



## Altruistic punishment in patients with Parkinson's disease with and without impulsive behaviour

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### ABSTRACT

Punishing violators of social norms when there is personal cost is known as altruistic punishment. We tested patients with Parkinson's disease (PD) with and without impulsive–compulsive behaviours (ICBs) and matched control subjects, on and off their regular dopamine replacement therapy on a task, in which the patients decided whether or not to invest a sum of money with a trustee. The sum was then quadrupled and the trustee could decide whether or not to return a portion of the investment. Participants could punish the trustee after they were informed of the trustee's decision. We found that PD patients without ICBs on or off medication punished more often than controls, whereas PD patients with ICBs punished more than controls on medication, but similar to controls off medication. These results suggest a role for dopamine in altruistic punishment decisions in PD patients with impulsive compulsive behaviour.

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### 1. Introduction

Violation of social norms or unfair behaviour by members of a group induces a desire for society to punish the miscreants (Fehr & Gächter, 2002). Punishing violators of social norms is gratifying, as people are prepared to accept personal loss in order to serve up justice. Punishment when there is personal cost is known as altruistic punishment, and has been shown to reduce the amount of unjust behaviour within groups (Boyd, Gintis, & Bowles, 2010; Fehr & Gächter, 2002; Sigmund, 2007).

A functional imaging study in healthy volunteers has shown that the dorsal striatum, in particular the caudate nucleus is critically involved in mediating punishment and greater activation in the ventral caudate is associated with higher altruistic punishment. This study also indicated that people derive satisfaction from punishing norm violations (de Quervain et al., 2004).

Other fMRI studies have demonstrated that the dorsolateral prefrontal cortex, the insula (Sanfey, Rilling, Aronson, Nystrom, & Cohen, 2003) and the caudate nucleus (King-Casas et al., 2005) play important roles in processing fair and unfair behaviour. The dorsolateral prefrontal cortex and the caudate are directly connected

in a frontal–striatal loop (Haber, Kim, Mailly, & Calzavara, 2006), and therefore both regions are likely to be relevant in mediating responses to fair and unfair behaviour.

The dopamine innervation of the dorsal striatum is severely depleted in Parkinson's disease (PD), leading to bradykinesia and rigidity. Dopaminergic replacement is used to correct the depleted dopamine levels and improve motor deficits. Patients with PD are commonly anhedonic (Todes & Lees, 1985), but there is a subgroup of patients who during chronic dopaminergic treatment exhibit a spectrum of biological impulsive compulsive behaviours (ICB) including pathological gambling, hypersexuality, compulsive shopping, binge eating, reckless generosity, punning and the compulsive use of dopaminergic medication (dopamine dysregulation syndrome or DDS) (American Psychiatric Association, 2000; Brewer & Potenza, 2008; Lawrence, Evans, & Lees, 2003; O'Sullivan, Evans, & Lees, 2009; Weintraub & Potenza, 2006). Clinical data suggest that dopamine replacement medication, especially dopamine agonists, directly provoke these compulsive behaviours (Potenza, Voon, & Weintraub, 2007; Voon, Hassan, Zurowski, Duff-Canning, et al., 2006; Weintraub et al., 2006) and a recent study has demonstrated a positive association between impulsivity and altruistic punishment (Crockett, Clark, Liebermann, Tabibnia, & Robbins, *in press*).

There were several motivations for this study. First, following recent work by our group where we described differences in learning from positive and negative feedback between PD patients with impulsive compulsive behaviors (PD + ICB) and PD patients without impulsive compulsive behaviors (PD) (Djamshidian et al., 2010), we

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hypothesized that PD + ICB patients might be less likely to punish as they might be less sensitive to the aversive aspects of the lack of reciprocation in the trust task. Second, as PD + ICB patients violate social norms themselves, we thought they might be less likely to punish others that violate social norms. Therefore, we tested PD patients with (PD + ICB) and without (PD) impulsive compulsive behaviour on and off medication and compared their results with healthy controls matched for age and education. We further hypothesized that on dopaminergic medication both groups of patients would punish to a greater amount and more frequently than when off medication given the role of the striatum in mediating punishment, and the important role of dopamine in modulating behaviours mediated by the striatum.

## 2. Patients and methods

Patients were recruited from a database of attendees at the National Hospital for Neurology and Neurosurgery Queen Square, London. All patients fulfilled the Queen Square Brain Bank criteria for the diagnosis of PD (Gibb & Lees, 1988) and were taking L-dopa medication. Controls were usually recruited from amongst the patient's spouses or partners. All participants provided written informed consent to protocols approved by the UCLH Trust local ethics committee. Patients who scored under 27/30 points on the Mini Mental State Examination (MMSE) (Folstein, Folstein, & McHugh, 1975) were excluded from this study. The study was performed between-groups, such that no patients were tested both off and on: this eliminates the possibility of order effects, which may be more likely with the task used in this study than other studies. Thirteen PD + ICB patients were tested off medication and 14 on medication. Similarly 12 PD patients were tested off medication and 14 on medication. We compared these results with 26 healthy controls. Table 1 includes detailed demographic information on all subjects. All patients were screened for sub-classes of ICBs. Pathological gambling was defined using the DSM IV criteria, compulsive shopping was defined using McElroy's criteria (McElroy, Keck, Pope, Smith, & Strakowski, 1994), hypersexuality was defined as suggested by Voon, Hassan, Zuroski, de Souza, et al. (2006). All patients were additionally screened for punning (Evans et al., 2004).

Patients who were tested "off" performed the test between 8.00 am and 9.00 am prior to their morning medication and had not taken their medication for at least 12 h. Patients who were tested on medication were tested at a similar time of the morning when they felt that their motor symptoms had been well controlled, about 1 h after their usual morning anti-Parkinson medication. The therapeutic motor response to L-dopa was assessed by UPDRS scores (PART 3) during "off" and "on" state. All patients had an excellent L-dopa response. Levodopa equivalent units (LEU—Table 1) were calculated as described previously (Evans et al., 2004). Testing was usually performed in patient's homes or a hotel room using a laptop computer. Distractions were minimized as much as possible.

The task was a computerized trust game (de Quervain et al., 2004) designed to assess altruistic punishment in fair and unfair rounds. Participants were told that they were playing live against 8 human players, but in fact all were playing against the computer. To ensure that the participants believed they were playing against

human participants we took several precautions. The tests were administered on a laptop, often in the participant's homes. We therefore used an external modem which initiated a connection to the internet. During this connection process the screen displayed "connecting to the first player" and later on during play "your decision has been sent to your first partner". Random time delays were also used while subjects waited to see if their "partner" would reciprocate.

Participants received an allowance at the start of play and were told that they could start the game by entrusting £10 or nothing to each of the eight trustees, as was done previously (de Quervain et al., 2004). Participants played with one trustee per round. Thus, a single decision at the start of play dictated the amount entrusted by the player in all subsequent rounds. None of the subjects chose not to entrust the £10 at the start of play. Participants were told that each trustee had been given £10 already and that in each round the invested £10 was quadrupled. Thus, each of the 8 players (trustees) received £50 in total. The trustee could either respond in a trustworthy manner and share (send back £25) or could keep all the money (£50). Following this the participants were given an additional £10, and had the option to punish the trustee which would result in a decrease in the amount of money the trustee was left with. However, the participant was informed that they would lose £1 for every £2 they chose to punish the trustee. Their punishment options were £0, £5, £10, £15 and £20, at costs to the participant of £0, £2.50, £5.00, £7.50 and £10. In three of the eight rounds participants were treated in a fair manner (receiving £25 back), in the rest of the rounds they were treated in an unfair manner (receiving £0 back). The researcher made sure that all participants understood the rules. Participants either pressed the necessary computer key by themselves or if more convenient gave verbal commands to the researcher who pressed the keys on their behalf. Participants were given the average outcome across all rounds of play. Within each group, controls received £14, PD + ICB patients off medication £13, PD patients off medication £10 and PD patients on medication from both groups £9 for completing this study, on average.

### 2.1. Data analysis

Analyses were carried out on the amount that the patients chose to punish in each round. The raw scores were 1 if participants did not punish or respectively 2 = £5, 3 = £10, 4 = £15 and 5 = £20. We carried out analyses using standard linear models and we present these in the results section. For the linear model, a mixed model ANOVA was performed with the scores as the dependent variable. Trials (round 1–8) and valence (fair and unfair) was modelled as within subject factors, with trial nested under valence. We also modelled group (PD off medication, PD on medication, PD + ICB off medication, PD + ICB on medication and Controls) and included subject as a random factor nested under group. Interactions between the fixed effects were also assessed. All post hoc comparisons were Bonferroni corrected.

We carried out a second ANOVA on just the PD and PD + ICB groups to examine explicit medication and group (PD vs. PD + ICB) effects. This model was identical in all other factors to the above model, except the group variable which had 5 levels in the first analysis was split into 2 factors each with 2 levels (as controls were excluded): patient diagnosis (+ICB/–ICB) and medication (on/off dopamine).

As the dependent variable values took on a discrete set of values, we also used a generalized linear model (SPSS) with a multinomial cumulative logit link function to assess significance (results in Appendix A). The cumulative logit maintains the ordinal relation of the responses without making the Gaussian assumption on the residuals. Wald chi-square was used to assess statistical significance. Thus, the

**Table 1**  
Participant demographic information.

	Controls	PD + ICB on med	PD + ICB off med	PD on med	PD off med	F-value except <sup>a</sup>	p-Value
Participants (no.)	26	14	13	14	12		
Age (yrs)	58 ± 11	55.0 ± 11.9	56.6 ± 6.4	66.3 ± 8.0	64.2 ± 8.3	3.5	0.01
Gender (male)	15	11	9	12	10	$\chi^2 = 5.1^a$	0.28
At disease onset	–	44 ± 10.5	49 ± 7.6	54.1 ± 9.5	53.1 ± 8.8	3.5	0.023
Disease duration (yrs)	–	11.3 ± 5.2	7.7 ± 4.7	12.2 ± 7	11.1 ± 6.9	1.45	0.24
Education (yrs)	13.5 ± 3.0	12.3 ± 2.3	14.7 ± 3.5	14.0 ± 4.3	15.2 ± 4.0	1.54	0.2
LEU dose (mg/day)	–	858 ± 348	801 ± 479	812 ± 346	825 ± 378	0.05	0.98
L-dopa (mg/day)	–	692.9 ± 281	521 ± 227	604 ± 315	466 ± 247	1.6	0.19
DA (patients)	–	8	9	10	9	$\chi^2 = 1.8^a$	0.6
UPDRS on	–	19.4 ± 8.0	14.1 ± 5.2	17.7 ± 10.9	12.5 ± 4.0	1.8	0.16
UPDRS off	–	36.8 ± 15.4	29.2 ± 11.1	27.7 ± 9.5	24.0 ± 7.0	2.3	0.09
Average change in UPDRS (%)	–	46	52	36	48		
Active ICB at time of testing	–	8	8	–	–		NS
Gambling	–	4	3	–	–		NS
Hypersexuality	–	6	8	–	–		NS
Shopping	–	6	8	–	–		NS
Punding	–	2	2	–	–		NS
Kleptomania	–	1	–	–	–		NS

UPDRS = Unified Parkinson's Disease Rating Scale; LEU = L-dopa equivalent units; DA = dopamine agonists. All values are mean ± s.e.m. NS = not significant.

<sup>a</sup> Chi-square.

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