



## Decisions under risk in Parkinson's disease: Preserved evaluation of probability and magnitude



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### ABSTRACT

**Introduction:** Unmedicated Parkinson's disease patients tend to be risk-averse while dopaminergic treatment causes a tendency to take risks. While dopamine agonists may result in clinically apparent impulse control disorders, treatment with levodopa also causes shift in behaviour associated with an enhanced response to rewards. Two important determinants in decision-making are how subjects perceive the magnitude and probability of outcomes. Our objective was to determine if patients with Parkinson's disease on or off levodopa showed differences in their perception of value when making decisions under risk.

**Methods:** The Vancouver Gambling task presents subjects with a choice between one prospect with larger outcome and a second with higher probability. Eighteen age-matched controls and eighteen patients with Parkinson's disease before and after levodopa were tested. In the Gain Phase subjects chose between one prospect with higher probability and another with larger reward to maximize their gains. In the Loss Phase, subjects played to minimize their losses.

**Results:** Patients with Parkinson's disease, on or off levodopa, were similar to controls when evaluating gains. However, in the Loss Phase before levodopa, they were more likely to avoid the prospect with lower probability but larger loss, as indicated by the steeper slope of their group psychometric function ( $t_{(24)}=2.21$ ,  $p=0.04$ ). Modelling with *prospect theory* suggested that this was attributable to a 28% overestimation of the magnitude of loss, rather than an altered perception of its probability.

**Conclusion:** While pre-medicated patients with Parkinson's disease show risk-aversion for large losses, patients on levodopa have normal perception of magnitude and probability for both loss and gain. The finding of accurate and normally biased decisions under risk in medicated patients with PD is important because it indicates that, if there is indeed anomalous risk-seeking behaviour in such a cohort, it may derive from abnormalities in components of decision making that are separate from evaluations of size and probability.

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### 1. Introduction

Among patients with Parkinson's disease, impulse control disorders, such as pathological gambling or compulsive shopping, are a common and devastating complication of treatment with dopaminergic medications (Dodd et al., 2005; Weintraub et al., 2010). This is in contrast to drug-naïve patients who are described as rigid and risk averse (Poletti & Bonucelli, 2012; Dagher & Robbins, 2009; Menza, Golbe, & Cody, 1993). Clinically apparent changes in reward-driven behaviour like impulse control disorders are mostly linked to treatment with dopamine agonists (Voon et al., 2006; Weintraub,

2008), possibly in a subset of patients with pre-existing higher novelty seeking traits (Poletti & Bonucelli, 2012). However, there is also some evidence that levodopa, the mainstay of treatment in Parkinson's disease, increases sensitivity to rewards in all Parkinson's patients (Cools, Lewis, Clark, Barker, & Robbins, 2007; Frank, Samanta, Moustafa, & Sherman, 2007; Frank, Seeberger, & O'Reilly, 2004; Kapogiannis et al., 2011; Moustafa, Cohen, Sherman, & Frank, 2008; Pine, Shiner, Seymour, & Dolan, 2010; Politis et al., 2013; Rutledge et al., 2009). The shift in behaviour caused by dopaminergic medications (both levodopa and dopamine agonists) may reflect underlying changes to decision-making strategies that occur first in the direction of risk aversion, as a result of the disease, and then towards risk-seeking, as a result of dopamine replacement.

This effect should not be surprising: neurophysiological and neuroimaging studies have shown that the processing of reward and risk involves dopaminergic systems (Schultz, 2006). Many

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neural networks have also been explored in decision-making, but a common theme is the contribution of dopamine signaling in these networks, largely through frontostriatal connections. Early insights into the neural basis of decision-making came from patients with frontal lesions who developed difficulty with daily problem solving, highlighting the importance of regions such as orbitofrontal and ventromedial prefrontal cortex for decision-making (Fellows, 2012). How dopamine impacts this processing is not clear, however. While the frontal cortex also plays key roles in executive function, working memory and cognitive flexibility, all processes involved in decision-making, problems with decision-making are not simply due to deficits in these processes, as decision-making can be dissociated from executive function (Toplak, Sorge, Benoit, West, & Stanovich, 2010). This is particularly relevant in Parkinson's disease, where, probably as a result of dopamine loss in the frontostriatal loops (Antonelli, Ray, & Strafella, 2010; Kaasinen et al., 2000), some degree of executive dysfunction is common, even very early in the disease. Similarly, reinforcement and reversal learning are important to decision-making since decisions are often informed by prior experiences. The striatum, with its role in encoding rewards, prediction errors and motivation, plays a critical role in learning (Shohamy & Foerde, 2011). Hence studies of decision-making in Parkinson's disease need to clarify if behavioural changes can be attributed simply to secondary effects of executive dysfunction or impaired learning, or if there are additional effects specific to decision-making itself.

Predicting decision-making deficits in Parkinson's disease is further complicated by the differential effects of the disease and of medications. In particular, the valence of feedback (i.e. positive for rewards and negative for punishments) can have opposite effects on behaviour depending on the dopamine state of a patient. For instance, unmedicated patients do well on tasks of reversal shifting but are not as susceptible to the effects of reward whereas medicated patients, who perform better on rewarded conditions, have deficits of reversal shifting when the reversal is signaled by an unexpected punishment (Bodi et al., 2009; Cools, Altamirano, & D'Esposito, 2006; Frank et al., 2007; Frank et al., 2004; Rutledge et al., 2009). Even bodily responses to decision-making either in anticipation of decisions or in response to feedback, as measured with electrodermal responses or skin conductance reactions, reflect the differential effect of gains versus losses in decision-making tasks (Euteneuer et al., 2009; Kobayakawa, Koyama, Mimura, & Kawamura, 2008).

In addition to distinctions based on valence, differences have been drawn between two main types of decisions; *decisions under ambiguity*, in which the probabilities and magnitudes of reward are not known to the subject, and *decisions under risk*, in which those properties are explicit. In medicated Parkinson's disease, *decisions under ambiguity* have been investigated with the Iowa Gambling task (Pagonabarraga et al., 2007; Poletti, Cavedini, & Bonuccelli, 2011; Rossi et al., 2010) while *decisions under risk* have been studied with the Cambridge Gambling task (Cools, Barker, Sahakian, & Robbins, 2003; Torta, Castelli, Zibetti, Lopiano, & Geminiani, 2009) and the Game of Dice task (Euteneuer et al., 2009; Rossi et al., 2010), for example. The results of these studies have been mixed, with some showing that patients with Parkinson's disease who are given either levodopa alone (Cools et al., 2003, 2007; Frank et al., 2007; Kapogiannis et al., 2011; Rutledge et al., 2009) or in combination with a dopamine agonist (Cools et al., 2006; Euteneuer et al., 2009; Frank et al., 2004; Pagonabarraga et al., 2007; Torta et al., 2009) make riskier choices, while others do not (Czernecki et al., 2002). The mixed results from these studies are not surprising considering that processing of risk and ambiguity might rely on partially separate neural networks. For example, one study comparing risky and ambiguous

decision-making showed greater activation of the ventral striatum under risky conditions whereas the orbitofrontal cortex showed greater involvement under ambiguous conditions (Hsu, Bhatt, Adolphs, Tranel, & Camerer, 2005).

New clinical or experimental tasks evaluating risk-related behaviours are important because they can demonstrate deficits that mirror the real-life problems that arise in these patients, problems that might not be detected with currently standard neuropsychological instruments. However, one of the challenges in understanding these aberrant behaviours is to determine which components of the complex decision-making process are anomalous. In neuroeconomic terms, decisions can be deconstructed into evaluation of magnitude of outcome, evaluation of probability of outcome, and attitudes towards the uncertainty present in the situation or choice (Glimcher, 2008; Platt & Huettel, 2008). Also, decisions are affected by personality traits such as impulsivity (Dagher & Robbins, 2009; Huettel, Stowe, Gordon, Warner, & Platt, 2006; Voon et al., 2010b), the perception of time frames and the tendency to delay discounting (Pine et al., 2009), gender (Harris, Jenkins, & Glaser, 2006) and age (Deakin, Aitken, Robbins, & Sahakian, 2004). Furthermore, reinforcement learning from positive or negative outcomes can influence the evolution of risk-related decisions via reward prediction error signals that inform the brain about whether a better or worse than expected outcome has occurred (Fiorillo, Tobler, & Schultz, 2003; Frank et al., 2004). One of the important needs in research on risk is a battery of tests that can isolate the contributions of these various components to the decisions made by a subject (Schonberg, Fox, & Poldrack, 2011).

Magnitude and probability of outcomes are basic factors of risk in many scenarios: reward prediction error incorporates information about magnitude and probability (Schultz, 1999), and in some tests of decisions under ambiguity such as the Iowa Gambling task, the results depend on subjects gradually discovering these properties in the choices they make. One of the major advances represented in *prospect theory* is the concept that decisions are not based on the objective size of reward and probability, but instead are based on the subject's perceptions of magnitude and probability, which are not veridical (Kahneman, 1981) (Fig. 1). For example, we tend to overestimate low probabilities and underestimate high probabilities, our perception of magnitude of reward is not linear, and we lend more weight to a loss than to a gain of equivalent size. Given the fundamental role of magnitude and probability in risk calculations, one important question is whether the subjective perception of these variables is anomalous in conditions associated with abnormal approaches to risky situations. Determining whether patients with Parkinson's disease evaluate probability and magnitude differently from healthy subjects is a key first step for interpreting reported abnormalities on other tests like the Iowa Gambling Task, in which many cognitive components are at play.

In this experiment we used the Vancouver Gambling task (Sharp, Viswanathan, Lanyon, & Barton, 2012) to examine how patients with Parkinson's disease make *decisions under risk*, when the subject is faced with choices (prospects) that have clearly defined probabilities and magnitude of gain or loss. By eliminating ambiguity and minimizing learning, we focused on how subjects trade off magnitude and probability of reward in their decisions. This task allowed us to determine how sensitive subjects are to differences in value between prospects that vary in both size and likelihood of reward, and also whether they show any decisional bias that favours choices with high probability over those with high reward. Furthermore, predictions based on *prospect theory* show that a shift in decisional bias caused by a change in perception of reward magnitude is associated with a different change in the response curve than when such a shift is generated by a change in perception of reward probability. This allows us to determine if a change in behaviour is due to anomalous perception of one or the other (Sharp et al., 2012), as illustrated in Fig. A1 of Appendix A.

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