CORTEX 70 (2015) 179–188

Available online at www.sciencedirect.com

ScienceDirect

Journal homepage: www.elsevier.com/locate/cortex

Special issue: Research report

Social intentions in Parkinson's disease patients: A kinematic study

Elisa Straulino [a], *Tomaso Scaravilli* [b] *and Umberto Castiello* [a,c,d,*]

[a] *Dipartimento di Psicologia Generale, Università di Padova, Padova, Italy*
[b] *Unità Operativa di Neurologia Ospedale di Dolo USL13, Venezia, Italy*
[c] *Cognitive Neuroscience Center, University of Padova, Italy*
[d] *Centro Linceo Interdisciplinare Beniamino Segre, Accademia dei Lincei, Roma, Italy*

ARTICLE INFO

Article history:
Received 13 November 2014
Reviewed 21 December 2014
Revised 19 January 2015
Accepted 14 February 2015
Published online 4 March 2015

Keywords:
Parkinson's disease
Basal ganglia
Motor intentions
Reward
Social interactions
Dopamine

ABSTRACT

Dysfunction of the dopaminergic system leads to motor, cognitive and motivational symptoms in brain disorders such as Parkinson's disease (PD). Moreover, the dopaminergic system plays an important role in social interactions. The dopaminergic input to the basal ganglia (BG) thought to integrate social cues during the planning and execution of voluntary movements remains, however, largely unexplored. Since PD provides a model to assess this function in humans, our study aimed to investigate the effects of social intentions on actions in non-demented PDpatients receiving dopamine replacement therapy (Levodopa = L-Dopa) and in neurologically healthy control participants. Patients' ability to modulate motor patterning depending on the intention motivating the action to be performed was evaluated both in "on" (with L-Dopa) and "off" (without L-Dopa) states. 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). A 'passive-observer' condition, which was similar to the 'individual' condition except for the presence of an onlooker who simply observed the scene, was also assessed to exclude the possibility that differences might be due to the presence of another person. Movement kinematics were recorded using a three-dimensional motion analysis system. Study results demonstrated that the controls and the PD patients in an 'on' state adopted different kinematic patterning for the 'social' and the 'individual' conditions; the PD patients in the 'off' state, instead, were unable to kinematically differentiate between the two conditions. These results suggest that L-Dopa treatment has positive effects on translating social intentions into specific motor patterns in PD patients.

* *Corresponding author*. Dipartimento di Psicologia Generale. Università di Padova, via Venezia 8, 35131 Padova, Italy.
E-mail address: umberto.castiello@unipd.it (U. Castiello).

http://dx.doi.org/10.1016/j.cortex.2015.02.012
0010-9452/

1. Introduction

While focussing their attention on social cognition, cognitive psychologists and neuroscientists developed paradigms to investigate isolated individual minds. The isolation paradigm approach has led to the paradox of studies investigating social interactions while examining individuals physically isolated in separate compartments without any face-to-face contact. These isolation experiments reflect an underlying assumption that social interaction is ultimately reducible to simply understanding individuals' mental states while they are interacting – or at least, think they are interacting, with other agents (e.g., Jacob & Jeannerod, 2005). Recent findings demonstrating that social interaction is deeply rooted in real social contacts have challenged that view (e.g., Knoblich & Sebanz, 2008; Sebanz, Bekkering, & Knoblich, 2006).

The theory that the social context influences action planning and execution has been tested by a variety of kinematical studies that have demonstrated that intention mechanisms modulate motor activation (Becchio, Sartori, & Castiello, 2010; Castiello, 2003; Castiello, Lusher, Mari, Edwards, & Humphreys, 2002; Edwards, Humphreys, & Castiello, 2003; Georgiou, Becchio, Glover, & Castiello, 2007; Mason & MacKenzie, 2005; Meulenbroek, Bosga, Hulstijn, & Miedl, 2007). That body of research established that kinematic movement patterns within a social context are different from those observed in the same participants carrying out movements with the same requirements in terms of speed and accuracy but performed in isolation, or more specifically, without any intention to interact socially. Becchio, Sartori, Bulgheroni, and Castiello (2008a), in particular, sought to determine if reach-to-grasp kinematics are, in fact, sensitive to social goals. Participants in their experiments were assigned individual and social experimental conditions. In the former, the participants were instructed to reach for and grasp an object; they were then told to move it from one place to another. In the latter, the participants were instructed to reach for and grasp the same object but instead of simply moving it, they were expected to hand it to another person. The study's results revealed that movement kinematics were sensitive to 'social' manipulation and provided compelling evidence that different motor patterns are at the service of different intentions.

In neural terms, a variety of studies on social interactions have revealed activations in the ventral striatum (VS), one of the key brain regions of the reward pathway (Báez-Mendoza & Schultz, 2013). VS activations are evident when people are engaged in online social interactions in which there is mutual contingency between the actors (Behrens, Hunt, Woolrich, & Rushworth, 2008; Walter, Abler, Ciaramidaro, & Erk, 2005). A wide range of social interactions characterized by various levels of complexity such as a simple interpersonal gaze (Kuzmanovic et al., 2009; Pfeiffer et al., 2014; Redcay et al. 2010; Schilbach et al., 2010; Williams, Waiter, Perra, Perrett, & Whiten, 2005), a ball game between virtual avatars (David et al., 2006), or more complicated actions producing cooperative behaviour such as neuroeconomic trust games (Rilling et al., 2002) have proved to activate this area. All of this suggests that social interaction generates a rewarding experience whenever mutual contingency characterizes individuals' behaviour.

The fact that the VS may be activated during social interaction implies that the basal ganglia (BG), the main recipient of VS outputs (Draganski et al., 2008), are involved in these endeavours. The BG are implicated in sensorimotor learning and receive a strong dopaminergic signal, which has been shown to play an important role in social interactions (Leblois, 2013). Despite this evidence, however, how the BG works to integrate social cues and how a dysfunction of the dopaminergic system can affect the ability to plan and to execute actions in a social context remains largely unexplored. Considering that the dopaminergic dysfunction causes motor, cognitive, and motivational outcomes in Parkinson's disease (PD) patients (Alexander & Crutcher, 1990), this group might offer an opportunity to investigate the role of the BG in socially-oriented motor interactions. The aims of the present study were then: (i) to investigate movement planning and execution by non-demented PD patients intending to interact socially or individually and, (ii) to evaluate the effect of dopaminergic therapy on these patients while in "on" (with L-Dopa) and "off" (without L-Dopa) states. PD patients in 'off' or 'on' states and neurologically healthy control participants were asked to carry out intentional actions in two different conditions: in an individual or in a social context. For the individual task, participants were instructed to reach for and grasp an object and then to move it from one place to another. For the social condition, participants were instructed to reach for and grasp the same object, but then to hand it to another person. Moving an object from one place to another and handing it to another person are both intentional actions, which involve object displacement. The critical difference lays in the value of the intentional component: while grasping an object with the goal of simply moving it implies a purely individual intention, grasping the same object with the goal of handing it to someone else implies a social one, i.e., the action was at least partially motivated by the intention to affect another person's behaviour. A 'passive-observer' condition, similar to the individual condition, was also tested to exclude the possibility that differences in the social conditions might be due to the simple presence of another person in the room.

We hypothesized that, as previously demonstrated, neurologically healthy participants would show differences in the kinematic parameterization depending on whether the action was performed with the intent of acting individually or socially. In addition, if the dopamine system plays a role in social interactions, then PD patients in 'off' state should not, according to this hypothesis, exhibit the same motor patterns observed within-subjects when experiencing 'on' state or as compared to neurologically healthy participants.

2. Methods

2.1. Participants

One group of participants ($N = 16$, 8F; age 53.5 ± 2.34 years; age range: 51–59 years) was made up of patients diagnosed with

Table 1 – Characteristics of the Parkinson's disease (PD) patients.

PD patient	Age (years)	Sex	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	52	M	1	I	L	24	27	30	.5–0–.5	–	+	+	+	–	–
2	55	F	2	II	R	42	56	30	1–1–1*	–	–	+	+	–	–
3	51	F	1	I	R	37	41	29	.5–0–.5	–	+	R	–	–	–
4	53	M	1	I	L	23	32	30	1–0–1*	–	+	+	+	–	–
5	56	M	2	I	L	45	58	30	1–1–1*	L	+	+	+	–	–
6	51	M	3	II	L	50	61	29	1.5–1.5–1.5*	–	+	R	+	–	–
7	53	F	1	I	L	43	54	28	1–0–1	–	+	+	–	–	–
8	55	M	1	I	R	27	31	30	.5–.5–.5	–	–	+	–	–	–
9	55	F	1	II	R	32	42	30	1–0–1	–	–	R	L	–	–
10	59	F	2	II	L	50	63	30	1–1–1	–	–	+	+	–	–
11	52	F	2	II	L	21	38	29	.5–.5–.5†	L	L	+	+	–	–
12	52	M	1	I	L	41	56	29	1–0–1	–	–	R	–	–	–
13	51	F	3	II	R	29	44	29	1–0–1	–	–	+	+	–	–
14	57	M	3	II	R	25	32	30	.5–.5–.5†	–	+	R	–	–	–
15	51	M	2	I	L	58	66	30	1–1–1	L	+	+	–	–	–
16	53	F	2	I	L	41	50	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 (range from 0 to 108; higher scores indicate greater impairments).

PD(see Table 1). The average duration of PD was 1.75 (±.77; range: 1–3 years) years and the mean age at onset was 51 yrs. All the PD patients were being treated with dopaminergic drugs. A board certified neurologist assessed the patients' parkinsonian status using two measures: the Hoehn and Yahr scale (Hoehn & Yahr, 1967) and the Unified Parkinson's Disease Rating Scale (UPDRS; Fahn & Elton, 1987). Each PD participant was first tested before receiving his/her first morning dose of Carbidopa-Levodopa, at least 12 h after the last dose (thus in 'off' state), and then a second time, one to 2 h after receiving the medication. Patients' response to medication was verified by administering the UPDRS (Fahn & Elton, 1987) during 'off' and 'on' states. None of the participants showed motor complications due to therapy that could interfere with the task at hand. Those patients and a gender- and age-matched control group ($N = 16$; age: 53.6 ± 2.57 years; age range: 51–59 years, PD age *vs* control: Mann–Whitney, U-value = 128, $Z = .0188$, $p = .98$) of neurologically healthy individuals without neurological or skeletomotor dysfunctions were administered the Mini-Mental State Examination (MMSE) which measures global cognition (Folstein, Folstein, & McHugh, 1975). The scores of the PD patients ranged between 28 and 30; the healthy participants all scored 30, indicating no significant differences among groups (Mann–Whitney, U-value = 96, $Z = -1.187$, $p = .23$). The average visual acuity of the PD patients was 18/20 and 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 purposes of the experiment. The study was approved by the ethics committee at the local institution and was performed in accordance with the principles of the Declaration of Helsinki. All participants gave written informed consent and were fully debriefed at the end of the experiment.

2.1.1. *Apparatus*

A schematic representation of the apparatus is illustrated in Fig. 1. The stimulus was an egg-shaped object (long axis = 5.7 cm) positioned on a holder in the middle of a black table (Fig. 1a). A starting switch was positioned on a pad (7 × 6 cm) located 15 cm from the edge of the table, immediately in front of the participant, in line with his/her mid-sagittal plane and positioned 21 cm far from the stimulus holder. Another pad, upon which a plastic concave frame was resting, was located 28 cm to the right of the stimulus holder on the table (see Fig. 1a). Reflective passive markers (diameter: .25 cm) were attached to (a) the ulnar styloid process of the wrist, (b) the tip of the index finger, and (c) the tip of the thumb of the participant's right hand (see Fig. 1a). The wrist marker was used to measure the *reaching component* of the action; the forefinger and the thumb markers were used to measure its *grasp component*. Another marker was attached to the top of the experimental stimulus. Movements were recorded using a SMART motion analysis system (Bioengineering Technology & Systems [B|T|S]). Six infrared cameras (sampling rate 200 Hz) positioned around and slightly above the table (see Fig. 1a) were utilized to capture the location of the markers in 3D space. Coordinates of the markers were reconstructed with an accuracy of 1/3000 mm over the field of view. The standard deviation of the reconstruction error was 1/3000 mm for the vertical (Y) axis and 1.4/3000 mm for the two horizontal (X and Z) axes.

2.1.2. *Procedure*

The participants were tested individually in a dimly lit room. Each participant was instructed to place his/her right hand in a prone position on the starting switch. The participant's index finger and thumb were slightly opposed on the pad

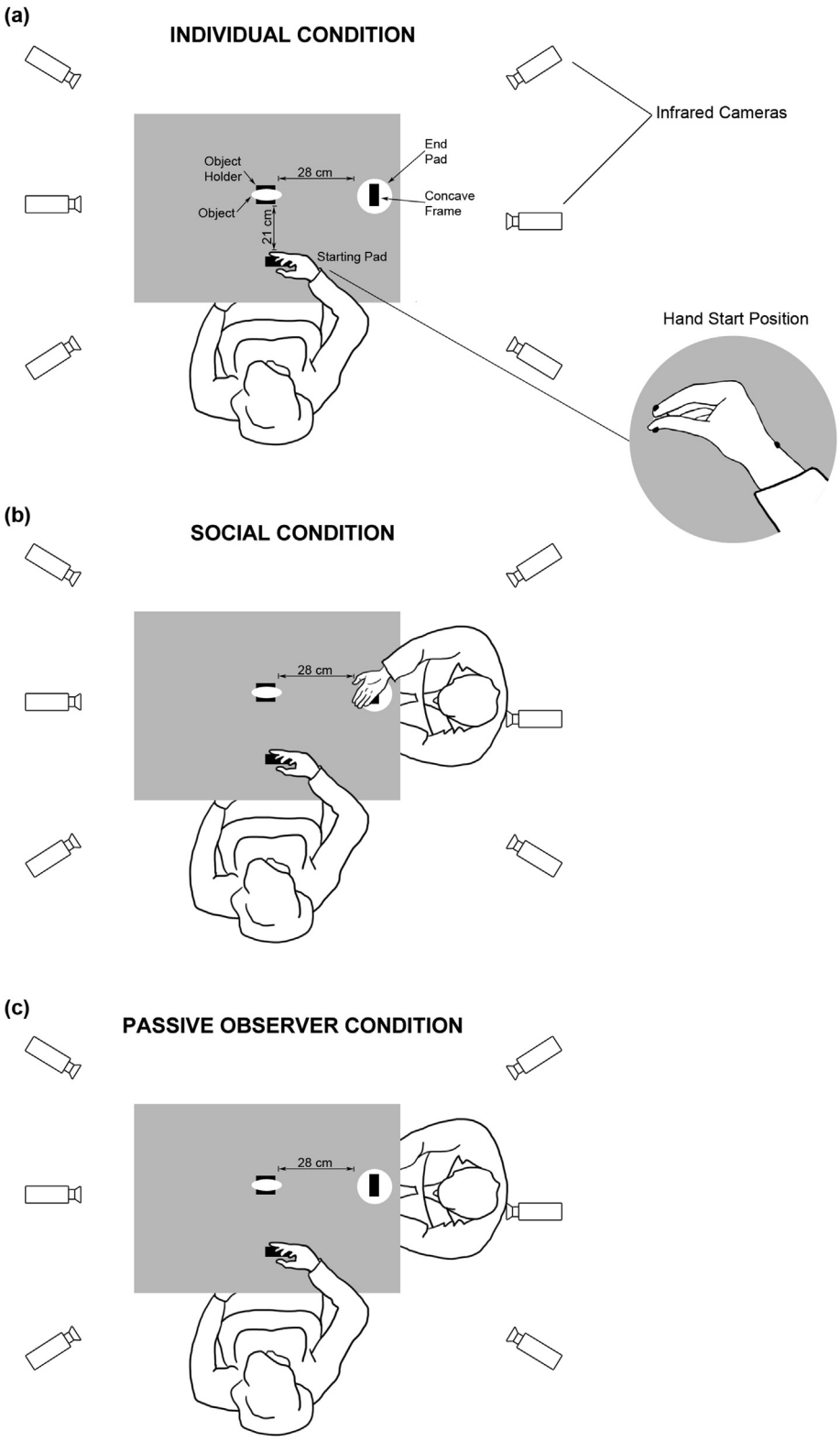

Fig. 1 – Graphical representation of the experimental set up for the individual condition (panel 'a'), the social condition (panel 'b') and the passive observer condition (panel 'c').

(starting position) along the subject's midsagittal axis (Fig. 1a). The participants were advised before each trial of which condition would have been tested next and, thus of which series of actions were expected of them when the signal (880 Hz/200 ms) was sounded. The three conditions and series of actions connected to the trials were:

(i) Individual Condition. Each participant was instructed to move his/her hand from the starting position, to reach for and grasp the stimulus sitting on the holder, and then to place it on a concave shaped frame matching the hand of the experimenter who was involved in the social condition (see below).
(ii) Social Condition. The starting position was the same as for the individual condition. Each participant was instructed to reach for and grasp the stimulus and to then hand the object to another person who was seated on the right side of the table (see Fig. 1b); that person was sitting at the table with his/her right hand resting on the concave frame in a supine position. The person took the object that was handed to him/her.
(iii) Passive Observer Condition. The starting position was the same as that of the individual condition. Each participant carried out the same action as that in the individual condition; the only difference was that in this case there was a passive observer seated on the participant's right side who simply observed the scene (see Fig. 1c).

For all conditions, at the end of each trial, the participant put the stimulus back in its original position in the holder, returned to the starting position and pressed the starting switch. Following a variable interval (2–4 sec) the subsequent trial started. The order of conditions was randomized in each of the participants. The neurologically healthy participants performed 10 trials for each condition. The PD patients performed 10 trials for each condition in both the 'on' and 'off' states.

2.1.3. *Data processing*

The SMART analyzer software package (B|T|S|) was used to analyse the data and provide a 3-D reconstruction of the marker positions as a function of time. The data were then filtered using a finite impulse response linear filter (transition band = 1 Hz, sharpening variable = 2, cut-off frequency = 10 Hz). Following this operation, the tangential speed of the wrist marker and the distance between the index finger and the thumb were computed. These data were used to determine the beginning and ending of the movement using a standard algorithm (i.e., the threshold for movement onset and offset was ~ 5 cm/sec). For the reach-to-grasp phase, movement onset was defined as the earliest point in time in which wrist movement was noted. The offset was defined as the last point in time in which movement of the thumb and index finger was noted. For the place phase, the onset and offset of the movement were calculated using the same algorithm (i.e., threshold for movement onset and offset was ~ 5 cm/sec). The tangential speed of the marker positioned at the top of the object was calculated.

2.1.4. *Data analysis*

Statistical analysis was confined to the dependent variables held to be specifically relevant to the hypothesis being tested. In particular, these variables (see below) were chosen because, as previously demonstrated, they proved to be sensitive to variations in social contexts (Becchio et al., 2008a, 2008b; Georgiou et al., 2007; Sartori, Becchio, Bulgheroni, & Castiello, 2009). The action was performed in two steps, namely reaching for and grasping the stimulus ('reach-to-grasp' phase) and placing the stimulus on the concave frame or in the other person's hand ('place' phase). Separate analyses were performed for each action step. The parameter linked to the grasp component was obviously considered only for the reach-to-grasp phase. Conversely, parameters concerned with the reaching component were analysed for both movement phases. The initiation time (i.e., the time at which the movement begins following the moment the signal sounded), the movement duration, the amplitude of the peak arm velocity, the deceleration time (i.e., the time from the peak velocity to the end of the movement), the time and the amplitude of the maximum distance between the markers positioned on the index finger and the thumb (i.e., the time of the maximum grip and the amplitude of the maximum grip aperture, respectively) were analysed for the 'reach-to-grasp' phase. The amplitude of peak velocity and the deceleration time for the 'place' phase were also calculated. These variables were considered suited to test our experimental hypothesis because we were dealing with a population (PD patients) showing impairment characterized by delayed movement onset (i.e., akinesia) and movement slowness (i.e., bradykinesia) during reach-to-grasp movements. Kinematic parameterization has instead been found to be largely unaltered with respect to the reach-to-grasp movement in neurologically healthy participants (Castiello, Stelmach, & Lieberman, 1993; Tresilian, Stelmach, & Adler, 1997). In view of the known movement delay in PD patients, absolute temporal values obtained from the two groups were expressed as a percentage of the movement duration (e.g., the absolute time at which the peak velocity occurred was expressed as a percentage of the movement duration). For each participant of the two groups, mean values per dependent measure were calculated for all experimental conditions. Given that the patients were assessed twice 'off' and 'on' medication, whereas the controls only once, three separate ANOVAs were conducted. Although this procedure could be considered redundant, it was applied to prevent the failure of ANOVA's assumption (i.e., independence of cases), which would invalidate the analysis. In the first ANOVA (A1), the effects of 'off' versus 'on' effects in PD are compared with 'group' as the within subjects factor (PD 'off' *vs* PD 'on'). In the second ANOVA (A2), PD 'off' medication were compared with control subjects (between-subjects factor group: PD 'off' *vs* controls). In the third ANOVA (A3), PD 'on' medication were compared with control subjects (between-subjects factor group: PD 'on' *vs* controls). For all three analyses the within-subject factor was experimental condition (individual, social, passive observer). 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 concerning violations were noted. Post-hoc comparisons were conducted using simple effects and Bonferroni's correction was applied (alpha level = .05).

3. Results

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

As revealed by the A1 analysis, the main factor 'group' (PD 'off' *vs* PD 'on') was significant for a number of dependent measures. These results mirror those of studies where the effects of dopaminergic medication on the organisation of the reach-to-grasp movement in PDin 'off' and 'on' states were assessed (Castiello, Bennett, Bonfiglioli, & Peppard, 2000a, Castiello, Bonfiglioli, & Peppard, 2000b). Thus, for the sake of brevity, these results will be briefly summarised.

3.1.1. *Reach-to-grasp phase*

Initiation time [$F(1,15) = 31.06$, $p < .0001$; 528 ± 78 *vs* 591 ± 65 ms] and movement duration [$F(1,15) = 44.23$, $p < .0001$; 1327 ± 156 *vs* 1665 ± 176 ms] were shorter for PD in the 'on' than in the 'off' state. For the reaching component, the amplitude of peak reaching velocity was higher [$F(1,15) = 44.23$, $p < .0001$; 690 ± 84 *vs* 598 ± 78 mm/sec] and deceleration time was shorter [$F(1,15) = 44.23$, $p < .0001$; 52 ± 7 *vs* 54 ± 6%] for patients in the 'on' than in the 'off' state. For the grasping component, the time of maximum grip aperture occurred earlier for PD patients in the 'on' than in the 'off' state [$F(1,15 = 37.21$, $p < .0001$; 72 ± 8 *vs* 75 ± 9%].

3.1.2. *Place phase*

Movement duration [$F(1,15) = 21.45$, $p < .0001$; 1363 ± 154 *vs* 1746 ± 189 ms] and deceleration time [$F(1,15) = 30.25$, $p < .0001$; 54 ± 7 *vs* 52 ± 9%] were shorter for the PD patients in the 'on' than in the 'off' state.

3.2. *Dopamine availability modulates the motor patterns of social intentions in PD patients*

3.2.1. *Reach-to-grasp phase*

As revealed by A1 the group by experimental condition interaction was significant for initiation time [$F(1,15) = 31.48$, $p < .0001$], movement duration [$F(1,15) = 47.36$, $p < .0001$], the amplitude of peak velocity [$F(1,15) = 56.21$, $p < .0001$], the time to peak velocity [$F(1,15) = 33.18$, $p < .0001$], deceleration time [$F(1,15) = 52.12$, $p < .0001$] and the time of maximum grip aperture [$F(1,15) = 44.35$, $p < .0001$]. Post-hoc comparisons revealed that for the PD patients in 'off' state there were no differences across conditions for any of the considered dependent measures ($p_s > .05$; Figs. 2 and 3). For the PD in 'on' state, however, differences across conditions were noticed. Initiation time and movement duration were longer for the 'social' than for the 'individual' and the 'passive observer' conditions ($p_s < .05$; Fig. 2a,b). For the reaching component, the amplitude of peak velocity was lower (Fig. 3a) and deceleration time was longer (Fig. 3b) for the 'social' than for the 'individual' and the 'passive observer' conditions

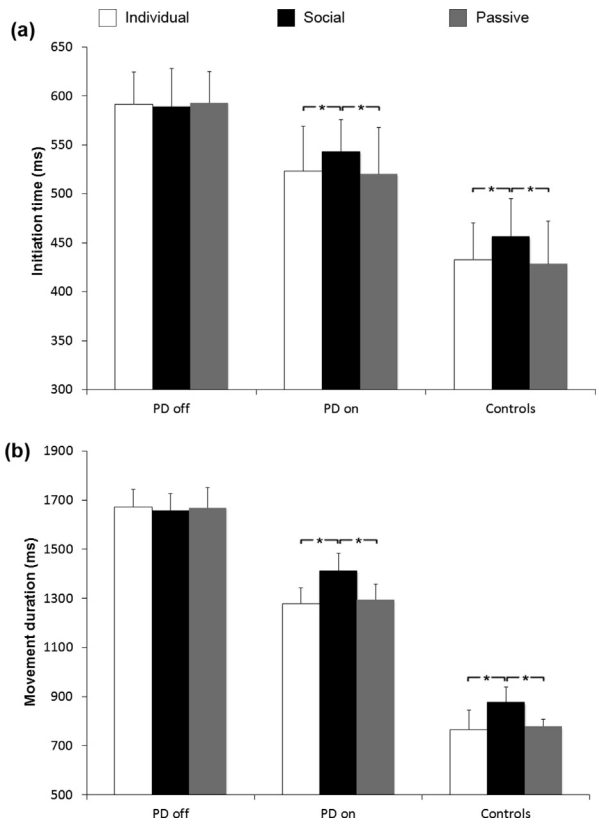

Fig. 2 – Graphical representation of the mean values for initiation time (panel 'a') and movement duration (panel 'b') per group and experimental condition. Bars represent the standard errors of the means. * = $p < .05$.

($p_s < .05$). For the grasping component, the time of maximum grip aperture was anticipated for the 'social' than for the 'individual' and the 'passive observer' conditions ($p_s < .05$; Fig. 3c). For the PD patients in the 'on' state, no significant differences between the 'individual' and the 'passive observer' condition for any of the dependent measures considered were noted (Figs. 2 and 3; $p_s > .05$). For A2 (PD 'off' *vs* controls), the group by experimental condition interaction was significant for initiation time [$F(1,15) = 37.06$, $p < .0001$], movement duration [$F(1,15) = 52.32$, $p < .0001$], the amplitude of the peak velocity [$F(1,15) = 48.13$, $p < .0001$], the time to peak velocity [$F(1,15) = 41.22$, $p < .0001$], deceleration time [$F(1,15) = 50.82$, $p < .0001$] and the time of maximum grip aperture [$F(1,15) = 39.75$, $p < .0001$]. Post-hoc comparisons revealed that for the PD patients in 'off' state there were no significant differences across conditions for any the dependent measures considered ($p_s > .05$; Figs. 2 and 3). For the controls initiation time and movement duration were longer (Fig. 2a,b), the amplitude of peak velocity was lower (Fig. 3a), deceleration time was longer (Fig. 3b) and the time of maximum grip aperture was anticipated (Fig. 3c) for the 'social' than for the 'individual' and the 'passive observer' conditions ($p_s < .05$). For this group no significant differences between the 'individual' and the 'passive observer' condition for any the dependent measures considered were noted (see Figs. 2 and 3; $p > .05$).

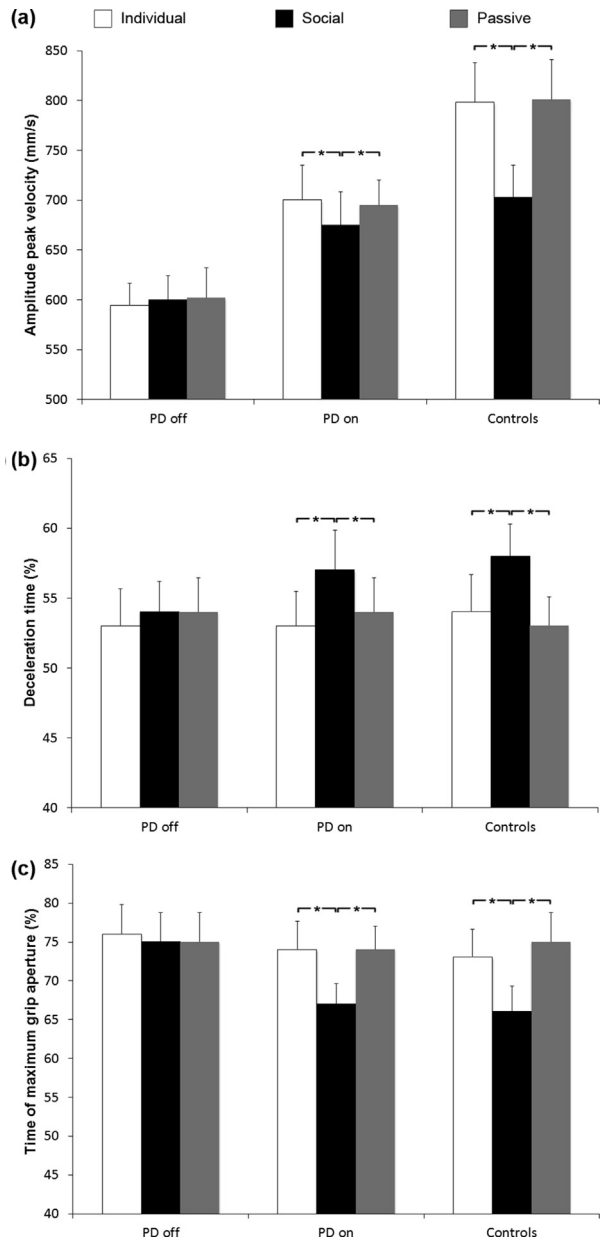

Fig. 3 – Graphical representation of the mean values for the amplitude of peak velocity (panel 'a'), deceleration time (panel 'b') and the time of maximum grip aperture (panel 'c') per group and experimental condition for the 'reach-to-grasp' phase. Conventions as for Fig. 2.

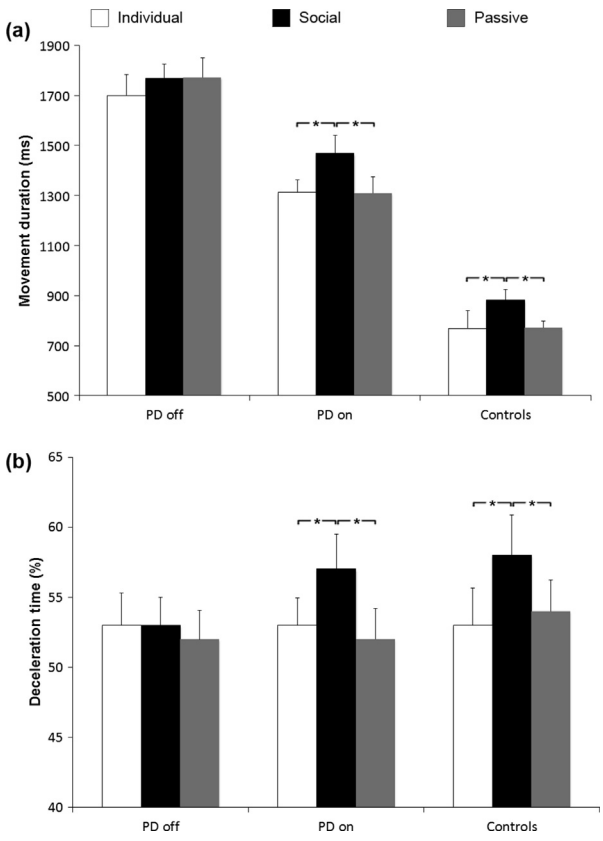

Fig. 4 – Graphical representation of the mean values for movement duration (panel 'a') and deceleration time (panel 'b') per group and experimental condition for the 'place' phase. Conventions as for Fig. 2.

3.2.2. *Place phase*

As revealed by A1 (PD 'off' *vs.* PD 'on'), the group by experimental condition interaction was significant for movement duration [$F(1,15) = 48.11$, $p < .0001$] and deceleration time [$F(1,15) = 34.28$, $p < .0001$]. Post-hoc comparisons revealed that when the PD patients were in 'off' state, both movement duration and deceleration were similar across conditions ($p_s > .05$; Fig. 4a,b). When the PD patients were in 'on' state movement duration and deceleration time were longer for the 'social' than for the 'individual' and the 'passive observer' conditions ($p_s < .05$; Fig. 4a,b). And no significant differences between the 'individual' and the 'passive observer' conditions for movement duration and deceleration time were noted ($p_s > .05$; Fig. 4a,b). When contrasting the performance of PD patients in 'off' state and controls (A2), the group by experimental condition interaction was significant for both movement duration [$F(1,15) = 41.09$, $p < .0001$] and deceleration time [$F(1,15) = 28.31$, $p < .0001$]. Post-hoc comparisons revealed that no differences for the PD patients in 'off' state across conditions were found ($p_s > .05$; Fig. 4a,b). For the controls movement duration and deceleration time were longer for the 'social' than for the 'individual' and the 'passive observer' conditions ($p_s < .05$; Fig. 4a,b). And no significant difference between the 'individual' and the 'passive observer' condition was noted ($p > .05$; Fig. 4a,b).

3.3. *PD patients in 'on' state and controls share kinematics for action intention*

3.3.1. *Reach-to-grasp phase*

When considering A3 (PD 'on' *vs.* controls), the interaction group by experimental condition was not significant for initiation time [$F(1,15) = 2.01$, $p > .05$] and movement duration [$F(1,15) = 1.21$, $p > .05$]. For both controls and PD patients in 'on' state initiation time and movement duration were longer, the amplitude of peak velocity was lower, deceleration time was longer and the time of maximum grip aperture was

anticipated for the 'social' than for the 'individual' and the 'passive observer' conditions (see Figs. 2 and 3).

3.3.2. *Place phase*

The interaction group by experimental condition was not significant for movement duration [$F(1,15) = 1.19$, $p > .05$] and deceleration time [$F(1,15) = 3.34$, $p > .05$]. For both controls and PD patients in 'on' state movement duration and deceleration time were longer for the 'social' than for the 'individual' and the 'passive observer' conditions (Fig. 4).

4. Discussion

This study investigated the effect of intention in PD patients who were asked to grasp an object and to move it from one place to another in two main conditions: in the first, an object was simply displaced (individual condition); in the second, the participant handed an object to a person (social condition). These effects were tested in PD patients undergoing dopaminergic treatment in 'on' or 'off' states, as well as in neurologically healthy participants.

Consistent with our initial hypothesis, neurologically healthy participants and PD patients in 'on' state exhibited different motor patterns for the individual versus social conditions. Both planning and execution of movement were found to be sensitive to the experimental conditions. The participants took longer to initiate the 'social' with respect to the 'individual' action and both the 'reach-to-grasp' and the 'place' phases were found to be sensitive to the experimental conditions. The kinematic parameters of the reach-to-grasp phase were found to be different for the 'social' condition: the longer movement duration, the lower peak velocity amplitude and the longer deceleration times imply that this phase required a more careful approach when the object was handed to another person. In the same way, an anticipated maximum grip aperture time for the social condition implies that a longer 'closing' time is needed to grasp an object when it has to be handed to another person. When the object was placed in the concave frame ('individual' condition), finger hand shaping and manipulation might be less crucial as the object could be placed there from any direction without compromising the action goal. In kinematic terms, these results are consistent with recent evidence showing that hand-shaping modulation depends on the need for end-goal accuracy (Ansuini, Santello, Massaccesi, & Castiello, 2006; Sartori et al., 2009, Sartori, Straulino, & Castiello, 2011).

Just as for the 'reach-to-grasp' phase, the kinematics of the 'place' phase were different for the 'social' with respect to the 'individual' and the 'passive-observer' conditions. Study results suggest that movements are more careful when the goal is linked to a social interaction. Longer movement duration and longer deceleration phase were, in fact, observed. In other words, handing an object to another person entails a more careful action with respect to placing the same object in an inanimate container (Becchio et al., 2008a, 2008b, Becchio et al., 2010; Sartori et al., 2009). 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 (Ansuini, Cavallo, Bertone, & Becchio, 2014).

The study's most significant finding is that the kinematics of the PD patients in 'off' state seem unaffected by the influence of social intentions. Evidence that dopamine-depleted PD patients are unable to translate social intentions into specific motor patterns implies that dopamine projections are indeed necessary in these situations. As postulated by some, engagement in social interaction and processing of rewards requires BG involvement (Izuma, Saito, & Sadato, 2008; Lebreton et al., 2009; Pfeiffer et al., 2014; Spreckelmeyer et al., 2009) and dopamine neurons play a central role in the reward circuit (Schultz, 2002; Wise, 2002). Behavioural and pharmacological studies on dopamine pathways have described associations between the mesolimbic and nigrostriatal pathways, reward and motor activity (Kobb & Le Moal, 1997; Panksepp, 1998; Phillips, Blaha, Pfaus, & Blackburn, 1992; Shizgal, 1997; Wise, 2004). Much of the causal evidence that the dopamine systems mediate rewards is rooted in studies on the pharmacological blockade of dopamine receptors in animals. Multiple evidence 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 & Robinson, 1998; Berridge, Robinson, & Aldridge, 2009). Positron emission tomography (PET) and functional magnetic resonance imaging (fMRI) studies in humans have revealed that the presentation of rewards modulates activity in dopamine target sites such as the nucleus accumbens, neostriatum or the prefrontal cortex (Breiter et al., 1997; Firestone et al., 1996; Koepp et al., 1998; Volkow et al., 1996). It follows that dopamine depletion might be associated to impaired reward components. As a result, although the PD patients in 'off' state retain the motor capacity to perform reach-to-grasp movements, they fail to modulate movements during social interactions, which may represent a reward in itself.

At this stage, the question is why do the kinematics of the PD patients in 'off' state seem unaffected by the influence of social intentions? A possible explanation is that dopaminergic therapy not only significantly improves clinical scores on the UPDRS and the intensive aspects of the movements (e.g., speed), but it also encodes implicit motivational signals for the motor system (Mazzoni, Hristova, & Krakauer, 2007). This would be in line with the role of tonic levels of ventral striatum dopamine in reward-seeking. In this framework, the fact that dopaminergic therapy re-establishes the ability to modulate movement kinematics depending on the kind of intentions guiding the action might indicate a role of tonic dopamine levels in encoding the motivation to act socially, which in turn translate into a different kinematic patterning.

Taken together, the results reported here might have implications regarding the effect of dopaminergic medication on the ability to modulate kinematic parameterization depending on the intention to act. Furthermore, they strengthen the idea that the engagement in social interaction and the processing of rewards share common anatomical substrates. Sectors of the BG encoding reward components may also be involved in motivating interactions in social contexts, thus supporting the hypothesis that the social nature of human

primates is based on the rewarding nature of the active participation in social interaction.

5. Limitations of the present study

Despite the novelty of our findings, there are a few limitations that need to be addressed with respect to study design and the interpretation of the results. First of all, it must be emphasized that given the highly complex functional anatomy of, for example, the frontostriatal connections and loops and also considering that PD compromises not only the dopaminergic neurotransmitter system, our findings might be taken with caution and be opened to different interpretations. One possibility is that neurotransmitters other than dopamine help mediate motor adaptation to social situations, since patients with PD are known to have deficits in multiple non-dopaminergic neurotransmitter systems (Fox, Brotchie, & Lang, 2008; Pifl et al., 2013) which contribute to the parkinsonian motor disorder. Second, the patients were always tested in the 'off' and then in the 'on' state. For recruitment problems the opposite order was never used. Although there is a possibility that the results obtained in the 'on' state could have been influenced by patients having already performed the task in the 'off' state, given the well-rehearsed nature of the task (i.e., people reach to grasp objects at all occasions), we feel that this might not be the case. Finally, we were not in the position to track the gaze of participants during the different tasks. Gaze direction is a potent social cue, which is indicative of other persons' goals. In everyday life, it is intuitively apparent that gaze may provide an important cue when acting on a shared goal. A possibility that we cannot exclude is that the effects reported for the PD patients in the 'off' state has to be partly ascribed to the fact that somewhat they were not engaging gaze with the partner during the social task and this produced a lack of understanding of the motor intention of others. In this respect, it is known that brain activity in the VS decreases when eye gaze is directed away during face processing (Kampe, Frith, Dolan, & Frith, 2001). Depending on the direction of gaze, face processing can activate dopaminergic regions that are strongly linked to reward prediction, indicating once again, that central reward systems may be engaged during the initiation of social interactions (Kampe et al., 2001). In future studies, it would be informative to further explore this aspect.

Altogether, we believe that in light of the scarcity of studies investigating the role played by subcortical structures during social encounters in real-time and, despite the limitations discussed above, the present study provides important insights into the mechanisms underlying the subjective experience of engagement in social interaction.

Acknowledgements

Our sincere gratitude to the patients who participated in the study. This work was supported by a grant from the MIUR (N. 287713), the FP7: REWIRE project and the Progetto Strategico, Universita di Padova (N. 2010XPMFW4) to Umberto Castiello.

REFERENCES

Alexander, G. E., & Crutcher, M. D. (1990). Functional architecture of basal ganglia circuits: neural substrates of parallel processing. *Trends in Neurosciences, 13*(7), 266–271.

Ansuini, C., Cavallo, A., Bertone, C., & Becchio, C. (2014). The visible face of intention: why kinematics matters. *Frontiers in Psychology, 5*, e815.

Ansuini, C., Santello, M., Massaccesi, S., & Castiello, U. (2006). Effects of end-goal on hand shaping. *Journal of Neurophysiology, 95*(4), 2456–2465.

Báez-Mendoza, R., & Schultz, W. (2013). The role of the striatum in social behavior. *Frontiers in Neuroscience, 7*, e233.

Becchio, C., Sartori, L., Bulgheroni, M., & Castiello, U. (2008a). The case of Dr. Jekyll and Mr. Hyde: a kinematic study on social intention. *Consciousness and Cognition, 17*(3), 557–564.

Becchio, C., Sartori, L., Bulgheroni, M., & Castiello, U. (2008b). Both your intention and mine are reflected in the kinematics of my reach to grasp movement. *Cognition, 106*(2), 894–912.

Becchio, C., Sartori, L., & Castiello, U. (2010). Towards you: the social side of actions. *Current Directions in Psychological Science, 19*(3), 183–188.

Behrens, T. E., Hunt, L. T., Woolrich, M. W., & Rushworth, M. F. (2008). Associative learning of social value. *Nature, 456*(7219), 245–249.

Berridge, K. C., & Robinson, T. E. (1998). What is the role of dopamine in reward: hedonic impact, reward learning, or incentive salience? *Brain Research Reviews, 28*(3), 309–369.

Berridge, K. C., Robinson, T. E., & Aldridge, J. W. (2009). Dissecting components of reward: "liking", "wanting", and learning. *Current Opinion in Pharmacology, 9*(1), 65–73.

Breiter, H. C., Gollub, R. L., Weisskoff, R. M., Kennedy, D. N., Makris, N., Berke, J. D., et al. (1997). Acute effects of cocaine on human brain activity and emotion. *Neuron, 19*(3), 591–611.

Castiello, U. (2003). Understanding other people's actions: intention and attention. *Journal of Experimental Psychology: Human Perception and Performance, 29*(2), 416–430.

Castiello, U., Bennett, K. M., Bonfiglioli, C., & Peppard, R. F. (2000a). The reach-to-grasp movement in Parkinson's disease before and after dopaminergic medication. *Neuropsychologia, 38*(1), 46–59.

Castiello, U., Bonfiglioli, C., & Peppard, R. F. (2000b). Dopaminergic effects on the implicit processing of distractor objects in Parkinson's disease. *Experimental Brain Research, 135*(2), 251–258.

Castiello, U., Lusher, D., Mari, M., Edwards, M., & Humphreys, G. (2002). Observing a human or a robotic hand grasping an object: differential motor priming effects. In W. Prinz, & B. Hommel (Eds.), *Common mechanisms in perception and action: Attention and performance, XIX* pp. 315–333). New York: Oxford University Press.

Castiello, U., Stelmach, G. E., & Lieberman, A. N. (1993). Temporal dissociation of the prehension pattern in Parkinson's disease. *Neuropsychologia, 31*(4), 395–402.

David, N., Bewernick, B. H., Cohen, M. X., Newen, A., Lux, S., Fink, G. R., et al. (2006). Neural representations of self versus other: visual-spatial perspective taking and agency in a virtual ball-tossing game. *Journal of Cognitive Neuroscience, 28*(6), 898–910.

Draganski, B., Kherif, F., Klöppel, S., Cook, P. A., Alexander, D. C., Parker, G. J., et al. (2008). Evidence for segregated and integrative connectivity patterns in the human basal ganglia. *The Journal of Neuroscience, 28*(28), 7143–7152.

Edwards, M. G., Humphreys, G. W., & Castiello, U. (2003). Motor facilitation following action observation: a behavioural study in prehensile action. *Brain and Cognition, 53*(3), 495–502.

Fahn, S., & Elton, R. L. (1987). UPDRS program members. unified Parkinson's disease rating scale. In S. Fahn, C. D. Marsden,

M. Goldstein, & D. B. Calne (Eds.), *Recent developments in Parkinson's disease*. Florham Park: Macmillan Healthcare Information, 153e163.
Firestone, L. L., Gyulai, F., Mintun, M., Adler, L. J., Urso, K., & Winter, P. M. (1996). Human brain activity response to fentanyl imaged by positron emission tomography. *Anesthesia and Analgesia, 82*(6), 1247–1251.
Folstein, M. F., Folstein, S. E., & McHugh, P. R. (1975). 'Mini-mental state': a practical method for grading the cognitive state of patients for the clinician. *Journal of Psychiatric Research, 12*(3), 189–198.
Fox, S. H., Brotchie, J. M., & Lang, A. E. (2008). Non-dopaminergic treatments in development for Parkinson's disease. *Lancet Neurology, 7*, 927–938.
Georgiou, I., Becchio, C., Glover, S., & Castiello, U. (2007). Different action patterns for cooperative and competitive behaviour. *Cognition, 102*(3), 415–433.
Hoehn, M. M., & Yahr, M. D. (1967). Parkinsonism: onset, progression and mortality. *Neurology, 17*(5), 427–442.
Izuma, K., Saito, D. N., & Sadato, N. (2008). Processing of social and monetary rewards in the human striatum. *Neuron, 58*(2), 284–294.
Jacob, P., & Jeannerod, M. (2005). The motor theory of social cognition: a critique. *Trends in Cognitive Sciences, 9*(1), 21–25.
Kampe, K. K., Frith, C. D., Dolan, R. J., & Frith, U. (2001). Reward value of attractiveness and gaze. *Nature, 413*(6856), 589.
Knoblich, G., & Sebanz, N. (2008). Evolving intentions for social interaction: from entrainment to joint action. *Philosophical Transactions of the Royal Society B: Biological Sciences, 363*(1499), 2021–2031.
Koepp, M. J., Gunn, R. N., Lawrence, A. D., Cunningham, V. J., Dagher, A., Jones, T., et al. (1998). Evidence for striatal dopamine release during a video game. *Nature, 393*(6682), 266–268.
Kobb, G. F., & Le Moal, M. (1997). Drug abuse: hedonic homeostatic dysregulation. *Science, 278*(5335), 52–58.
Kuzmanovic, B., Georgescu, A. L., Eickhoff, S. B., Shah, N. J., Bente, G., Fink, G. R., et al. (2009). Duration matters: dissociating neural correlates of detection and evaluation of social gaze. *NeuroImage, 46*(4), 1154–1163.
Leblois, A. (2013). Social modulation of learned behavior by dopamine in the basal ganglia: insights from songbirds. *Journal of Physiology Paris, 107*(3), 219–229.
Lebreton, M., Barnes, A., Miettunen, J., Peltonen, L., Ridler, K., Veijola, J., et al. (2009). The brain structural disposition to social interaction. *The European Journal of Neuroscience, 29*(11), 2247–2252.
Mason, A. H., & MacKenzie, C. L. (2005). Grip forces when passing an object to a partner. *Experimental Brain Research, 163*(2), 173–187.
Mazzoni, P., Hristova, A., & Krakauer, J. W. (2007). Why don't we move faster? Parkinson's disease, movement vigor, and implicit motivation. *Journal of Neuroscience, 27*, 7105–7116.
Meulenbroek, R. G., Bosga, J., Hulstijn, M., & Miedl, S. (2007). Joint-action coordination in transferring objects. *Experimental Brain Research, 180*(2), 333–343.
Oldfield, R. C. (1971). The assessment and analysis of handedness: the Edinburgh inventory. *Neuropsychologia, 9*(1), 97–113.
Panksepp, J. (1998). *Affective neuroscience: The foundations of human and animal emotions*. Oxford: Oxford University Press.
Pfeiffer, U. J., Schilbach, L., Timmermans, B., Kuzmanovic, B., Georgescu, A. L., Bente, G., et al. (2014). Why we interact: on the functional role of the striatum in the subjective experience of social interaction. *NeuroImage, 101*, 124–137.
Phillips, A. G., Blaha, C. D., Pfaus, J. G., & Blackburn, J. R. (1992). Neurobiological correlates of positive emotional states: dopamine, anticipation, and reward. In K. T. Strongman (Ed.), *International review of studies on emotion* (vol. 2, pp. 31–50). New York: John Wiley.
Pifl, C., Hornykiewicz, O., Blesa, J., Adanez, R., Cavada, C., & Obeso, J. A. (2013). Reduced noradrenaline, but not dopamine and serotonin in motor thalamus of the MPTP primate: relation to severity of parkinsonism. *Journal of Neurochemistry, 125*, 657–662.
Redcay, E., Dodell-Feder, D., Pearrow, M. J., Mavros, P. L., Kleiner, M., Gabrieli, J. D., et al. (2010). Live face-to-face interaction during fMRI: a new tool for social cognitive neuroscience. *NeuroImage, 50*(4), 1639–1647.
Rilling, J., Gutman, D., Zeh, T., Pagnoni, G., Berns, G., & Kilts, C. (2002). A neural basis for social cooperation. *Neuron, 35*(2), 395–405.
Sartori, L., Becchio, C., Bulgheroni, M., & Castiello, U. (2009). Modulation of the action control system by social intention: unexpected social requests override pre-planned action. *Journal of Experimental Psychology-Human Perception and Performance, 35*(5), 1490–1500.
Sartori, L., Straulino, E., & Castiello, U. (2011). How objects are grasped: the interplay between affordances and end-goals. *PLoS ONE, 6*(9), e25203.
Schilbach, L., Wilms, M., Eickhoff, S. B., Romanzetti, S., Tepest, R., Bente, G., et al. (2010). Minds made for sharing: initiating joint attention recruits reward-related neurocircuitry. *Journal of Cognitive Neuroscience, 22*(12), 2702–2715.
Schultz, W. (2002). Getting formal with dopamine and reward. *Neuron, 36*(2), 241–263.
Sebanz, N., Bekkering, H., & Knoblich, G. (2006). Joint action: bodies and minds moving together. *Trends in Cognitive Sciences, 10*(2), 70–76.
Shizgal, P. (1997). Neural basis of utility estimation. *Current Opinion in Neurobiology, 7*(2), 198–208.
Spreckelmeyer, K. N., Krach, S., Kohls, G., Rademacher, L., Irmak, A., Konrad, K., et al. (2009). Anticipation of monetary and social reward differently activates mesolimbic brain structures in men and women. *Social Cognitive and Affective Neuroscience, 4*(2), 158–165.
Tresilian, J. R., Stelmach, J. E., & Adler, C. H. (1997). Stability of reach-to-grasp movement patterns in Parkinson's disease. *Brain, 120*(Pt 11), 2093–2111.
Volkow, N. D., Fowler, J. S., Gatley, S. J., Logan, J., Wang, G. J., Ding, Y. S., et al. (1996). Pet evaluation of the dopamine system of the human brain. *Journal of Nuclear Medicine, 37*(7), 1242–1256.
Walter, H., Abler, B., Ciaramidaro, A., & Erk, S. (2005). Motivating forces of human actions: neuroimgaing reward and social interaction. *Brain Research Bulletin, 67*(5), 368–381.
Williams, J. H. G., Waiter, G. D., Perra, O., Perrett, D., & Whiten, A. (2005). An fMRI study of joint attention experience. *NeuroImage, 25*(1), 133–140.
Wise, R. A. (2002). Brain reward circuitry: Insights from unsensed incentives. *Neuron, 36*(2), 229–240.
Wise, R. A. (2004). Dopamine, learning and motivation. *Nature Reviews. Neuroscience, 5*(6), 483–494.