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Novelty seeking behaviour in Parkinson's disease

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ABSTRACT

Novelty seeking can be a positive trait leading to creativity and innovation, but it is also related to increased risk of damaging addictive behaviour. We have assessed novelty seeking with a three armed bandit task, in which novel stimuli were occasionally introduced, replacing choice options from which the participants had been choosing. This allowed us to assess whether or not they would be prone to selecting novel stimuli. We tested 25 non impulsive patients with Parkinson's disease (PD) and 27 PD patients with impulsive compulsive behaviours (ICBs). Both patient groups were examined "on" and "off" dopaminergic medication in a counterbalanced order and their behaviour was compared with 24 healthy controls. We found that PD patients with ICBs were significantly more prone to choose novel options than either non impulsive PD patients or controls, regardless of medication status. Our findings suggest that attraction to novelty is a personality trait in all PD patients with ICBs which is independent of medication status.

1. Introduction

Humans and animals are inherently attracted to new stimuli as these can be potentially rewarding (Daffner et al., 1998; Ennaceur & Delacour, 1988; Hughes, 2007). High novelty seeking is part of adolescence and may help in normal development and the acquisition of independence (Kelley et al., 2004): adults with novelty seeking personality traits on the other hand often have increased impulsivity, addiction, inability to delay gratification, recklessness and aggressive behaviour (Barratt, 1985, 1994; Belin et al., 2008). A subgroup of patients with Parkinson's disease (PD) develop impulsive compulsive behaviours (PD + ICB) in relation to their dopamine replacement therapies. These include pathological gambling, compulsive sexual behaviour and shopping and the inappropriate, excessive overuse of dopaminergic medication (dopamine dysregulation syndrome, DDS) (Evans et al., 2005, 2006; Voon et al., 2007b). While self-report questionnaires have suggested that the subgroup of PD + ICB patients with DDS (Evans et al., 2005) and those with pathological gambling (Voon et al., 2007b) have high levels of novelty seeking, this has not been formally studied using metric tests.

The trade-off between choosing options of known value and exploring novel options is known as exploration vs. exploitation (Daw et al., 2006). Exploring novel choices and learning the value of stimuli based on reward feedback have been linked to the ventral striatum, the substantia nigra and the ventral tegmental area of the midbrain (Guitart-Masip et al., 2010; Wittmann et al., 2008) as well as the hippocampus (Guitart-Masip et al., 2010; Voon et al., 2010). These areas either contain dopamine neurons or receive strong dopaminergic innervation. Additional studies have examined the dopamine link to learning and exploration. For example, behavioural studies in PD have shown that dopamine levels play an important role in reward learning (Cools et al., 2002; Djamshidian et al., 2010; Frank et al., 2004; Seo et al., 2010; Voon et al., 2010). Complimenting this work, functional magnetic resonance imaging (fMRI) studies in healthy controls and positron emission tomography (PET) studies in PD + ICB patients have localized reward responsivity to the ventral striatum (Evans et al., 2010; O'Doherty et al., 2003; O'Sullivan et al., 2011; Steeves et al., 2009). An important role for striatal dopamine D2 receptors in the exploration vs. exploitation trade-off has been suggested by genetic studies (Frank et al., 2009). It seems probable therefore that there is an overlap between the networks which mediate reward learning and novelty seeking, and both processes can be conceptualized as assigning value to choice options.

One of the circuits that has been proposed to mediate novelty effects includes the hippocampal projection to the ventral striatum. Specifically, the hippocampus forms a functional loop with

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the ventral striatum and the mid-brain dopamine neurons. The hippocampus is activated by novel information (all information that is not stored in long term memory) and regulates, via the ventral striatum, dopamine neuron firing rates (Lisman & Grace, 2005). Neuropathological studies have shown that the parahippocampal gyrus is affected in later stages of PD (Braak et al., 2004). Thus, abnormal and increased activity in the ventral striatum might be triggered by earlier neuropathological changes in the hippocampus in PD + ICB patients.

The aim of the present study was to compare novelty seeking between impulsive and non-impulsive PD patients, and also to examine the role of dopaminergic medication on novelty seeking. We hypothesized that PD + ICB as a group would be more novelty seeking than PD − ICB patients on a task which allows for exploration of novel options. We tested PD + ICB and PD patients without ICB (PD − ICB) on and off their dopaminergic medication on a modified "three armed bandit" choice task (Wittmann et al., 2008), where all participants played for real money. We compared the choices of PD − ICB and PD + ICB patients on and off their medication with a group of healthy controls who were matched for age and education to the patients group.

2. Patients and methods

PD 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. Patients with structural lesions on their brain scans were excluded from this study. Some of the patients also had raclopride PET scanning and results of this study are presented elsewhere (O'Sullivan et al., 2011). We included patients who were moderately impaired by PD. All patients showed a significant improvement (>35% improvement) after L-dopa intake which was assessed by the UPDRS (part 3) motor score. There was no significant difference in UPDRS motor scores between the 2 patient groups. L-Dopa equivalent units (LEU) of patients' regular daily dopamine replacement therapies were calculated as described elsewhere (Evans et al., 2004). Controls were usually recruited from among the patient's spouses or partners. Participants who provided written informed consent to protocols approved by the UCLH Trust local ethics committee were included. Patients who scored under 27/30 points on the Mini Mental State Examination (MMSE) (Folstein et al., 1975) were excluded from this study.

27 PD + ICB and 25 PD − ICB patients were recruited and results were compared with 24 healthy controls. PD + ICB patients were diagnosed using proposed criteria (Evans et al., 2004; Lawrence et al., 2003; Voon et al., 2007a). Most PD + ICB patients had more than 1 ICB. The ICBs included compulsive sexual behaviour (12 patients), pathological gambling (11 patients), compulsive buying (8 patients), punding (4 patients) and kleptomania (1 patient).

3. Novelty task

We performed a three-armed bandit task, modified from the "four armed bandit choice task" used previously (Wittmann et al., 2008). The task was administered on a laptop computer. Participants performed 60 trials of the task. In each trial three black and white picture post-cards were presented on the screen (Fig. 1). After presentation of the pictures, the participant was required to select one of the three pictures, and after the option was selected, they were told whether they had "won" or "lost". We also provided auditory feedback (5 kHz for winning and 2.5 kHz for losing) to reinforce feedback learning. Following an inter-trial interval, during which the screen was blank, the participants were again presented with the 3 choice options and they could make another decision. The location of each picture was randomized from trial to trial to prevent habituation. The participants were told to pick the most often rewarded picture as many times as possible to maximize their winnings.

During the task, as the participants were making their choices and learning the reward value of the pictures, novel stimuli were introduced. This was done by replacing one of the images from which participants had been choosing with a new image, which was then a novel choice option. A novel choice option was introduced on 20% of trials, or on average every 5 trials. These novel choices were of two types — unfamiliar and familiar. Unfamiliar stimuli were images that the patients had never seen before, whereas familiar stimuli were images that the patients had seen in pre-task training. It is important to note that both unfamiliar and familiar images refer to pictures that were introduced into the ongoing 3-armed bandit task, replacing one of the pictures that the participants had been selecting from. Familiarization was done by sending 18 black and white pictures to participant's homes prior to the experiment, and asking them to guess which country each picture was taken from. We called all participants prior to testing to ensure that participants were familiar with the set of images. On the day of testing and prior to each session we familiarized participants again. We used different sets of pictures for each session. Therefore, we re-familiarized participants with 9 of the 18 pictures prior to the first session, and the other 9 pictures prior to the second session. We also counterbalanced the pictures from the set with which the subjects were familiarized across medication conditions, so approximately half the subjects were familiarized with one half the pictures for their medicated session, and the other half of the subjects were familiarized with the other half of the pictures for their medicated session. None of the subjects knew the purpose of familiarization. There were no differences in reward values between familiar and unfamiliar pictures in the choice task. At the beginning of each of the two choice experiments, in the first trial, all participants were asked: "which picture is unfamiliar?" They all recognized the unfamiliar image among the three in the first trial.

PD patients were tested prior and after their usual anti-Parkinson medication in a counterbalanced sequence to account for order effects. All patients who were tested in their "off medication state" did not take their usual anti-Parkinson medication, including both L-dopa and any dopamine agonists, for at least 12 h. Results were compared with 24 controls who were matched for age to the PD + ICB group. Patients who were tested first prior to their usual anti-Parkinson medication ("off medication") performed the task between 8.00 am and 9.00 am. They were then retested in their "on medication" state 1 h after taking their first dopaminergic medication of the day. Those patients who were tested "on medication" first performed this task usually in mid-morning when their motor symptoms were well controlled. They were re-visited on the following day prior to their medication for the second test. Controls were tested in the same way but did not take any anti-Parkinson medication. At the end of the study all participants got a modest amount of money depending on their final score (usually £5 to £10).

Statistical analyses were performed using SPSS, version 18. For the demographic variables, age, gender, years of education, age of disease onset UPDRS scores, LEU dose were used as dependent variables and group (PD − ICB, PD + ICB and control) was modelled as a between subject factor. We used ANOVA, t-test or χ^2 test where appropriate. For the behavioural variables we first fit models to the choice data of individual participants to parameterize the value they assigned to novel stimuli, which in effect characterized the probability that they would select a novel stimulus. A higher value indicates a higher probability of selecting a novel stimulus. We then fit an ANOVA to the parameters derived from the model comparing the effect of novel stimuli in PD and ICB groups off and on medication.

4. Reinforcement learning model

We have fitted a reinforcement learning model to the choice behaviour of the subjects to assess whether or not they were disposed to selecting novel stimuli. This model computes the value of a novel stimulus, to the participant, before it has had any reward