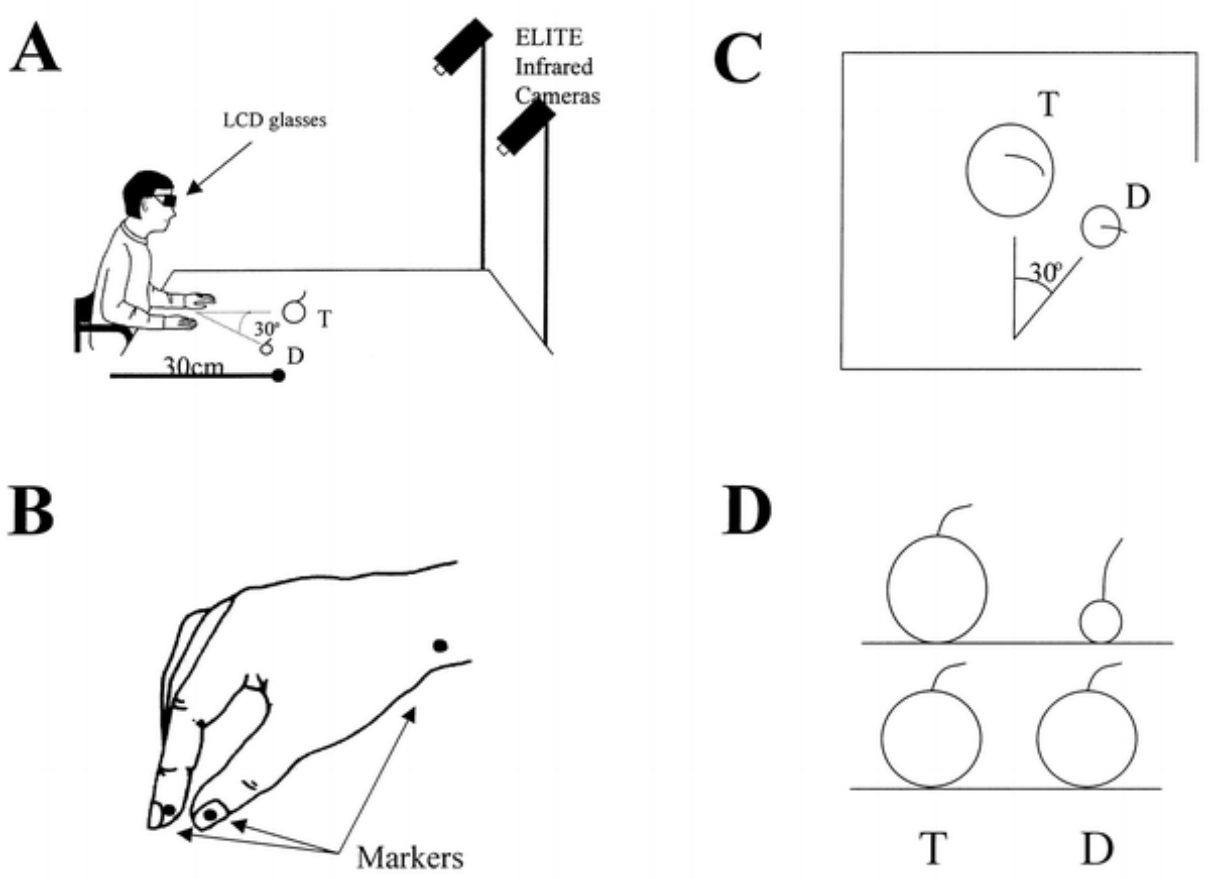

Fig. 1A-D. Experimental setup. **A** Subject, stimuli and camera position. **B** The position of the markers on the subject's hand. **C** The central target and the distracter from above. **D** The target with the compatible (same object) and the incompatible (different object) distracters seen from the front (*T* target, *D* distracter)

Recording

Reflective passive markers (0.25 cm in diameter) were attached to three points, the wrist (the radial aspect of the distal styloid process of the radius), the index finger (the radial side of the nail) and thumb (the ulnar side of the nail). Movements were recorded with the ELITE system (Ferrigno and Pedotti *1985*). This system 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 surface was a parallelepiped (60 cm long × 30 cm wide × 60 cm high) from which the spatial error

measured from stationary and moving stimuli was 0.4 mm.

Procedure

Thirty trials were performed altogether: ten trials for the no-distracter condition, ten trials for the compatible-distracter condition, and ten trials for the incompatible-distracter condition. These conditions were presented in random order and counterbalanced for right and left position of the distracter objects.

For each trial, as soon as the spectacles cleared, the participant was required to reach and grasp the centrally located object and to lift it briefly from its position on the working surface. Movement initiation time was the time taken between the opening of the spectacles, which acted as a go signal, and the release of the starting switch. The start of the movement was recorded as the time the participant's hand left the pressure sensitive switch. The end of the movement was recorded as the time the fingers closed on the target. The movement after the target had been grasped was not relevant to the experiment and was not assessed. There were no instructions about maximising the speed of the movement. It was stressed that a normal movement, similar to that used for reaching and grasping familiar objects, was a requirement for the purposes of the experiment.

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 FIR linear filter with a transition band of 1 Hz (sharpening variable 2; D'Amico and Ferrigno *1992*). Analysis of the acceleration and velocity of the wrist marker allowed assessment of the reaching component. Analysis of the markers on the thumb and index finger allowed assessment of the grasp component. The start of the movement was signalled by the release of the pressure starting switch. The end of the movement was taken as the time when movement of the fingers ceased after they had closed on the object. No further assessment took place after finger closure. The dependent variables specifically relevant to the scientific hypothesis under investigation were analysed. Given previous results of interference on the movement due to the presence of distracters, an increase in initiation time and movement duration when both the target and the distracter were presented was expected (Castiello *1996*; Tipper et al. *1997*). To investigate whether the temporal occurrence of the reaching component parameters varied when the target was presented with a distracter rather than in isolation, the times to peak velocity, peak acceleration and the time from peak velocity to the end of the movement (deceleration time) were analysed. To test whether the movement showed a more direct trajectory to the object, analyses were conducted upon the mean maximum deviation along the mediolateral and antero-posterior horizontal axis, and along the vertical axis (Chieffi et al. *1993*; Jackson et al. *2000*). For the grasp component, measurements for the opening and closing phases of the hand movement related to the rate of maximum velocity, and the time at which this occurred, were considered (Jervis et al. *1999*). In particular, the parameters under consideration were time to maximum peak grip aperture, the time from the maximum grip aperture to the end of the movement (closing time), time to peak grip velocity, the amplitude of peak grip aperture and the amplitude of peak grip velocity. Each temporal parameter has been expressed in relative terms as a percentage of the total movement duration. Subsequent statistical analyses have been carried out on relative values, which allow for a more informative comparison between groups and conditions.

Statistical analyses

For each participant of the two groups, mean values for each of the dependent measures were calculated for each distracter combination. Given that the patients were assessed twice (On and Off medication), whereas the control only once, three ANOVAs were conducted. Even if in some respects the three analyses may appear redundant, this was done in order to meet ANOVA assumptions. In the first ANOVA, the effects of On versus Off effects in PD are compared with Group as the within-subjects factor (PD Off vs PD On). In the second ANOVA, PD On medication was compared with control subjects (between-factor Group: PD On vs Controls). In the third ANOVA, PD Off were compared with control subjects (between-factor Group: PD Off vs Controls). For all three analyses, the within-subject factor was Type of distracter (Compatible, Incompatible, No distracter). Given the number of dependent variables and analyses involved, the significance level for the number of

comparisons was adjusted to $P<0.01$. Where necessary, significant effects were further analysed using the Neuman-Keuls test for pairwise comparisons. An analysis was conducted in order to investigate whether the effects for right and left distracter objects were asymmetric. For this analysis, the between-subject factor was Group (PD Off, PD On, Controls) and the within subjects factors were Type of distracter (Compatible, Incompatible) and Distracter position (Right, Left). No significant effects due to position (right or left) or interaction between groups, position and type of distracter for any of the dependent measures of our interest were found. Thus, data for distracter position were averaged and entered into the analyses.

Results

Global effects of the dopaminergic medication

As revealed by the first analysis, the main factor Group (PD Off vs PD On) was significant for a number of dependent measures. These results mirror those of a study where the effects of dopaminergic medication on the organisation of the reach-to-grasp movement in PD in Off and On states were assessed (Castiello et al. *1999*). Thus, for the sake of brevity, these results will be briefly summarised (see Table 2).

Table 2. Mean and SD for the kinematic parameters comparing the Parkinson's disease (*PD*) group in the On and the Off state

	PD Off		PD On		$F_{1,11}$	*P*-value
	Mean	SD	Mean	SD		
Movement duration (ms)	1291	743	1063	118	85.03	<0.0001
Deceleration time (%)	58	7	54	8	10.31	<0.001
Amlitude peak velocity (mm/s)	784	200	539	121	9.31	<0.001
Amplitude peak Acceleration (mm/s^2)	4001	1140	2529	543	15.28	<0.001
Amplitude peak deceleration (mm/s^2)	3744	898	2132	441	27.44	<0.0001

Movement duration and the time spent in arm deceleration were significantly less in the On than in the Off state. The amplitudes of peak reaching velocity, acceleration and deceleration were all higher in the On than in the Off state. Further, in the On state, the acceleration profile no longer exhibited small, irregular adjustments, and the movement was more direct in both the mediolateral horizontal and vertical planes. Along the same lines, the present results confirm that dopaminergic medication is of benefit in reducing bradykinesia and in fine-tuning kinematic parameterisation of a selected reach-to-grasp action.

Distractor effects and dopamine depletion

In this section, statistical values refer to the first analysis where PD Off and PD On were compared. The performance for the control and the PD On groups was very similar. Thus, for the sake of clarity and brevity, the results for the control group are mentioned in this section, but they refer to the second and the third analyses (see Statistical analyses section).

For the PD group in the Off state, the time to initiate the movement was longer for the incompatible-distracter condition than for the compatible- and the no-distracter condition ($F_{1,11}$=9.45, P<0.001; see Fig. 2). No differences for the PD group in the On state and the control group were found. This result suggests that processing time before the start of the action was affected by the relationship between the target and the distracter object for PD subjects off medication. When the PD subjects were in the Off state, but not when they were in the On state, movement duration was significantly longer in the incompatible- than in the no-distracter condition ($F_{1,11}$=7.02, P<0.01; see Fig. 2). Similarly for the control group, movement duration was significantly longer in the incompatible- than in the no-distracter condition (see Fig. 2). For the PD subjects in either the Off or the On state and the control subjects, the time from peak velocity to the end of the movement (deceleration time) was longer for the incompatible- than for the compatible- and the no-distracter conditions ($F_{1,11}$=32.76, P<0.0001; see Fig. 2). However, the length of the deceleration phase was more pronounced for the PD subjects in the Off state (Newman-Keuls, P<0.01; see Fig. 2). For the spatial trajectories, no specific effects due to the presence of the distracter were found.

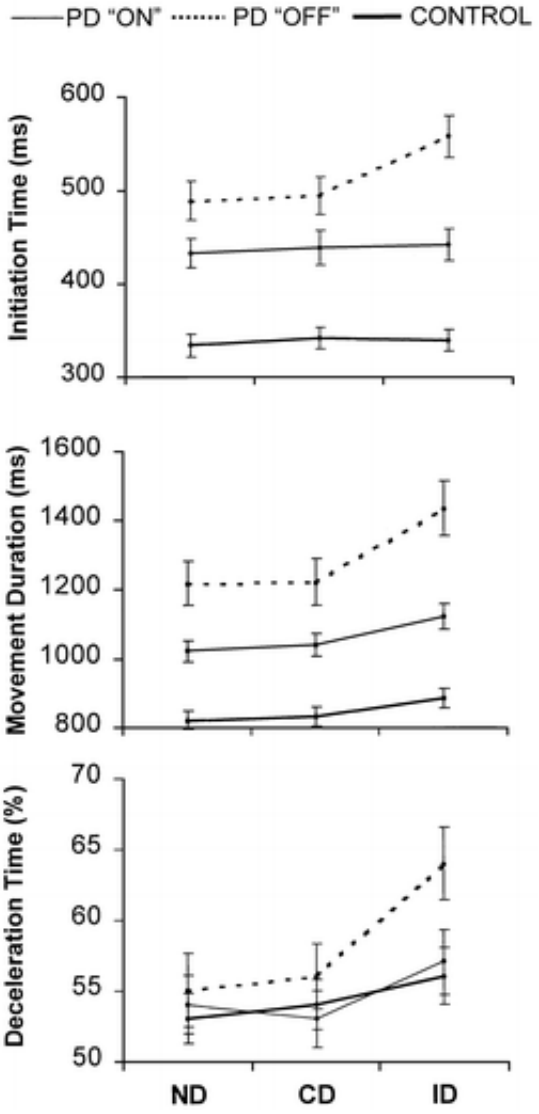

Fig. 2. Initiation time, movement duration and deceleration time for the three distracter conditions for Parkinson's disease subjects in On and Off states and for control subjects. *Bars*, standard error

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Consistent results within the prehension literature are the longer movement duration and deceleration time for small stimuli than for large stimuli (Castiello *1996*; Gentilucci et al. *1991*; Jakobson and Goodale *1992*; Marteniuk et al. *1990*). The current result of a longer movement duration and a longer deceleration time suggests that for both groups the implicit processing of the smaller distracter influenced kinematics parameterisation for the large object (Bonfiglioli and Castiello *1998*; Castiello *1996*). However, the fact that differences were found between the PD subjects in the Off state and the other two groups suggests that the "size-distracter" effect was more pronounced and affected more severely the organisation of the reach-to-grasp movement following dopamine depletion.

Several parameters of the grasp component reached significance. We observed that for all groups there was a significant difference between the no-distracter and the compatible-distracter condition compared with the incompatible-distracter condition for the velocity and acceleration of finger opening. Examination of the relative values at which the significant kinematic landmarks occurred shows that there was a consistent trend in which these events, in the incompatible-distracter condition,

occurred significantly earlier than in the no-distracter condition. These changes to the kinematic parameters of the grasp component were accommodated within a movement time that differed significantly for the three conditions for the PD group in the Off state but that did not differ for the PD in the On state and the control groups (see Fig. 2). For the hand-opening phase, time to peak acceleration and velocity (referring to the maximum rate of acceleration and velocity at which the thumb and forefinger moved apart as the hand opened), occurred earlier in the incompatible condition than the compatible- and the no-distracter condition (acceleration: $F_{1,11}=8.23$, $P<0.01$; velocity: $F_{1,11}=10.04$, $P<0.001$; see Fig. 3). Thus, the finger and thumb began to open and reached the greatest opening rate earlier when an incompatible distracter was presented compared with no distracter being present. The time of maximum grip aperture occurred earlier in the incompatible condition compared with the compatible condition and the no-distracter condition ($F_{1,11}=11.12$, $P<0.001$). This anticipation, however, was much greater for the PD in the Off state than for the PD in the On state and the control participants (post hoc comparisons, $P_s<0.01$; see Fig. 3). These early effects may reflect a compensatory strategy that allows the fingers a longer deceleration and positioning time. This statement is supported by the significantly greater percentage of movement time spent from the time of maximum grip aperture to the end of movement (closing time) for the incompatible-distracter condition than the compatible- and the no-distracter conditions ($F_{1,11}=34.76$, $P<0.0001$; see Fig. 3). Post hoc comparisons also revealed that for the PD subjects in the Off state this percentage of movement duration was different when compared with the percentage obtained for the same group in the On state and for the control group ($P_s<0.01$). The amplitude of maximum grip aperture was also more affected for the PD in the Off state than for the PD in the On state ($F_{1,11}=6.31$, $P<0.05$). When the small incompatible distracter was presented, the amplitude of grip aperture was smaller for the PD in the Off state than that for the PD in the On state and the control subjects for the same condition (94 mm, 100 mm and 101 mm, respectively).

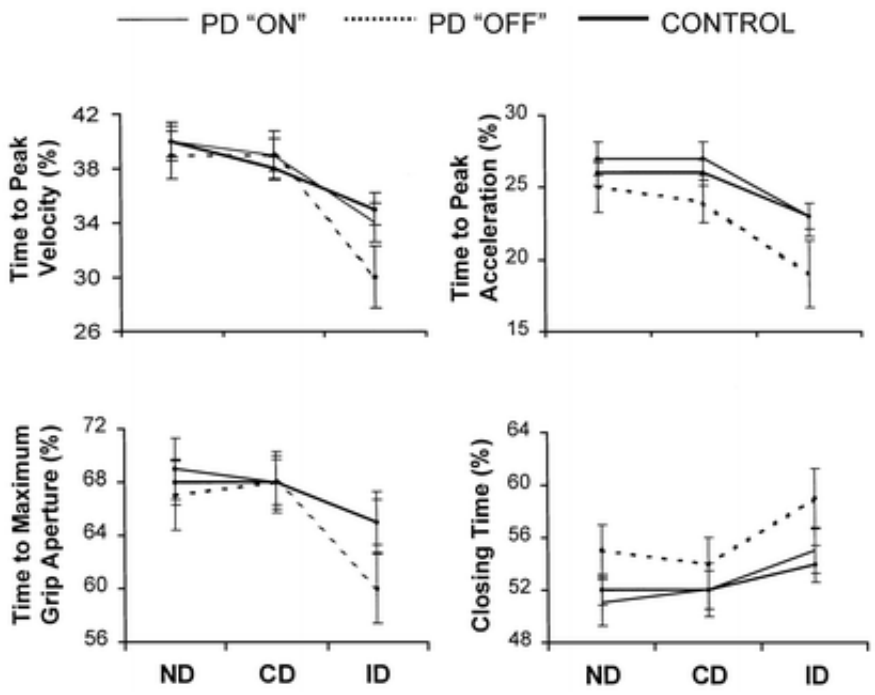

Fig. 3. Time to peak velocity opening, time to peak acceleration opening, time of maximum grip aperture and closing time for the three distracter conditions for Parkinson's disease (PD) subjects in On and Off states and for control subjects. *Bars*, standard error

In conclusion, these results indicate interference with the normal patterning of grasp kinematics. In other words, processing of the visual information from a distracter object of a different size to the target led to a reorganisation of the grasp component, with the anticipation of the kinematic parameters. This interference, however, was greater for PD subjects during the Off than the On state. The pattern observed for the PD participants in the On state was similar to that observed for the control participants (see Fig. 3).

Discussion

Two issues were at stake in the present study. The first issue was whether PD subjects were "distracted" by the presence of non-relevant objects during a goal-directed action (Castiello *1996*; Jackson et al. *1995*; Tipper et al. *1997*). The second issue follows from the first and was whether, in PD subjects, the lack of dopaminergic medication determines greater distractibility.

The present results confirm that reach-to-grasp movements were affected when performed in the presence of irrelevant objects in both normal and PD subjects (Jackson et al. *1995*). This conflict appeared to be sensitive to whether particular attributes of irrelevant objects do not match those of the relevant target object. One of the distracter objects utilised in the present study required a different type of prehension (precision grip) than the target object (whole-hand prehension). Thus, parallel computations for different types of grasp, one for the target and one for the distracter, may be at the origin of the changes found for the kinematics of the action directed to the target. This view is supported by neurophysiological and behavioural evidence. In the former case, different neural populations subserve different types of grasp or given types of action (Rizzolatti et al. *1988*; Sakata and Taira *1994*). In the latter case, the kinematics differ for contrasting types of grasp. For instance the time course of the manipulation component and its temporal relations with the transport component

change with the type of grasp (Castiello *1996*; Gentilucci et al. *1991*; Jakobson and Goodale *1992*). Conflicts can emerge when the distracter and target objects require different prehensile patterns, in order to be grasped or manipulated. Neuronal populations, kinematic planning and functional properties for an irrelevant distracter object can interfere with those activated by and executed for the target object. Given this automatic process of converting perceptual input into the action afforded by the distracter objects, different objects in a visual scene can evoke the parallel implementation of actions. If more than one motor pattern is kept active simultaneously, this parallel activation determines mutual interference (Tipper et al. *1997*).

It is thus the process of inhibiting the motor program evoked by the distracter that is particularly dysfunctional for PD subjects in the Off state. The present findings suggest that the level of interference for the PD subjects in the On state is equal to that of control subjects, but it is much greater during the Off state. The increased interference noticed in the PD subjects in the Off state may be related to a dysfunctional sensory gating mechanism for sensorimotor selection due to dopamine depletion in the striatum (Bernheimer et al. *1973*; Schneider *1987*). The striatum plays an important role in the subconscious planning, execution and inhibition of motor programs (Kemp and Powell *1970*). Accordingly, we found that dopamine had acted upon a dysfunction in the ability to enhance inhibitory activity to avoid activated motor programs from interfering with each other.

These conclusions, however, may be challenged by the fact that both the manipulated variables (medication and distracter size) may have led to the same effect. That is, smaller objects usually produce small grip apertures, and PD subjects generally produce smaller grip apertures than controls (Muller and Stelmach *1992*). Thus, any difference between control and PD subjects may be simply due to symptomatic characteristics such as hand rigidity. However, results for the amplitude of maximum grip aperture suggest that this is not the case. Firstly, movements directed to a large object (target), which in principle should reveal greater dysfunctional finger aperture, do not differ between PD and control subjects. Secondly, there is no difference for this parameter with respect to distracter condition between PD in the On state and the control subjects. Thirdly the differences found between PD subjects in the Off state and PD subjects in the On state and control subjects clearly demonstrate that the effects due to amplitude size and dopaminergic medication can be disentangled.

The longer time taken by PD in the Off state to initiate the movement compared with PD in the On state and control subjects suggests that the premovement planning phase is affected when the distracter differs from the target. In this view, the longer initiation time for the incompatible-distracter condition suggests that, when the choice is between objects that require different motor programs, the selection load is such that the effects of dopamine depletion become more evident.

The role played by basal ganglia during response selection is a matter of debate. A possible candidate for the modulation of information within this neural structure is the striatum, which, as proposed by Robbins and Brown (*1990*), may be implicated in assigning probability of selection from the range of available responses (response set). Thus, following striatal dopamine depletion, the selection for action process for the PD subjects of the present study may become looser and the action evoked by the incompatible distracter may not be maintained at a level of threshold so as not to influence the action to the target. The consequence is a sensorimotor disinhibition that determines an increased susceptibility to interference (Caligiuri et al. *1992*).

The impairment in efficiently inhibiting the action evoked by the incompatible distracter may be dependent on a circuit alternative to the striatal circuit. For example, it is thought that the basal ganglia-thalamocortical pathways are critical for higher cortical processing and complex motor behaviour (Brooks *1986*). Further, this circuit seems dependent on dopaminergic mechanisms, given that the malfunctioning of the caudate outflow causes abnormalities in the prefrontal cortex. It is well

established that neurons from the basal ganglia complex are massively connected with the prefrontal cortex and have functional resemblance to prefrontal neurons (Cummings *1993*). Taylor et al. (*1986*) suggested that, because the prefrontal cortex is the cortical target of caudal activity and also the terminal projection for the dopaminergic mesocortical system, it can be particularly vulnerable. Consequently, if the frontal cortex is involved in the regulation of selective attention, a dopamine deficit in the mesocortical system may cause a frontal deficit type in the performance of parkinsonian patients in efficiently separating irrelevant from relevant information for action (Riddoch et al., *in press*). Again, this dysfunction in using adequately inhibitory strategies re-proposes the similarities, attributable to frontal-subcortical circuits, between behaviours of patients with basal ganglia disorders and patients with frontal lobe injury.

In conclusion, the present study demonstrates that the selection-for-action mechanisms are dysfunctional in PD following dopamine depletion. The notion that subjects with PD present impaired inhibition systems similar to those that characterise frontal lobe patients has been proposed. Hypotheses have been advanced regarding the possible systems responsible for the results obtained for the PD subjects in the Off state. However, further studies are needed to disentangle the contribution of the striatal and the mesocortical dopaminergic subsystems in order to understand the role played by the basal ganglia in the selection-for-action mechanisms.

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