

## Abstract

*Objective:* In addition to the well-known motor symptoms, Parkinson's disease (PD) patients also frequently experience disabling non-motor symptoms, such as impulse control disorders (ICDs). The present study aimed to assess the predictive value of depression and anxiety, and the interaction of these factors with dopaminergic replacement therapy (DRT), for ICD development in *de novo* PD patients. *Methods:* Using the Parkinson's Progression Markers Initiative database, a total of 334 *de novo* PD patients with a negative ICD screen at baseline (assessed with the Questionnaire for Impulsive-Compulsive Disorders short form [QUIP-S]) were included in the present study. Baseline depression and anxiety were measured by the Geriatric Depression Scale (GDS-15) and the State-Trait-Anxiety Inventory (STAI-Y), respectively. The outcome measures were ICD presence (a positive QUIP-S score) at follow-up visits, and ICD onset duration (time in months from baseline until ICD development). Binominal logistic regression and multiple regression analyses were performed to assess predictors for ICD presence and duration until ICD onset, respectively. *Results:* In total, 149 participants (44.6%) developed an ICD and the time of ICD onset was on average 34.54 months ( $SD=24.74$ ) after baseline. Baseline STAI-Y scores were a significant predictor of ICD presence at follow-up visits, and higher scores were associated with an increased likelihood of developing an ICD ( $OR=1.02$ , 95% CI [1.00,1.05],  $p=.036$ ). The first DRT type also significantly predicted ICD incidence, and dopamine agonists were associated with 2.34 higher odds (95% CI [1.45,3.86],  $p=.001$ ) of developing an ICD, compared to levodopa or other medication types. Both effects were not confounded by age, gender or UPDRS motor score. GDS-15 scores and the interaction terms GDS-15 x DRT type and STAI-Y x DRT type did not significantly predict ICD presence (all  $ps>.299$ ). None of the investigated factors significantly predicted ICD onset duration (all  $ps>.091$ ). *Implications:* The finding that increased anxiety levels in *de novo* PD patients represent an ICD risk factor highlights the need for early and routine based anxiety screening in these patients. Additionally, clinicians should carefully consider the first choice of DRT, given that patients who received dopamine agonists as their first medication type encountered an increased ICD risk.

This work has been published in the Journal of Parkinson's disease and can be found here:

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