Personality and addictive behaviours in early Parkinson's disease and REM sleep behaviour disorder

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1. Introduction

While still controversial, a pre-morbid personality has been associated with Parkinson's disease (PD) since 1913 [1]. Assessment of personality varies depending on the model used, however some report that patients with established PD have a profile of less novelty seeking and more harm avoidance [2]. Other features relate to over controlled personality traits with introversion, mental rigidity, tenseness, social alertness and cautiousness [3]. It has been argued that reduced striatal dopaminergic signalling may cause these personality traits. There is also evidence that PD patients engage in less addictive behaviours than the general population, such as smoking, alcohol and caffeine use, which may or may not be secondary to these personality differences [4,5]. Conversely, a significant proportion of patients can develop impulsive-compulsive behaviours (ICB) when treated with dopamine agonists [6]. In the general population, novelty seeking behaviour is associated with impulsive/addictive syndromes, linked to an exaggerated dopaminergic response to novel or rewarding stimuli [7]. These
observations strengthen the view of dopamine as a central factor in both personality traits and reward or novelty based behaviour.

There have been few well-designed prospective studies investigat- ing personality in this earliest stage of the disease process [2] or in the prodromal phase. The latter can be investigated with a cohort of patients with REM sleep behaviour disorder (RBD) because of their high risk of future conversion to PD and evidence, even at this stage, of a functional change in dopamine circuitry [8]. We have examined the following questions using the Oxford Dis- covery study comprising a large well-phenotyped PD cohort, RBD patients and population controls. (1) Does the personality of PD patients differ from controls in the early and pre-motor stages? (2) Can one explain differing patterns in addiction prone behaviours, such as smoking, caffeine and alcohol consumption in PD, by different personality profiles?

2. Materials and methods

2.1. Participants

Full details of the protocol have been described elsewhere [9]. In brief, PD patients diagnosed within 3.5 years were recruited be- tween September 2010 and February 2014. Cases were eligible for inclusion if they met the UK PD Brain Bank criteria for diagnosis [10] irrespective of their age at PD onset, family history or cognitive status, while atypical cases were excluded. Cases diagnosed with dementia within one year of diagnosis were excluded as cases of Lewy body dementia.

The control population were clinically assessed to ensure they did not have PD or a first-degree relative with PD. The ‘RBD’ group comprised of participants with a diagnosis made by clinical assessment and polysomnography according to standard Interna- tional Classification of Sleep Disorders-II criteria [11].

2.2. Clinical assessment

Personality was assessed using the Big Five Inventory (BFI-44). This is a self-rated questionnaire that uses a 5-point scale to rate 44 short phrases of character to evaluate the five factor model of personality: extraversion; neuroticism; agreeableness; openness; and conscientiousness (see supplemental tables 1 and 2) [12].

The addictive behaviours assessed were smoking, alcohol and caffeine use, each scored using the Mini Environmental Risk Questionnaire for PD. Current and past use for each was assessed, with consumption before diagnosis used for pre-morbid assess- ment in the PD group. A broad range of non-motor symptoms (NMS) were assessed, details of the tests and thresholds for positive symptoms are shown in supplemental table 3.

Motor function was assessed using MDS-UPDRS III and Hoehn and Yahr staging. PD patients were classified into three motor phenotypes (postural instability and gait difficulty (PIGD), tremor dominant (TD) and indeterminate) based on their MDS-UPDRS motor score [13].

We also collected data on socioeconomic status (type of ac- commodation and vehicle ownership) and education level (using years in formal education) to adjust for the potential confounding effect of socio-economic position on addiction prone behaviours that are socially patterned.

2.3. Statistical analysis

Continuous demographic variables were compared using ANOVA or Kruskall-Wallis tests (if distribution was not Gaussian). The chi-squared test was used for categorical data. Missing data was excluded from the analysis.

We initially tested whether there were differences in personality (outcome) by our three exposure groups (PD, RBD, controls). Each personality domain was categorised into quintiles and ordinal logistic regression was used to calculate the odds ratio (OR) for a unit change in the outcome as the assumptions required for linear regression were not valid. The Wald test of parallel lines assump- tions was used to test the model was appropriate. We used multi- variable models in our comparison between groups, incrementally adjusting for age, gender, affective disorders (anxiety and depres- sion) and cognition. For comparison of PD subtypes, our regression models also included disease duration, motor severity and levo- dopa equivalent daily dose (LED).

We then tested whether disease status predicted our three addiction prone behaviours: smoking, alcohol and caffeine beverage consumption, which we had categorised into ordinal variables (see supplemental table 3). Our initial models adjusted for age, gender, socioeconomic status and educational level. We then adjusted for each of the 5 personality factors (the log of the total individual score was used due to non-normality) to see if this attenuated the associations. Finally to look at how personality predicted addiction prone behaviours, we pooled together all subjects (regardless of disease status) and adjusted for age, gender, socio-economic position and educational level.

We used a threshold of 0.05 as a level of statistical significance, but due to multiple testing, p-values between 0.05 and 0.001 should be interpreted with caution as they may reflect a type I error.

3. Results

Baseline data from 1361 participants (941 PD, 128 RBD and 292 controls) were included (Fig. 1). Basic demographics are shown in Table 1. Missing data in each variable was less than 3% except for the BDI (5.2%) and the QUIP-S (4.7%) leaving us with 1112 (81.7%) complete cases.

3.1. Comparison of personality in the early PD, RBD and control groups

The PD group was older than the control (p < 0.001) and the RBD groups (p = 0.01), which had similar age. There were substantially fewer women in the RBD group (13.3%) compared to both controls (51.0%) and PD group (35.2%) (both p values < 0.001) and the PD group also had fewer women than the controls. The control group were wealthier and more educated than both the PD and RBD groups (all p-values < 0.05). The PD group owned more of their own accommodation (p = 0.007) and had more bedrooms than the RBD group (p = 0.008).

Neuroticism and extraversion showed the biggest absolute differ- ences between the control group and the others (see supplemental Fig. 1). Adjusting for age and gender, PD cases were more neurotic (OR 2.03, 95% CI 1.59, 2.58, p < 0.001), less extraverted (OR 0.53, 95% CI 0.42, 0.68, p < 0.001) and less open than the control group (OR 0.55, 95% CI 0.44, 0.70, p < 0.001) (see Table 2). The same pattern was seen when comparing the RBD group with controls, who were more neurotic (OR 3.07, 95% CI, 2.09, 4.52, p < 0.001), less extraverted (OR 0.65, 95% CI 0.44, 0.95, p = 0.03) and less open (OR 0.49, 95% CI 0.34, 0.72, p < 0.001). The addition of mood (depression and anxiety) and cognition as additional co- variates in the regression model had little effect on most of the results, except for neuroticism, which showed moderate attenuation with the addition of mood (OR for PD cases versus controls went from 2.03 to 1.49). Again the same pattern was seen in the RBD group following this adjustment, so they remained more neurotic and less open, but there was moderate attenuation for
extraversion after including mood in the model (OR for RBD cases versus controls went from 0.65 to 0.85).

PD patients with the PIGD phenotype were less extraverted than the tremor dominant phenotype (OR 0.66, 95% CI 0.51, 0.87, p = 0.003) and more neurotic (OR 1.47, 95% CI 1.21, 1.92, p = 0.005) but were otherwise similar [see supplementary Table 4]. PD patients with RBD were more neurotic (OR 2.02, 95% CI 1.59, 2.58, p < 0.001), which was consistent with the other patterns, but were also less agreeable (OR 0.71, 95% CI 0.56, 0.90, p = 0.005) and less conscientious (OR 0.69, 95% CI 0.54, 0.88, p = 0.002). Treated PD patients (not on dopamine replacement therapy) were less open than untreated PD patients (OR 0.64, 95% CI 0.44, 0.92, p = 0.02) but were otherwise similar [see supplementary Table 5]. Differences between untreated PD patients and controls were attenuated compared to the whole PD group comparison, particularly the differences in openness were no longer evident (OR 0.81, 95% CI 0.55, 1.20, p = 0.30).

We undertook a number of sensitivity analyses by excluding younger (<50 years) or demented (MOC  < 24) subjects in the comparison of personality between the patient groups, which had little effect on the results.

3.2. Smoking, alcohol and caffeine consumption

PD patients were less likely to have smoked regularly (at least 1 cigarette a day for 6 months) than controls (OR 0.72, 95% CI 0.54, 0.96, p = 0.03). However, the difference was greater following diagnosis, with a greater proportion of PD patients having given up
smoking (OR went from 0.72 to 0.44). Looking at total cigarette consumption (pack years smoked) (see Table 3), this showed the same pattern of PD patients smoking less than controls (OR 0.71, 95% CI 0.54, 0.93, p = 0.02). However, there was modest evidence that RBD patients possibly smoked more than controls (OR 1.55, 95% CI 0.54, 0.93, p = 0.05). Adjusting for personality in the model made little difference to the results except for alcohol consumption, which showed modest attenuation for PD versus controls (OR 0.70–0.79). PD patients with RBD symptoms may have had a modestly higher rate of smoking than those without (OR 1.33, 95% CI 0.99, 1.79, p = 0.06), but this difference was not statistically significant. 

Personality traits were associated with addictive behaviours (see supplementary table 6). Being more extravert (OR 1.74, 95% CI 1.16, 2.60, p = 0.007) and less agreeable (OR 0.23, 95% CI 0.13, 0.56, p < 0.001) was associated with higher smoking consumption. Higher scores in extraversion (OR 2.14, 95% CI 1.44, 3.17, p < 0.001) and openness (OR 2.98, 95% CI 1.75, 5.06, p < 0.001), as well as lower neuroticism scores (OR 0.55, 95% CI 0.40, 0.76, p < 0.001), predicted higher alcohol consumption. These associations remained despite adjusting for mood and cognition, although the affect of neuroticism was less pronounced.

4. Discussion

4.1. Personality in PD and prodromal PD

Our findings support and build on some of the previous studies.
which suggest a ‘Parkinsonian personality’ is associated with being more introverted and neurotic. The presence of these personality differences in RBD and in the early stages of PD infers that these changes start before the onset of motor symptoms. Most previous studies have used personality assessments based on Cloninger’s psychobiological model [14]. They demonstrated that PD patients had less novelty seeking and more harm avoidance characteristics than control populations [2,15]. Using the five factor model, PD patients were shown to be more neurotic and less extraverted than controls if the patient was depressed [16]. Two other studies have shown less extraversion and conscientiousness in the PD group [17] or no differences in personality [18]. However these studies were small and potentially underpowered to detect differences. A major strength of this study is that the personality differences largely persisted despite adjusting for mood and cognition, which can affect the assessment of personality traits [15].

Sieurin et al. recently published the results of a prospective twin study which found neuroticism and introversion to be more common in subjects who converted to PD [19], in support of a prodromal PD personality. Postuma et al. found that RBD patients scored higher on harm avoidance than controls using the Tridimensional Personality Questionnaire [20]. Importantly these personality differences did not predict conversion to PD, implying that they remained relatively stable through the prodromal stage to conversion [21]. However Sasai et al. were unable to replicate these findings in an independent cohort using a five-factor model (NEO-PIR), although the study may have been too small to detect a difference [22]. This study adds considerable evidence to the concept of a prodromal personality profile, with the differences detected reflecting the same pattern of differences as the early PD group.

Proposed subtypes of PD may have different disease mechanisms, with the prevalence and severity of NMS being key distinguishing features. The same pattern of differences seen between PD and controls was again reflected in the differences between the PD and TD groups, consistent with a more severe NMS disease burden and more aggressive disease process. That PD patients with RBD were more neurotic than those without may also be a reflection of this, consistent with previous evidence that these patients have different phenotypic features [23,24]. It remains unclear whether these differences are a direct result of the underlying pathophysiology or a consequence of disrupted sleep.

The attenuation of the differences, particularly in openness, between the untreated PD participants and controls, may be driven by these patients having a less aggressive disease process. As the study design recruited subjects with early Parkinson’s rather than at the time of diagnosis, this result could just reflect a milder subtype of PD. The phenotypic differences between subtypes is more complex than primarily driven by dopamine dysfunction [25]. Thus while we have provided evidence of personality differences between subtypes, the similarities between treated and untreated PD cases may reflect that these effects are due to changes in alternative pathways.

4.2. Addictive behaviours in PD

There is a body of epidemiological evidence that suggests that
PD is associated with lower rates of smoking [4,26]. We had postulated that this inverse association with addictive behaviours may be a reflection of the personality traits associated with PD, driven by disruption of dopaminergic signalling. Analyses, when adjusted for differences in personality as a potential confounder, still found a robust difference in smoking rates between the PD group and controls. This suggests personality and certain reward-based activities are independent factors, consistent with the Swedish twin registry study (n = 197) [19] that also found a direct effect of neuroticism increasing the risk of PD using mediation analysis (i.e. conditioning out any indirect effect through a smoking mediator pathway).

PD patients were more likely to have given up smoking than controls, potentially a result of disease progression affecting reward sensitivity in this group. A similar finding was reported in early, untreated PD patients although we are unable to comment on the reasons for individuals quitting smoking [27].

Somewhat surprisingly, the RBD patients were more likely to have smoked than either the control or PD population, replicating the results of a previous large study of RBD patients [28]. The reasons for this are not clear and the trend of PD patients with RBD to smoke more than those without RBD replicates the finding of a previous study [29]. This may provide further support for PD heterogeneity with possibly different pathophysiological mechanisms or reflect behavioural changes due to the symptoms of the condition. A large population study using a screening questionnaire to diagnose probable RBD did not find this association with smoking, but this may be due to misclassification due to the assessment method [30].

Alcohol consumption was similar in the RBD group and controls, but less in the PD group. Personality accounted for more of the differences between the cases and controls than in the smoking comparison, but the overall effect was still small. Caffeine beverage consumption was similar across groups, possibly because the absolute caffeine value of different drinks was not assessed.

Extraversion was the only trait that predicted both higher smoking and alcohol consumption. Being more extravert is thought to represent an underlying sensitivity to reward, thus its association with addictive behaviour is intuitive. In addition to extraversion, openness was positively associated with higher alcohol use and neuroticism was inversely associated. This pattern of personality traits predicting more alcohol use is the inverse of the personality changes occurring before motor symptom onset. Extraversion, which has been linked with reward sensitivity, is positively associated with smoking and alcohol consumption. The lower rates of addictive behaviours before and after the onset of motor symptoms in PD are not explained by the personality changes alone, at least as measured by the five factor model. However, the same personality characteristics that are affected in PD are associated with addictive behaviours, which is strongly suggestive of a common link.

**5. Conclusion**

This study supports the concept of personality differences between PD and control subjects, even in the earliest stages of the motor phase of the disease. The similar pattern found in RBD patients (a surrogate for prodromal PD) is strongly suggestive of these personality changes occurring before motor symptom onset. Extraversion, which has been linked with reward sensitivity, is positively associated with smoking and alcohol consumption. The lower rates of addictive behaviours before and after the onset of motor symptoms in PD are not explained by the personality changes alone, at least as measured by the five factor model. However, the same personality characteristics that are affected in PD are associated with addictive behaviours, which is strongly suggestive of a common link.

**Ethics approval**

Ethical approval for this study was granted by the Berkshire Ethics Committee, South Central, National Research Ethics Service (UK): reference number 10/H0505/71. All participating subjects provided informed written consent.

**Financial disclosure/conflict of interest**

The authors have no conflicts of interest to declare. The OPDC Discovery cohort is funded by the Monument Trust Discovery Award from Parkinson’s UK (grant number J-1403) and supported by the National Institute for Health Research (NIHR) Oxford Biomedical Research Centre based at Oxford University Hospitals NHS Trust and University of Oxford, and the Dementias and Neurodegenerative Diseases Research Network (DeNDRoN).

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**Author roles**

1. Research Project: A. Conception, B. Organization, C. Execution;
2. Statistical Analysis: A. Design, B. Execution, C. Review and Critique; 3. Manuscript Preparation: A. Writing the First Draft, B. Review and Critique.

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Competing interests
None.

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Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.parkreldis.2017.01.017.

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