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It's all in the type of the task: Dopamine modulates kinematic patterns during competitive vs. cooperative interaction in Parkinson's disease

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ABSTRACT

Increasing evidence suggests that a dysfunctional dopaminergic system affects the ability to socially interact. Since Parkinson's disease (PD) provides a model for assessing dopaminergic dysfunctions in humans, our study was designed to investigate social interactions in PD patients receiving dopamine replacement therapy (Levodopa=L-Dopa) and in neurologically healthy controls. We focused on the kinematics of one action, reaching to grasp a wooden block, which was performed within the context of two basic modes of social cognition, namely cooperation and competition. During the cooperative tasks, two participants were instructed to reach and grasp their respective objects and to cooperate in forming a specific configuration on the working table. During the competitive tasks, two participants were instructed to compete to place their own object at the bottom of a tower to be built on the working table. PD patients' ability to modulate motor patterning depending on the intention motivating the action they were about to perform was evaluated in both "on" (with L-Dopa) and "off" (without L-Dopa) states. Study results revealed that both the healthy controls and the 'on' PD patients had distinct kinematic patterns for cooperative and competitive actions and that these differed from patterns mirroring similar actions performed by those same participants in non social conditions. The kinematic patterns of the healthy controls and the 'on' patients were highly correlated during the cooperative tasks. The 'off' PD patients were, instead, unable to differentiate between isolated and social conditions. These results support the hypothesis that dopaminergic neurotransmission is involved in shaping the mechanisms underlying social interactions.

1. Introduction

Although exciting advances have recently been made in understanding the links between the mind, the brain and behaviour, these have been almost entirely based on studies in which individual participants were considered strictly as isolated units. It has thus become an ever more pressing challenge to understand the mechanisms underlying actions carried out in social contexts, such as cooperation or competition (Schilbach et al., 2013).

Accumulating evidence indicates that both cooperation and competition involve specific, often distinct psychological and cortical mechanisms. Both necessitate monitoring self-other awareness, which implicates anticipating/predicting the behaviour of a social partner (Decety and Sommerville, 2003). Only a few neuroimaging studies have, however, investigated cooperation and competition in humans. In one functional magnetic resonance imaging (fMRI) study, participants played an economic trust game following a fixed probabilistic strategy (McCabe et al., 2001). The results showed a significant activation of the right medial prefrontal cortex during interaction. During another study in which cerebral activity was examined while participants played a cooperative game, the Prisoner's Dilemma (Rilling et al., 2002), ventromedial frontal cortex activation was detected when the players engaged in mutual cooperation. When Decety et al. (2004) assessed individuals playing a specially designed computer game during which players compete or collaborate with one another, it was found that both stances activated a common frontoparietal network subserving executive functions (Decety et al., 2004). Activity in the dorsal sector of the middle pre-frontal cortex has,

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likewise, been detected during cooperative and competitive tasks (Becchio et al., 2012). Taken together, these findings suggest social interaction conditions that require self-other monitoring are the province of the prefrontal cortex.

Although the prefrontal cortex is a vital component of the circuitry subserving cooperative and competitive tasks, subcortical structures are also in the position to mediate successful social behaviour. Indeed, Alexander et al. (1986) hypothesized that the corticostriatal circuitry is a crucial organising principle of the brain that intimately links the regions of the frontal cortex to striatal structures via the thalamus and globus pallidus. This model suggests a functional as well as anatomical connectivity between the frontal cortex and striatum. Support for this hypothesis was provided by an animal study showing that lesions to the caudate nucleus lead to deficits resembling those following prefrontal ablation (Divac et al., 1967).

Evidence that subcortical structures are important in human social behaviour has been provided by recent studies showing that Parkinson's disease is characterised by social impairments that are evident in unmedicated patients (Straulino et al., 2015, 2016). In these studies, patients' ability to modulate motor patterning depending on the social intention motivating the action to be performed was evaluated both in "on" (with L-Dopa) and "off" (without L-Dopa) states. In one study (Straulino et al., 2015), participants were instructed to reach for and to grasp an object; they were then told to hand it to another person (social condition) or to place it on a concave frame (individual condition). In another study (Straulino et al., 2016), participants were requested to reach toward, grasp an object, and either simply lift it (individual condition) or lift it with the intent to communicate a meaning to a partner (communicative condition). Results from these studies demonstrated that the PD patients in an 'on' state adopted different kinematic patterning for the 'social/communicative' and the 'individual' conditions; the PD patients in the 'off' state, instead, were unable to kinematically differentiate between the two conditions. Altogether, these findings suggest that L-Dopa treatment has positive effects on translating social intentions into specific motor patterns in PD patients. In other words, deficits concerned with social behaviour appear to be a genuine concomitant of basal ganglia damage, depending not on the isolated prefrontal cortex but on the intact functioning of corticostriatal circuitry mediated by dopaminergic neurotransmission.

Given these premises, here we further explore the links between the dopaminergic system and social interactions in the realm of cooperative and competitive behaviour. We capitalized on a paradigm which has been able to show the influence that cooperative and competitive contexts might have on action in neurologically healthy participants (Georgiou et al., 2007). Participants were instructed to carry out the same action – reaching-to-grasp a wooden block – in two different contexts: one in a cooperative situation and the other in a competitive one. For the 'cooperative' task, two participants were instructed to reach for and grasp their respective blocks and to cooperate in forming a tower on the working table. The 'competitive' task was similar to the cooperative one, except that once the block was grasped the two participants were instructed to compete to be the first to place theirs at the very bottom of the tower to be built. To highlight the differences in kinematic patterns characterizing actions preparatory to both a social interaction and an isolated condition, 'single-agent' trials were also contemplated. In one of these, participants were instructed to reach and grasp the block at a natural speed and to place it in a predefined position. In another, they were instructed to carry out the same action, but this time as quickly as possible. The interest was in comparing the kinematics of a reach-to-grasp movement carried out at a natural speed performed by a participant in an isolated condition with a cooperative condition presumably requiring a slower, careful movement. The results revealed different kinematic signatures, depending on whether the action being performed was triggered by the intent to act individually or motivated by cooperative or competitive intentions. For instance, movement duration was longer, the amplitude of wrist peak velocity was lower and the maximum distance reached by the wrist with respect to the working surface was lower for the cooperative than for the 'natural speed' condition. In addition, the time of the maximum grip aperture was reached later for the former than for the latter condition. When the differences between the fast-speed, single-agent condition and the competitive conditions were considered movement duration was faster, the amplitude of wrist peak velocity was higher and the maximum distance reached by the wrist with respect to the working surface was higher for the competitive than for the 'fast' isolated condition. Furthermore, the time of the maximum grip aperture was anticipated for the former than for the latter condition. It is important to remember that this study analysed the kinematics of only the first part of the reach-to-grasp movement. In the single agent conditions, that movement preceded the action of placing the block on the table; in the cooperative and competitive tasks, it was preparatory to but (not part of) the interaction itself. The trials were thus designed in such a way that differences in the kinematics of the reach-to-grasp movements in the various conditions could hypothetically be ascribed to the agent's intention.

In the current study, we administered the very same paradigm to neurologically healthy controls, PD patients in "on" (with L-Dopa) and "off" (without L-Dopa). We hypothesized that controls and PD patients in "on" state would show different kinematic signatures depending on whether the action being performed was triggered by the intent to act individually or motivated by cooperative or competitive intentions. In addition, if the dopamine system does indeed play a role in shaping social functions – in terms of motor planning and control - underlying competitive and cooperative behaviour, then 'off' state PD patients should not exhibit the same motor patterns as 'on' state ones or controls.

2. Methods

2.1. Participants

Twelve patients (N=12, 4 F; age 54 ± 2.34 years; age range: 51–59 years) diagnosed with Parkinson's disease were enlisted in our study (see Table 1). The average disease duration was 1.83 (± .83; range: 1–3 years) years, and the mean age of disease onset was 52 yrs. All the PD patients were being treated with dopaminergic drugs. Each patient was tested both before they received their first morning dose of Carbidopa-Levodopa which was at least 12 h after the last one (thus in an 'off' state) and at least two hours after they had received medication (thus in 'on' state). The order of sessions was counterbalanced with respect to the order of the medication state. A board certified neurologist assessed the patients' parkinsonian status using two measures: the Hoehn and Yahr scale (Hoehn and Yahr, 1967) and the Unified Parkinson's Disease Rating Scale (UPDRS; Fahn and Elton, 1987). The trials for the PD participants were scheduled during sessions that were held on two different days. For each session, four participants came to the laboratory and on the basis of the counterbalanced order they entered the laboratory and performed the experimental conditions. The patients' response to medication was verified by the UPDRS (Fahn and Elton, 1987). None of the patients showed any therapy-related motor complications due to therapy that could interfere with the tasks the experiments contemplated. A gender- and age-matched group (N=12; age: 53 ± 2.2 years; age range: 51–58 years, PD age vs control: Mann–Whitney, U-value=117, Z=.0163, p=.93) of neurologically healthy individuals without neurological or skeletomotor dysfunctions was also enlisted. All of the PD patients and the controls were administered the Mini-Mental State Examination (MMSE) which measures global cognition (Folstein et al., 1975). The scores of the PD patients ranged between 29 and 30; the healthy participants all scored 30, indicating no significant differences between the groups (Mann–Whitney, U-value=101, Z =−1.011, p=.30). The average visual acuity of the PD

Table 1
Characteristics of the Parkinson's disease (PD) patients at the time of testing.

PD patient	Age (years)	Gender	Years since diagnosis	Stage of the disease	Most affected upper limb	UPDRS (on meds)	UPDRS (off meds)	MMSE score	Dopaminergic Medication	Clinical signs					
										T	R	B	A	P	F
1	55	F	3	II	L	30	43	30	1 – 0 – 1*	–	–	+	+	–	–
2	52	M	1	I	L	36	40	30	.5 – 0 – .5*	–	+	+	+	–	–
3	54	M	3	I	L	42	52	30	1 – 1 – 1*	L	–	+	+	–	–
4	53	F	1	I	L	44	53	30	1 – 0 – 1*	–	+	+	–	–	–
5	55	M	1	I	R	28	31	30	.5 – .5 – .5†	–	–	+	–	–	–
6	55	F	1	II	R	32	41	30	1– 0 – 1*	–	–	R	L	–	–
7	59	F	2	II	L	51	62	30	1– 1 – 1†	–	–	+	+	–	–
8	52	F	2	II	L	22	39	30	.5– .5 – .5†	L	L	+	+	–	–
9	52	M	1	I	L	40	55	29	1 – 0 – 1*	–	–	R	–	–	–
10	57	M	3	II	R	30	43	30	.5– .5 – .5†	–	+	R	–	–	–
11	51	M	2	I	L	57	61	30	1 – 1 – 1*	L	+	+	–	–	–
12	53	F	2	I	L	42	51	30	1 – 0 – 1*	–	–	+	R	–	–

Note. Medication: number of tablets morning–midday–evening (dopaminergic medication, *50 mg; †125 mg). Clinical signs: signs when medicated, according to examination at time of testing and self report: T=resting and/or postural tremor, R=rigidity, B = bradykinesia, A=akinesia, P= problems with static and dynamic upright posture, F=freezing; '+'=both sides affected; '–'=neither side noticeably affected; 'L'=left side mainly affected; 'R'=right side mainly affected. MMSE=Mini-Mental State Examination (Folstein et al., 1975). Stage of the disease was determined on the basis of the Hoehn & Yahr's scale. UPDRS, United Parkinson's Disease Rating Scale, Motor section

patients was 18/20; it was 20/20 in the healthy participants. All the participants showed right-handed dominance (Edinburgh Inventory; Oldfield, 1971) and were naive about the experimental design and the purpose of the experiment. The study was approved by the local ethics committee and was performed in accordance with the principles of the Declaration of Helsinki. All the participants gave written informed consent and were fully debriefed at the end of the experiment.

2.2. Stimuli

The objects utilized were a pair of blue wooden blocks (4×4×8 cm) (Fig. 1a) which were placed in the middle of a work table 18 cm away from one another and 21 cm away from the hand starting position (Fig. 1a).

2.3. Procedures

The experiments were conducted under normal lighting conditions. Two participants were seated opposite one another at a work table (122×60 cm; Fig. 1a). Before each trial, the right hand of each participant was resting on a starting pad (green velvet cloth 6×4 cm) with the index finger and the thumb nearly touching. The starting pad was located approximately 3 cm away from the edge of the table in a midsagittal position, 21 cm away from the midsection (Fig. 1a). Each of the subjects were tested in 8 experimental conditions, 10 trials for each condition, all triggered by an acoustic signal (880 Hz/200 ms):

2.3.1. Same group cooperation

Two participants were seated opposite to one another and were instructed to reach for their respective blocks. One of the two was instructed to place it at the bottom; the other was instructed to put it on top of the other one to form a tower (Fig. 1d, e). The top/bottom order was counterbalanced across the subjects. The two participants assigned to this trial belonged to the same group (controls, PD 'on', PD 'off').

2.3.2. Different group cooperation

This condition was similar in every respect to the same group cooperation condition except for the fact that the two participants belonged to different groups (control/PD 'on'; control/PD 'off'; PD 'on'/PD 'off'). In this condition each subject performed the same task twice. More precisely, a PD 'on' performed the task both with a control participant and with a patient PD 'off'.

2.3.3. Same group competition

This condition was similar in every respect to the cooperation condition except for the fact that the subjects were instructed to compete with one another in order to place their block at the very bottom of the tower (Fig. 1d, e). In this trial both participants belonged to the same group (controls, PD 'on', PD 'off').

2.3.4. Different group competition

This condition was similar in every respect to the same group competition condition except for the fact that the two participants belonged to different groups (control/PD 'on'; control/PD 'off'; PD 'on'/PD 'off'). In this condition each subject performed the same task twice. More precisely, a PD 'on' performed the task both with a control participant and with a patient PD 'off'.

2.3.5. Single-agent: natural speed bottom

In this condition, each participant was instructed to reach and grasp, *at a natural speed*, the object positioned in front of his/her right hand and to place it at the center of the work table (Fig. 1b, c). Each participant performed the action in the presence of another participant seated in front of him/her on the other side of the table who observed the scene. The PD participants were tested in this condition twice, once during an 'on' state and in the context of another session during an 'off' state.

2.3.6. Single-agent: natural speed top

In this condition, each participant was instructed to reach and grasp, *at a natural speed*, the block positioned in front of his/her right hand and to place it on top of a block already lying in the middle of the work table (Fig. 1b, c). Each participant performed the action in the presence of another participant seated in front of him/her on the other side of the table who observed the scene. The PD participants were tested in this condition twice, once during an 'on' state and in the context of another session during an 'off' state.

2.3.7. Single-agent: fast speed bottom

In this condition, each participant was instructed to reach and grasp *as quickly as possible* the block positioned in front of his/her right hand and to place it in middle of the work table (Fig. 1b, c). Each participant performed the action in the presence of another participant seated in front of her/him on the other side of the table who observed the scene. The PD participants were tested in this condition twice, once during an 'on' state and in the context of another session during an 'off' state.

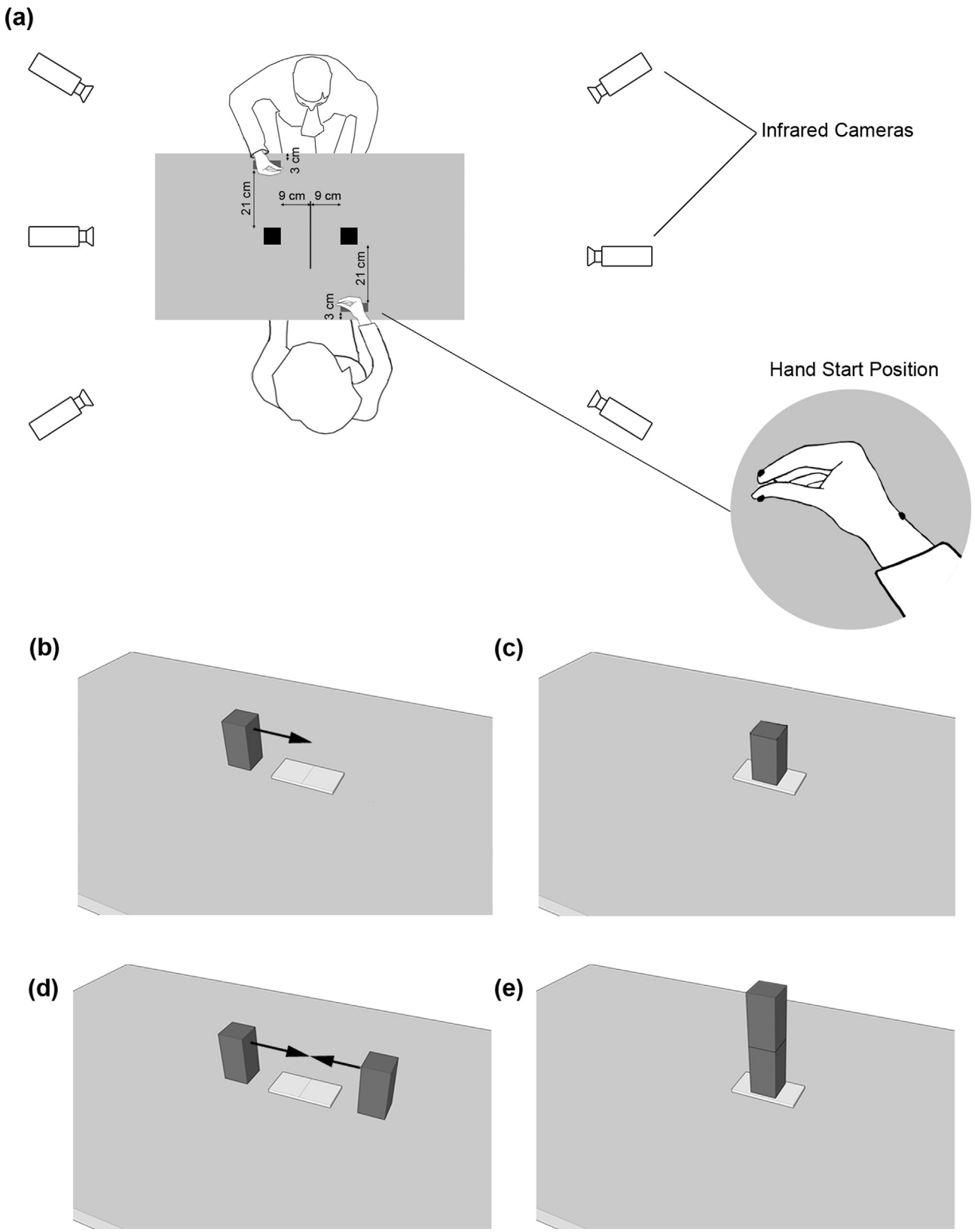

Fig. 1. Experimental set up. Panel 'a' represents the subjects' posture, the positioning of the stimuli and the positioning of the infrared cameras. Panel 'b' represents the direction of movement for the single agent conditions. Panel 'c' represents the final stimulus configuration for the single agent conditions. Panels 'd' and 'e' represent the direction of movement and the final stimuli configuration for the cooperation and competition tasks.

2.3.8. Single-agent: fast speed top

In this condition, each participant was instructed to reach and grasp *as quickly as possible* the block positioned in front of his/her right hand and to place it on top of another block lying in the middle of the work table (Fig. 1b, c). Each participant performed the action in the presence of another participant seated in front of her/him on the other

side of the table who was observing the scene. The PD participants were tested in this condition twice, once during an 'on' state and in the context of another session during an 'off' states.

2.4. Recording techniques

Infrared reflective markers (.25 mm diameter) were taped to the following points on the participants' right upper limb (Fig. 1a): (1) the wrist – the dorsodistal aspect of the radial styloid process; (2) the thumb – the ulnar side of the nail; and (3) the index finger – the radial side of the nail. Markers were also attached to the top of each object (block of wood). The markers were fastened using double-sided tape. The wrist marker was used to measure the reaching component of the action. The finger and thumb markers were used to measure the grasping component of the action. When two subjects were acting simultaneously (cooperation and competition conditions) the kinematics of both were computed. The movements were recorded using a SMART motion analysis system (Bioengineering Technology & Systems [B|T|S]). Six infrared cameras (sampling rate 100 Hz) placed in a circle around the table captured the movements of the markers in 3D space (Fig. 1a). The co-ordinates of the markers were reconstructed with an accuracy of .2 mm over the field of view. The standard deviation of the reconstruction error was .2 mm for the vertical (Y) axis and .3 mm for the two horizontal (X and Z) ones.

2.5. Data processing

An in-house software package was used to analyse the data. To test our experimental hypothesis, we utilized dependent measures which, as has been demonstrated, show differences when cooperative versus competitive attitudes are analysed in neurologically healthy participants (Georgiou et al., 2007). These were (a) movement time; (b) the wrist peak velocity amplitude; (c) the amplitude of the maximum height of the wrist trajectory (i.e., the maximum distance that the wrist reached with respect to the working surface); and (d) the time of the maximum grip aperture. Since we expected the kinematic patterns for natural-speed and fast movements and for cooperative and competitive tasks to differ as far as movement speed was concerned, the absolute temporal values obtained from the participants (i.e., the time of maximum grip aperture) were expressed as a percentage of the movement duration (i.e., relative values). Furthermore, given the known slowness of PD patients, we hypothesized that the procedure would help to clarify differences in kinematic signatures within and across the groups studied.

2.6. Data analysis

Although the subjects' movements were performed in two steps (the first step was reaching/grasping the object and the second was putting it down in a specific place) the kinematic analyses were restricted to the phase leading up to the grasping part of the movement. This procedure was adopted so that the differences could be attributed to the mind set of the agent/s and not to the dynamics of the interaction itself. The means of the kinematic parameters measured during the 8 experimental conditions were calculated for all of the participants. A series of preliminary analyses of variance were performed (ANOVA) to check for top/bottom differences in the kinematic parameters for each condition for each group. This was done to determine whether slight changes in movements caused modifications in the kinematics. The results indicated that there were no top/bottom differences in the kinematic parameters considered (all $p_s > .05$). As a consequence, the top/bottom data were collapsed. Since the PD patients were assessed twice, once during 'off' and another time during 'on' states, and the controls were assessed only once, three separate ANOVAs were conducted. Although this procedure could seem redundant, it was applied to prevent the failure of the ANOVA's assumption (i.e., independence of cases), which would invalidate the analysis. In the first ANOVA (A1), the effects of the 'off' vs 'on' states in the PD patients were compared with 'medication' as the within subjects factor (PD 'off' vs PD 'on'). In the second ANOVA (A2), the kinematics of the 'on' PD patients were compared with those of the control subjects (between-subjects factor group: 'on' PD vs controls). The within-subject factor for all three analyses was the experimental condition (alone/natural, alone/fast, same group cooperation, different group cooperation, same group competition, different group competition). In the third ANOVA (A3), the kinematics of the 'off' PD patients were compared with those of the control subjects (between-subjects factor group: 'off' PD vs controls). Preliminary analyses were conducted to check for normality, sphericity (i.e., Mauchly test), linearity, univariate and multivariate outliers, the homogeneity of variance-covariance matrices, and the multicollinearity. No violations were noted. Post-hoc comparisons were conducted using simple effects and Bonferroni's correction was used (alpha level =.05). The performance of the PD patients who were tested in an 'on' state during their first session did not differ from that of the patients who were tested in an 'on' state for their second session (all $p_s > .05$). Likewise, the performance of the PD patients who were tested in an 'off' state during their first session did not differ from that of the patients who were tested in an 'off' state during their second session (all $p_s > .05$). Correlation analyses were also conducted to examine whether there was a linear relationship within the movements of each pair in the 'cooperation' and the 'competition' conditions. The time to maximum peak height trajectory and the time of maximum grip aperture, parameters that reflect an index of the degree of cross-talk between two agents during a social action (Georgiou et al., 2007), were analysed using the Pearson product-movement correlation coefficient. The time to maximum grip aperture is the time it takes – beginning with the sound of the signal – for the fingers to start to wrap around the object. The time to maximum peak height is the time that it takes – beginning with the sound of the signal – for the participant to reach towards and to begin to grasp the object being utilized in that particular trial. During cooperative tasks the two agents could presumably use self-other monitoring to coordinate their actions in time (Georgiou et al., 2007). During competitive tasks, the rapidity or the nature of the action precluded any attempts to coordinate the actions that were involved (Georgiou et al., 2007).

3. Results

3.1. The global motor effects of dopaminergic medication in PD patients

The A1 analysis showed that the main factor 'medication' ('off' PD vs 'on' PD states) was significant for a number of dependent measures. The results were in agreement with those produced by studies examining the effects of dopaminergic medication on the organisation of reach-to-grasp movements in 'off' and 'on' states (Castiello et al. 2000a, 2000b). The results can be summarized as follows: the movement duration was shorter for the patients in 'on' with respect to 'off' PD states [$F(1,11)=76.05$, $p < .0001$, $\eta^2_p=.81$; 1305 ± 156 vs 1812 ± 234 ms]. The amplitude of the peak reaching velocity was higher [$F(1,11)=56.23$, $p < .0001$, $\eta^2_p=.68$; 733 ± 95 vs 508 ± 71 mm/s] for the 'on' than for the 'off' PD states. The maximum trajectory height amplitude was lower in the 'on' with respect to the 'off' PD state [$F(1,11)=33.12$, $p < .0001$, $\eta^2_p=.57$; 108 ± 15 vs 122 ± 20 mm/s]. The time of the maximum grip aperture occurred earlier for the 'on' than for the 'off' PD states [$F(1,11=20.11$, $p < .001$, $\eta^2_p=.59$; 68 ± 8 vs $72 \pm 9\%$]. In summary, the lack of dopaminergic medication determined longer movement duration together with lower amplitudes of peak velocity and trajectory height and a delayed occurrence of the time of maximum grip aperture.

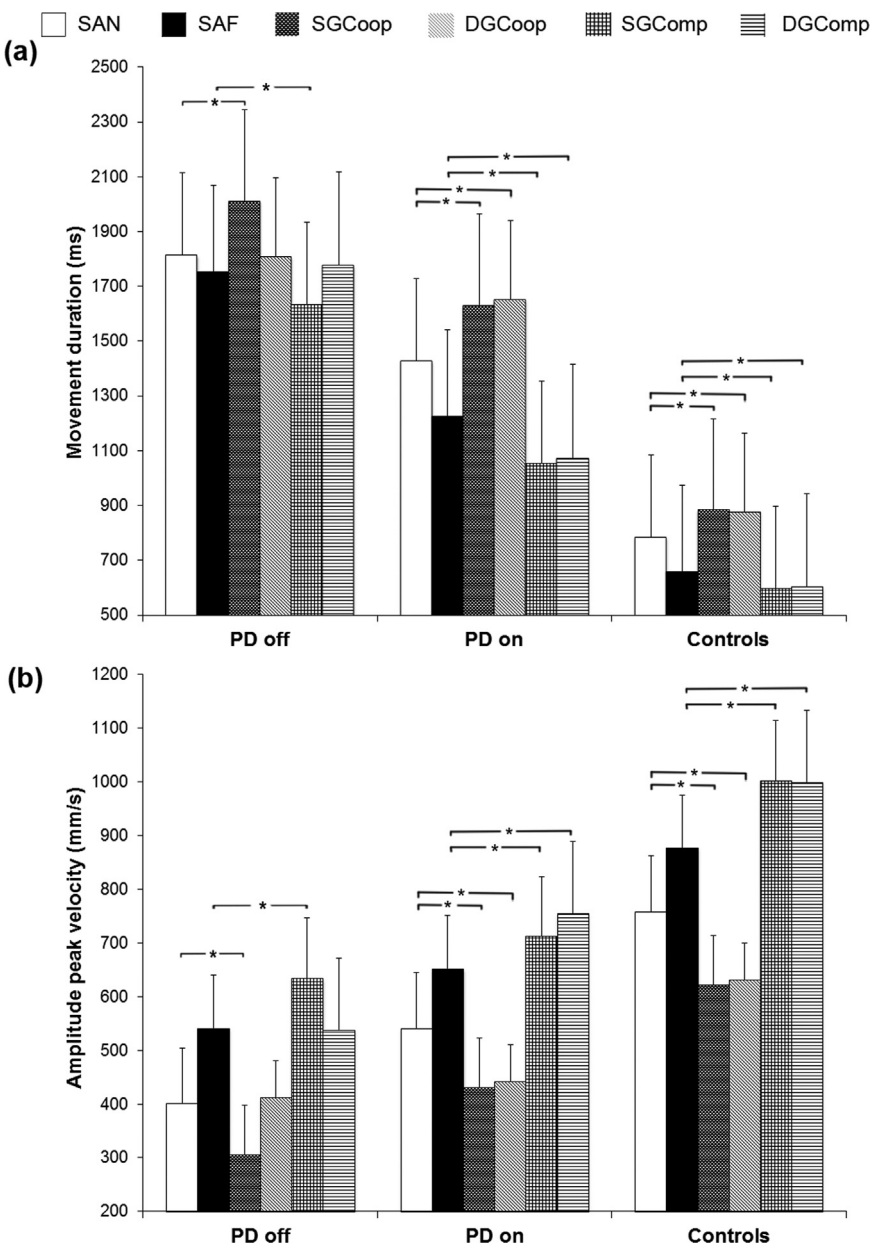

Fig. 2. Movement time (Panel 'a') and the amplitude of maximum peak velocity (Panel 'b') for the different experimental conditions. SAN=Single-Agent Natural; SAF=Single-Agent Fast, SGCoop=Same Group Cooperation; DGCoop=Different Group cooperation; SGComp=Same Group Competition; DGComp=Different Group Competition. Error bars represent the standard error of means. Horizontal bars with asterisks indicate significant differences when comparing the Single-Agent with the Social conditions.

3.2. 'On' state PD patients and controls share differential kinematics for the single-agent, cooperation/competition conditions

According to A2 (PD 'on' vs. controls), the main factor experimental condition was significant for the movement duration [$F(1,11)=68.82$, $p < .0001$, $\eta^2_p = .64$], the amplitude of peak velocity [$F(1,11)=51.22$, $p < .0001$, $\eta^2_p = .70$] the amplitude of maximum trajectory height [$F(1,11)=20.31$, $p < .001$, $\eta^2_p=.50$] and the time of maximum grip aperture [$F(1,11) =35.12$, $p < .0001$, $\eta^2_p=.55$]. The interaction group by experimental condition was not significant for any of the dependent measures considered ($p_s > .05$). The actions performed by a single agent at a natural speed exhibited a shorter movement duration, lower amplitudes of peak velocity and maximum trajectory height, and an earlier time of maximum grip aperture than for the same and different group 'cooperative' conditions (ps < .05; see Figs. 2 and 3). The actions performed by a single agent at a rapid speed exhibited a longer movement duration, lower amplitudes of peak velocity and maximum trajectory height, and a delayed time of maximum grip aperture than for the same and different group 'competitive' conditions ($p_s < .05$; see Figs. 2 and 3). No differences between the same and different group cooperative and competitive conditions for all the considered dependent measures were found ($p_s > .05$; see Figs. 2 and 3). Taken together, the findings in the control participants and in the PD patients in 'on' state show how different intentions are mirrored in action kinematics: specific patterns connote and distinguish actions executed with a social goal from those motivated by an individual one. In other words, when dopamine is available, different motor intentions emerge in the kinematic pattern of actions with different social meaning.

3.3. Comparison of the single-agent conditions with the cooperation and competition ones: the effects of dopamine depletion

According to the A1 analysis (PD 'off' vs. PD 'on'), the medication by experimental condition interaction was significant for movement

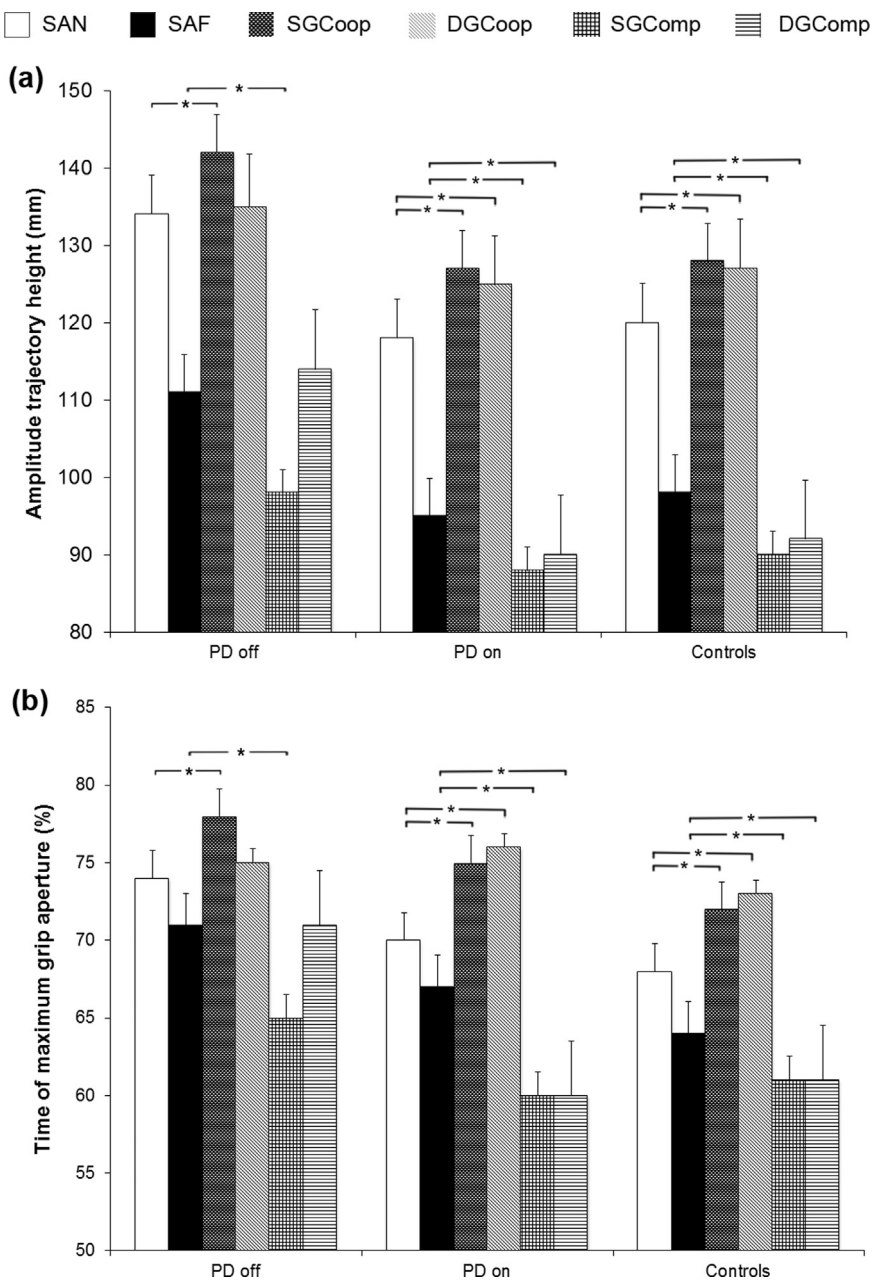

Fig. 3. Amplitude of maximum wrist trajectory height (Panel 'a') and time of maximum grip aperture for the different experimental conditions. Conventions as for Fig. 2.

duration [F(1,11)=53.21, $p < .0001$, η^2_p=.65], the amplitude of peak velocity [F(1,11)=52.15, $p < .0001$, η^2_p =.77], the amplitude of maximum trajectory height [F(1,11) =25.34, $p < .001$, η^2_p=.54] and the time of maximum grip aperture [F(1,11) =39.22, $p < 0.001$, η^2_p =.67]. For the 'on' state PD patients, the pattern for movement duration and the kinematics for all the considered dependent measures were similar to those reported above for the A2 analysis (all $p_s < .05$; see Figs. 2 and 3). For the 'off' state PD patients, the differences between the single agent natural and rapid speed conditions and the cooperation and competition conditions outlined above for the 'on' state PD patients and the controls, emerged only when they acted with a participant in a similar state (i.e., same group conditions; $p_s < .05$; see Figs. 2 and 3). According to the A3 analysis (PD 'off' vs. controls), the group by experimental condition interaction was significant for the movement duration [F(1,11)=56.28, $p < .0001$, η^2_p =.72], the amplitude of peak velocity [F(1,11)=61.12, p < .0001, η^2_p=.70] the amplitude of maximum trajectory height [F(1,11)=70.23, $p < .0001$, η^2_p=.60] and the time of maximum grip aperture [F(1,11) =36.08, $p < .001$, η^2_p=.52]. For the controls, the pattern of results for all dependent measures mirrors that reported above for the A2 analyses ($p_s < .05$; see Figs. 2 and 3). For the 'off' state PD patients the pattern of results mirrored that already described above for the A1 and A2 analyses (all $p_s < .05$; see Figs. 2 and 3). In summary, controls and the PD patients in an 'on' state adopted different kinematic patterning for the 'social' and the 'individual' conditions. PD patients in the 'off' state, instead, were able to kinematically differentiate between the two conditions only when they interacted with a partner in a similar state.

3.4. Cooperation vs. competition

Post-hoc contrasts conducted to explore the significant interaction medication by experimental condition for A1 and A3 and the significant main factor experimental condition for A2 revealed that for the 'on' state PD patients and the controls the movement duration was shorter ($p_s < .05$; see Fig. 2a) and amplitude of peak velocity was lower ($p_s < .05$; see Fig. 2b) for competition than for cooperation. Differences in

Table 2
Pearson correlations within the six couples cooperating with respect to time of maximum grip aperture and the time of maximum trajectory height.

Subject pair	Time to maximum grip aperture						Time to maximum trajectory height					
	Controls		PD 'on'		PD 'off'		Controls		PD 'on'		PD 'off'	
	Same group	Different group	Same group	Different group	Same group	Different group	Same group	Different group	Same group	Different group	Same group	Different group
1–2	.70	.87	.69	.78	.93	.27*	.87	.72	.64	.73	.71	.22*
3–4	.77	.79	.83	.69	.84	.31*	.92	.61	.66	.58	.33*	.34*
5–6	.81	.97	.77	.84	.21*	.22*	.79	.66	.83	.77	.67	.30*
7–8	.89	.82	.79	.90	.58	.26*	.85	.76	.63	.81	.88	.42*
9–10	.91	.75	.62	.88	.64	.34*	.92	.88	.86	.67	.26*	.37*
11–12	.90	.88	.88	.69	.38*	.40*	.88	.65	.79	.85	.66	.28*

Note. All significant correlations were at the $p < .01$ level. * non significant correlations.

the planning of the two social actions also emerged with regard to the spatial trajectory results for these groups. The maximum height from the table surface of the wrist trajectory was lower for competition than for the cooperation ($p_s < .05$; see Fig. 3a). Similar results were found for the 'off' PD group, but only for the same group condition ($p_s < .05$; see Figs. 2 and 3). Finally, for both the 'on' state PD patients and the controls results for the correlation analyses revealed a significant correlation between the time to maximum trajectory height and the time of maximum grip aperture during both the same and different group cooperation conditions (see Table 2). In some cases, for the 'off' state PD patients a significant correlation emerged for the same group cooperation condition (Table 2). No significant correlations for these parameters were found for all the groups for the competition task.

4. Discussion

The study, which was designed to investigate how a functional and dysfunctional dopaminergic system affects social planning, showed that the kinematics of reach-to-grasp movements in neurologically healthy participants and in PD patients in 'on' state are influenced by the action context. And that the kinematics of actions performed in an isolated context differ from those performed preparatory to social interaction. The PD patients in the 'off' state, instead, were unable to kinematically differentiate between the two conditions. Cooperative reach-to-grasp actions were found, in fact, to entail a longer deceleration time than normally paced ones performed by an agent in an isolated condition. An opposite pattern was found when competitive reach-to-grasp actions were compared with single-agent, rapid actions, and a higher peak velocity was associated to competitive tasks with respect to quick actions carried out in isolated conditions. Study data showed then that the same action – reaching towards and grasping an object - is executed in different ways depending on whether it embodies a social or an individual intent. A high level of correlation was also found for key kinematic landmarks in the movements being carried out by paired agents during a cooperative task, thus suggesting that individuals can calibrate their actions depending on those of other/s when a shared goal is involved. The lack of correlation in the kinematics of competitive tasks could be explained by a greater self-other merging underlying cooperative with respect to competitive ones (DeCremer and Stouten, 2003; Decety et al., 2004).

The most striking finding emerging from the present study was that kinematic patterns in 'on' state PD patients and in controls are dramatically different from those in 'off' state patients who do not seem to be affected by the influence of a social context. Although PD patients in the 'off' state retain the motor capacity to perform reach-to-grasp movements, they seem to be unable to modulate movements during social interactions, thus inferring that dopamine projections are indeed necessary in those situations (e.g., Plavén-Sigray et al., 2014; Cervenka et al., 2010; Egerton et al., 2010; Reeves et al., 2007).

It is well known that PD patients' performance in different forms of social interaction depends on dopaminergic replacement therapy (Schröder and Dengler, 2013), which has been shown to improve emotional speech production (De Letter et al., 2007) and recognition of emotional facial expression (Sprengelmeyer et al., 2003). Previous studies have already shown that dopamine depletion in PD patients affects the ability to plan, sequence, self-monitor and to carry out socially-oriented activities (e.g., Straulino et al., 2016). The current study takes our knowledge about the effects the dopamine system's role in shaping intentional mechanisms (Searle, 1983) a step further. Here we demonstrate that when the dopamine system is dysfunctional, patients' kinematic patterns do not reflect cooperative or competitive intentions. Dopamine depletion, in fact, appears to disrupt the coordinated blending of the various processes needed to achieve a particular goal in a flexible manner. The hypothesis that dopamine and prefrontal function are intimately linked concurs with the evidence that PD patients, who have dopamine depletion due to degeneration of the nigrostriatal pathway, exhibit a wide range of deficits attributable to prefrontal dysfunction (e.g., Taylor et al., 1986).

The fact that the 'off' state PD patients were unable to calibrate their own actions depending on actions performed by another person during a cooperative condition provides circumstantial evidence that the dopaminergic system plays an important role in other abilities needed during social interactions (Abu-Akel, 2003). Cooperative interactions, in fact, necessitate self–other monitoring, that is, the ability to foresee other/s behaviour by attributing mental states to them which are different from one's own (Decety and Sommerville, 2003). In accordance with Abu-Akel's findings (2003), our current data provide circumstantial evidence confirming the role of the dopaminergic system in mentalizing abilities. First, the dopaminergic system innervates regions such as the prefrontal cortex and the temporo-parietal region that have been showed to be critical for theory of mind (ToM) performance, an ability that plays a central role in social interaction (Adolphs et al., 2001). Second, abnormalities in the dopaminergic system lead to the disruption of cognitive abilities that influence ToM performances (Russell et al., 1991). Third, ToM deficits have been extensively observed in pathologies such as in Parkinson's disease (Saltzman et al., 2000; Mengelberg and Siegert, 2003) and schizophrenia (Corcoran et al., 1995; Bosia et al., 2011) in which there is a known disruption of the dopaminergic system. Our results suggest that a disruption of neurochemical processes that modulate the dopamine system could contribute to 'social' impairments.

An unexpected finding of the current study concerns the importance of similarity. Although the 'off' state PD patients were unable to modulate the kinematics of their actions depending on their context, they were able to synchronize their movements with those of their partner during a cooperation task when they were paired with another 'off' state PD patient. This could appear logical in the context of movement atypicalities in clinical populations. It is important to remember that individuals who tend to move differently with respect to others may also have different motor and visual action experiences.

Some theories concerning the relationships between the visual and motor systems hypothesize that the greater the similarity of two persons' actions the higher is the likelihood that they will engage in motor resonance when they observe each other's actions (Kilner et al., 2007; Friston et al., 2011). A number of studies suggest that a by-product of motor resonance is facilitating various socio-cognitive functions, including inferring others' mental states, imitating, and developing positive social attitudes (Cook, 2016). In our case, we could hypothesize that individuals who move in a similar way are more successful in synchronizing their actions because of an enhanced motor resonance, promoting a better mental state inference (Kilner et al., 2007). They may, for example, feel more confident about their own and the other's movements (Patel et al., 2012) and develop a more positive attitude toward themselves and others which translates into more positive interpersonal mindsets (Hove and Risen, 2009).

Accumulating evidence suggests that behavioral correlates of motor resonance such as movement synchronicity may be intrinsically rewarding. As postulated by some, engagement in social interaction and rewards processing require basal ganglia (BG) involvement (Izuma et al., 2008; Spreckelmeyer et al., 2009; Lebreton et al., 2009; Pfeiffer et al., 2014), and dopamine neurons play a central role in the reward circuit (Schultz, 2002; Wise, 2002). Behavioral and pharmacological studies on dopamine pathways have described associations between the mesolimbic and nigrostriatal pathways and reward and motor activity (Koob and Le Moal, 1997; Panksepp, 1998; Phillips et al., 1992; Shizgal, 1997; Wise, 2004). Much of the causal evidence supporting the hypothesis that the dopamine mediates the brain reward system is based on studies examining the pharmacological blockade of dopamine receptors in animals. Many studies have shown that dopamine antagonists reduce reward-directed behaviour in a subtle although clear way that cannot be explained by sensorimotor impairments alone (for review see Berridge and Robinson, 1998; Berridge et al., 2009). Positron emission tomography (PET) and fMRI studies in humans have revealed that the presentation of rewards modulates activity in the dopamine target sites such as the nucleus accumbens, neostriatum and the prefrontal cortex (Breiter et al., 1997; Firestone et al., 1996; Koepp et al., 1998; Volkow et al., 1996). It would follow that dopamine depletion is associated to impaired reward processing and, consequently, although 'off' state PD patients retain the motor capacity to perform reach-to-grasp movements, they are unable to modulate movements during social interactions, which probably represent rewards in themselves. This theory would concur with the hypotheses that tonic dopamine levels play a role in reward-seeking behaviour (Mazzoni et al., 2007). The fact that dopaminergic therapy re-establishes the ability to modulate movement kinematics depending on the intentions guiding the action might, in this framework, indicate that tonic dopamine levels play a role in encoding the intent to act socially, which, in turn, translates into different kinematic patterns.

In conclusion, the current study proposes new ways to examine the links between the dopaminergic system and social interactions. The results suggest that L-Dopa treatment has positive effects on translating a variety of social intentions into action, and may provide further evidence that subcortical structures collaborate with the prefrontal cortex to mediate the mechanisms involved in cooperative and competitive behaviour.

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