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Intertemporal choice in Parkinson's disease and restless legs syndrome

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ABSTRACT

Background: Impulse control disorders in Parkinson's disease are a potential consequence of dopaminergic therapy. Impulse control problems might be revealed by intertemporal choice tasks which entail to forgo an immediately available reward in favor of a larger but later reward. The steepness of the discounting curve can be quantified by the parameter *k*.
Methods: Participants (37 Parkinson patients [13 de novo, 24 medicated], 24 patients with restless legs syndrome, and 22 controls) were offered 54 choices between immediate smaller rewards and delayed larger and the *k* value was estimated from the participants' responses. Participants had the chance of winning one of their decisions. None of the participants had impulse control disorders.
Results: Unmedicated Parkinson patients had a higher discounting rate than controls and medicated patients with restless legs syndrome. The *k* values of medicated Parkinson patients and patients with restless legs syndrome did not differ from those of controls. No correlation was found between the *k* value and the dopamine agonist dose.
Conclusion: Impulsive decision making in patients with Parkinson's disease may occur as part of the disease rather than as a consequence of dopamine agonist therapy.

1. Introduction

Several studies have demonstrated an association between impulse control disorders (ICD) in patients with Parkinson's disease (PD) and therapy with dopamine agonists (DAs) and, albeit less pronounced, L-DOPA [1–4]. Research has also revealed an association between the development of impulse control disorders in patients with restless legs syndrome (RLS) and treatment with DAs [5]. The DOMINION study [6] involving 3090 patients with PD reported that 13% of patients who were treated with DAs developed impulse control disorders including pathological gambling. Pathological gambling can be characterized as a disturbance of the balance between an immediate reward process (associated with parts of the limbic system) favoring the selection of immediately available rewards and a delayed gratification process (associated with the prefrontal cortex) which allows us to forego an immediate reward in order to wait for later, greater reinforcements [7]. The interplay of these opposing mechanisms can be investigated by "delay discounting" or "intertemporal choice" paradigms, in which participants choose between a smaller immediate reward and a larger delayed reward.

Importantly, it has been demonstrated that future rewards are discounted roughly following a hyperbolic function. A simple equation which captures real-life discounting quite well is the following [8]:

$$V = \frac{A}{1 + kD}$$

where V is the present discounted value of a delayed reward, A is the amount of the delayed reward, k is the delay discount rate, and D (days) is the duration of the delay. The delay discount rate k shows great interindividual variation and indicates the steepness of the discounting curve. For example, assuming that $k = 0.016$, the present value of an €80 reward that is available after a delay of 30

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days is €54. A higher *k* value indicates a steeper discount rate and a preference for a devaluation of future rewards. Research has found that pathological gamblers and patients with substance addiction (e.g, tobacco, alcohol, heroin, and cocaine) have higher *k* values than HCs [9–13]. Note, that there is no *best* choice in intertemporal choice paradigms. Rather, these paradigms are about individual preferences of the participants.

Several studies have looked at delay discounting in PD [14–16]. While these previous studies [14–16] clearly suggest abnormalities in intertemporal choice behavior in PD, the pattern of results raises some questions. First, the fact that two studies [14,15] did not find significantly elevated discount rates in PD without ICD, whereas Milenkova et al. [16] did, calls for a replication of Milenkova et al. [16] in a new sample of PD without ICD. Moreover, Voon et al. [14] described an effect of dopaminergic medication on discount rate (albeit only in PD with ICD), whereas Milenkova et al. [16] did not find such an effect. To tackle these questions, we performed the current study. To assess, whether an elevated discount rate might be considered a trait feature of PD, we investigated delay discounting in de novo, i.e. previously unmedicated PD patients. To test the question whether DA medication in and of itself leads to elevated discounting rates, we also assessed patients with restless legs syndrome on dopamine agonist medication. In addition to these groups, we also investigated PD patients on dopaminergic medication and a control group.

2. Participants and methods

All participants had normal or corrected-to-normal vision, no history of pathological gambling, hypersexuality, compulsive buying, or binge eating as assessed by clinical interview and no depression (score < 18 on Beck Depression Inventory II [17]). Screening for cognitive deficits in PD was carried out with the Parkinson Neuropsychometric Dementia Assessment (PANDA) [18].

PD patients were recruited from the local outpatient clinic and diagnosed in accordance with the UK brain bank criteria [19]. Of the 37 PD patients, 13 were unmedicated de novo patients. In addition, 24 patients with RLS diagnosed according to Allen et al. [20] and medicated with L-DOPA and/or DAs, participated in the study. Finally, 22 unmedicated HCs with a similar age range were included (Table 1).

2.1. Neuropsychological testing

Neuropsychological tests (Table 2) covered the following cognitive domains: Attention was tested with a simple speeded reaction time test that required a button press to a visual stimulus (Alertness test with and without warning tone) as well as a go/nogo test. Executive function was tested with a version of the color word interference test (Farb–Wort-Interferenz-Test, FWI), a verbal fluency test (Regensburger Wortflüssigkeitstest, RWT) and two tests assessing deductive reasoning (LPS 3 and 4). Memory was assessed with the California Verbal Learning test (CVLT). Finally, the PANDA test, an instrument for the assessment of cognitive abilities in PD [18], was administered.

2.2. Intertemporal choice

We used a variant of the task described by Kirby et al. [9] with 54 instead of 27 choices to allow a better differentiation of k-values. The additional choices covered intermediate k-values. The order of the trials was fixed (Table 3) and did not correlate with the size of the rewards or k-values. A computerized presentation was used with the display comprising the smaller immediate reward (on the left of a fixation point), the larger delayed reward (to the right) and the delay for the delayed reward (below the fixation point). There was no time limit for making the decision. The next choice was presented 2 s after a reaction. The participants were informed to make each decision as if it were real. At the end of the participation, they were allowed to throw a die; if they scored a 6, they were allowed to draw a number between 1 and 54 (each number represented 1 decision). Participants then received a reward based on their choice for that particular decision. If they had chosen the smaller immediate reward, they were given cash. If they had chosen the delayed reward, the respective sum was paid by bank transfer after the specified delay.

2.3. Statistical analysis

Four different *k* values were calculated per subject using the method described by Kirby et al. [9] a global *k* value based on all decisions and one *k* value each for small, medium, and large rewards.

To investigate the potential impact of group and reward size on impulsive behavior, an ANOVA with the between-subjects factor group (4 levels: de novo PD, medicated PD, RLS, HC) and the within-subjects factor reward size (3 levels: k values for small, medium, and large reward sizes) was calculated. Group differences between categorical data were tested with the chi-square test. Following the hypothesis that DA treatment is linked to increased k values,

Table 1
Demographic and clinical characteristics.

Characteristics	PD de novo N = 13	PD medicated N = 24	RLS N = 24	HC N = 22
Age (yrs), mean (SD)	69.9 (11)	67.2 (11.8)	68.4 (6.5)	69.3 (8.1)
Sex w/m	4/9	6/18	16/8	13/9
Education (yrs), mean (SD)	12.6 (4.2)	13.7 (3)	12 (2.4)	14 (3.8)
Disease duration (yrs), mean (SD)	2.2 (1.2)	6.4 (4.4)	13.8 (12.4)	–
Symptom onset to diagnosis (yrs), mean (SD)	0.2 (0.5)	5.5 (4.2)	7.2 (3.6)	–
Familiar history for movement disorder, n (%)	0	2 (7.7)	7 (27)	1 (4)
Reported Smoking, n (%)	1 (7.7)	3 (12.5)	1 (8.3)	3 (9.1)
Alcohol consumption (occasionally), n (%)	2 (15.3)	6 (25)	7 (19)	10 (36.6)
Reported Sleep disturbance, n (%)	3 (23)	16 (67)	21 (88)	6 (27)
DA-LEDD (mg), mean (SD)	–	158.5 (118)	66 (69)	–
Total-LEDD (mg), mean (SD)	–	440 (247)	123 (99)	–
UPDRS III, mean (SD)	23.5 (10.5)	21.1 (6.7)	–	–
Hoehn and Yahr, mean (SD)	1.5 (0.5)	2.0 (0.6)	–	–
BDI II, mean (SD)	6.9 (8.7)	8.4 (7.2)	8.5 (7.5)	6.6 (6.1)

DA-LEDD, dopamine agonist-L-DOPA equivalent daily dose; LEDD, L-DOPA equivalent daily dose; UPDRS, Unified Parkinson's Disease Rating Scale; BDI II, Beck Depression Inventory II.