

Screening for impulse control symptoms in patients with de novo Parkinson disease

A case-control study

Daniel Weintraub, MD
Kimberly Papay, BS
Andrew Siderowf, MD,
MSCE
For the Parkinson's
Progression Markers
Initiative

Correspondence to
Dr. Weintraub:
daniel.weintraub@uphs.upenn.edu

ABSTRACT

Objective: To determine the frequency and correlates of impulse control and related behavior symptoms in patients with de novo, untreated Parkinson disease (PD) and healthy controls (HCs).

Methods: The Parkinson's Progression Markers Initiative is an international, multisite, case-control clinical study conducted at 21 academic movement disorders centers. Participants were recently diagnosed, untreated PD patients ($n = 168$) and HCs ($n = 143$). The outcome measures were presence of current impulse control and related behavior symptoms based on recommended cutoff points for the Questionnaire for Impulsive-Compulsive Disorders in Parkinson's Disease (QUIP)-Short Form.

Results: There were 311 participants with complete QUIP data. Frequencies of impulse control and related behavior symptoms for patients with PD vs HCs were as follows: gambling (1.2% vs 0.7%), buying (3.0% vs 2.1%), sexual behavior (4.2% vs 3.5%), eating (7.1% vs 10.5%), punning (4.8% vs 2.1%), hobbyism (5.4% vs 11.9%), walkabout (0.6% vs 0.7%), and any impulse control or related behavior (18.5% vs 20.3%). In multivariable models, a diagnosis of PD was not associated with symptoms of any impulse control or related behavior ($p \geq 0.10$ in all cases).

Conclusions: PD itself does not seem to confer an increased risk for development of impulse control or related behavior symptoms, which further reinforces the reported association between PD medications and impulse control disorders in PD. Given that approximately 20% of patients with newly diagnosed PD report some impulse control or related behavior symptoms, long-term follow-up is needed to determine whether such patients are at increased risk for impulse control disorder development once PD medications are initiated. *Neurology*® 2013;80:176-180

GLOSSARY

HC = healthy control; **ICD** = impulse control disorder; **MoCA** = Montreal Cognitive Assessment; **PD** = Parkinson disease; **PPMI** = Parkinson's Progression Marker Initiative; **QUIP** = Questionnaire for Impulsive-Compulsive Disorders in Parkinson's Disease; **UPDRS** = Unified Parkinson's Disease Rating Scale.

Impulse control disorders (ICDs), including compulsive gambling, buying, sexual behavior, and eating, are common and clinically significant in Parkinson disease (PD).¹ Other compulsive behaviors reported to occur include punning (excessive repetition of non-goal directed activity),² hobbyism (excessive repetition of more complex activities),³ and walkabout (aimless wandering).² In a recent large observational study of patients with treated PD, an ICD was identified in 14% of patients.⁴ Prevalence rates for punning range from 1% to 14%,^{5,6} whereas the prevalence of hobbyism and walkabout are not known.

The association between PD medications and ICDs in PD is well established.^{4,7} However, an important unanswered question is whether PD itself confers an altered risk for ICDs. Preliminary comparison studies suggest that ICDs are more common in *treated* PD patients than in healthy controls (HCs).^{8,9} In the only published study assessing newly diagnosed, *untreated* PD patients, 18% screened positive for impulse control symptoms, a number similar to HCs.¹⁰

Supplemental data at
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Supplemental Data



From the University of Pennsylvania School of Medicine (D.W., K.P., A.S.); and Parkinson's Disease and Mental Illness Research, Education and Clinical Centers (D.W.), Philadelphia Veterans Affairs Medical Center, Philadelphia, PA.

Parkinson's Progression Markers Initiative coinvestigators are listed on the *Neurology*® Web site at www.neurology.org.

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However, this study used a general impulse control instrument not validated for use in PD, did not query for compulsive eating, and included control data that were published in a separate report.¹¹

Determining the frequency of impulse control symptoms in patients with de novo, untreated PD would help answer the question of whether PD itself confers an increased risk for experiencing such symptoms. Analyzing baseline data from a large observational study of patients with newly diagnosed, untreated PD and an HC group of similar age and education, we hypothesized that the frequency of impulse control symptoms would be similar in the 2 groups.

METHODS Participants. Patients with newly diagnosed, untreated PD and unmatched HCs were enrolled in the Parkinson's Progression Marker Initiative (PPMI), a study for which the aims and methodology have been published.¹² At baseline, PD patients are required to 1) have an asymmetric resting tremor or asymmetric bradykinesia or 2) of bradykinesia, resting tremor, and rigidity, 2) be recently diagnosed (within 2 years), and 3) be untreated. HCs must have no significant neurologic dysfunction, no first-degree family member with PD, and a Montreal Cognitive Assessment (MoCA) score >26.

Standard protocol approvals, registrations, and patient consents. Each participating PPMI site 1) received approval from an ethical standards committee on human experimentation before study initiation, and 2) obtained written informed consent for research from all individuals participating in the study.

Study design. PPMI is an observational, international, multicenter (16 US and 5 European sites) study designed to identify PD progression biomarkers, with a goal to enroll 400 PD patients and 200 HCs. The study was launched in June 2010, and the data used in the preparation of this article were obtained from the PPMI database (www.ppmi-info.org [accessed February 24,

2012]). At this time, 432 people had been screened for the study. Of this total, 329 consented and provided complete baseline data (PD = 186, HC = 143). Of the patients with PD, 18 were identified as having dopamine transporter brain scans without evidence of dopaminergic deficit and were removed from the PD population for the purposes of this study, leaving a total sample size of 311 participants (PD = 168, HC = 143).

Study outcomes. A self-report and self-completed screening instrument, the Questionnaire for Impulsive-Compulsive Disorders in Parkinson's Disease (QUIP), was recently developed and validated specifically to detect the presence of clinically significant impulse control (compulsive gambling, buying, sexual behavior, and eating) and related behavior (punding, hobbyism, and walkabout) symptoms reported to occur in PD.¹³ A short-form version of the QUIP was shown to have similar psychometric properties in secondary analyses.¹³ As a screening instrument, the QUIP is designed to be sensitive for the detection of ICDs and related disorders, but is not highly specific (i.e., it overidentifies patients), so many individuals with a positive QUIP do not meet diagnostic criteria for an ICD or related disorder. A positive QUIP for a particular disorder was based on previous research with the QUIP-Short Form (i.e., a positive response to either of the 2 questions for each of the 4 ICDs, and a positive response to the single question each for punding, hobbyism, and walkabout).¹³

Other measures included basic demographic variables, Unified Parkinson's Disease Rating Scale (UPDRS) motor score¹⁴ and Hoehn and Yahr stage¹⁵ as measures of disease severity, the MoCA (scores range from 0 to 30, lower scores indicating greater cognitive impairment) for assessment of global cognitive abilities,¹⁶ and the 15-item Geriatric Depression Scale (scores range from 0 to 15, higher scores indicating greater depression severity) to assess severity of depressive symptoms.¹⁷

Statistical methods. To compare medians, χ^2 tests, *t* tests (with the Levene test for equality of variances), and nonparametric tests were used for between-group comparisons of clinical, demographic, neuropsychological, and imaging variables. Normality assumptions were checked with the Kolmogorov-Smirnov test whenever the tests required normality assumption, and a Mann-Whitney *U* test was run for variables that were not normally distributed.

Variables either reported to be associated with ICDs in PD (e.g., age⁴) or for which we found between-group differences (PD patients vs HCs) on bivariate analysis at *p* value <0.05 (table 1) were entered into stepwise logistic regression models to determine the independent effects of different covariates on the occurrence of impulse control and related behavior symptoms. Because walkabout was uncommon, it was not examined separately, but was included in the category "any ICD or related behavior."

All statistical tests were 2-sided. Statistical significance was set at *p* ≤ 0.05. Analyses were conducted with PASW Statistics (version 20.0) software.¹⁸

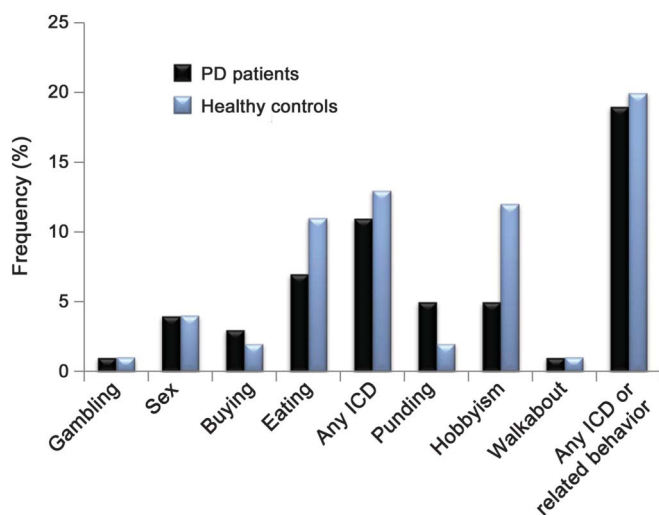
RESULTS Participant characteristics. Demographic and clinical information for the 168 PD patients and 143 HC individuals is listed in table 1. On bivariate analysis, there were no significant differences between the 2 groups for age (*p* = 0.12), race (*p* = 0.17), or education (*p* = 0.51), but PD patients were more likely to be male (*p* = 0.007). PD patients performed statistically worse on the MoCA (*p* < 0.001), with 19% of PD patients screening

Table 1 Demographic and clinical characteristics of the study population

Variable	Patients with PD (n = 168)	Healthy controls (n = 143)	Statistic (t test, Mann-Whitney U test, or χ^2)
Age, y, mean (SD)	61.5 (9.5)	59.1 (12.0)	<i>z</i> = -1.6, <i>p</i> = 0.12
Sex (% male)	71.4	56.6	7.4 (1), <i>p</i> = 0.007
Race (% white)	96.4	93.0	1.9 (1), <i>p</i> = 0.17
Education, y, mean (SD)	15.8 (2.7)	16.0 (2.8)	<i>z</i> = -0.7, <i>p</i> = 0.51
UPDRS motor score, mean (SD)	21.6 (8.6)	—	—
Hoehn and Yahr stage, median	2.0	—	—
MoCA, mean (SD), range	27.1 (2.2), 20-30	28.3 (1.1), 27-30	<i>z</i> = -5.0, <i>p</i> < 0.001
GDS-15, mean (SD)	2.2 (2.4)	1.4 (2.3)	<i>z</i> = -4.2, <i>p</i> < 0.001

Abbreviations: GDS-15 = 15-item Geriatric Depression Scale; MoCA = Montreal Cognitive Assessment; PD = Parkinson disease; UPDRS = Unified Parkinson's Disease Rating Scale.

Figure Frequencies of self-reported impulse control disorder (ICD) and related behavior symptoms in patients with Parkinson disease (PD) and in healthy controls



positive for a cognitive disorder based on the recommended cutoff score of <26 .¹⁹ PD patients also demonstrated a higher 15-item Geriatric Depression Scale score ($p < 0.001$), with 12.5% of PD patients screening positive for depression based on the recommended cutoff score of >4 .²⁰

Frequency of ICD and related behavior symptoms. The frequencies of impulse control and related behavior symptoms are illustrated in the figure, and for patients with PD vs HCs were as follows: compulsive gambling (1.2% vs 0.7%), compulsive buying (3.0% vs 2.1%), compulsive sexual behavior (4.2% vs 3.5%), compulsive eating (7.1% vs 10.5%), punding (4.8% vs 2.1%), hobbyism (5.4% vs 11.9%), walkabout (0.6% vs 0.7%), and any impulse control or related behavior symptoms (18.5% vs 20.3%). There

were no significant differences between the 2 groups regarding the frequency of symptoms of any of the 4 impulse control behaviors, either individually or as a group. Regarding related behaviors, although there was no significant difference in the frequency of punding or walkabout, HCs were more likely to report symptoms of hobbyism ($p = 0.04$). There were no significant between-group differences when impulse control and related behavior symptoms were combined into a single group.

Correlates of impulse control and related behavior symptoms. Given the significant differences between PD patients and HCs in gender, cognition, and depression severity, as well as research documenting an association between younger age and ICDs in PD, logistic regression models were run including these variables as covariates, with impulse control or related behavior symptoms as the dependent variable (table 2). A diagnosis of PD was not associated with the presence of symptoms of any impulse control or related behavior, either individually or as a group. The only significant correlate in the multivariable model was increasing severity of depressive symptoms. On subanalysis, increasing severity of depression was associated with the presence of compulsive-eating symptoms (β [SE] = 0.17 [0.06], $p = 0.007$), but not with other impulse control or related behavior symptoms (data not shown).

Examining PD patients and HCs separately, increasing severity of depression was associated with presence of any impulse control or related behavior symptoms in HCs (β [SE] = 0.21 [0.09], $p = 0.02$) and with presence of impulse control symptoms in PD patients (β [SE] = 0.21 [0.09], $p = 0.02$).

Examining for other correlates in PD patients, there were no significant associations between the presence of any impulse control symptoms or any

Table 2 Logistic regression models examining predictors of impulse control and related behavior symptoms in the entire study population

	Any impulse control behavior ^a (n = 37)	Punding or hobbyism ^b (n = 33)	Any impulse control or related behaviors ^c (n = 60)
Diagnosis (PD vs HC)	-0.48 (0.39), $p = 0.23$	-0.70 (0.42), $p = 0.10$	-0.43 (0.33), $p = 0.19$
Age	-0.02 (0.02), $p = 0.20$	-0.02 (0.02), $p = 0.40$	-0.01 (0.01), $p = 0.37$
Sex	0.07 (0.39), $p = 0.86$	0.14 (0.41), $p = 0.74$	0.01 (0.32), $p = 0.97$
MoCA	-0.08 (0.11), $p = 0.46$	-0.17 (0.11), $p = 0.10$	-0.14 (0.09), $p = 0.11$
GDS-15	0.18 (0.06), $p = 0.002$	0.09 (0.07), $p = 0.17$	0.17 (0.06), $p = 0.002$

Abbreviations: GDS-15 = 15-item Geriatric Depression Scale; HC = healthy control; MoCA = Montreal Cognitive Assessment; PD = Parkinson disease.

^aAny impulse control behavior is participant with symptoms of ≥ 1 of the 4 impulse control disorders. $\chi^2 = 12.6$ ($df = 5$), $p = 0.03$ for the model. β coefficient (SE) and p value presented for each variable for all analyses.

^b $\chi^2 = 6.8$ ($df = 5$), $p = 0.24$ for the model.

^cAny impulse control or related behavior is participant with symptoms of ≥ 1 of the 4 impulse control disorders, punding, hobbyism, or walkabout. $\chi^2 = 15.2$ ($df = 5$), $p = 0.01$ for the model.

impulse control or related behavior symptoms and age, sex, education, MoCA score, Hoehn and Yahr stage, and UPDRS motor score (data not shown).

DISCUSSION The primary finding of this study is that the broad range of impulse control and related behavior symptoms that are reported to occur in patients with established, treated PD is equally common (approximately 20%) in patients with de novo, untreated PD and the general population. Additional findings are that increasing severity of depression is associated with these symptoms in both the entire population and PD patients, but global cognitive abilities are not. The major strengths of our study are that it is the first to use an impulse control assessment tool developed and validated for use in PD, as well to enroll PD patients and HCs concurrently and to have both groups undergo an identical assessment process.

Given that all research to date examining the frequency and correlates of ICDs and similar behaviors in PD has been cross-sectional, an important unanswered question is to what extent the increased frequency reported in PD patients compared with the general population is attributable to treatment with PD medications vs a disease-related effect.

Our results suggest that PD itself does not confer an increased risk for experiencing ICDs and related disorders. Therefore, the excess occurrence of these disorders in PD is likely driven by exposure to PD pharmacotherapy and possibly other PD treatments (e.g., deep brain stimulation surgery²¹), with certain clinical and demographic variables (e.g., younger age, family or personal history of similar behaviors^{3,4}) moderating an individual's risk for developing an ICD. It also supports recent case reporting of ICDs occurring with dopamine agonist treatment in other clinical populations (e.g., restless legs syndrome²² and fibromyalgia²³).

Despite the fact that impulse control and related behavior symptoms were not more common in PD patients compared with HCs, almost 20% of PD patients did screen positive for one or more of these disorders. Perhaps these patients also have a personal or family history of similar behaviors that has been suggested to be a risk factor for ICDs in PD based on results from cross-sectional studies.⁴ Long-term follow-up of patients newly diagnosed with PD is necessary to determine whether those patients who report impulse control and related behavior symptoms at the time of PD diagnosis are at increased risk of developing an actual ICD after treatment with PD medications is initiated.

The only correlate of impulse control symptoms in PD patients was increasing severity of depression, which has been reported previously for ICDs in PD.²⁴ However, because depression was also associated with impulse control or related behavior

symptoms in controls, this finding does not seem to be specific to PD.

We did not find a correlation in PD patients between impulse control and related behavior symptoms and global cognitive abilities as measured by the MoCA, similar to what was reported in a previous case-control study in PD patients with ICDs.²⁴ Administration of more sensitive and specific cognitive tasks, as previously done in PD ICD studies,^{25–27} may be needed to detect cognitive changes with ICD symptoms.

Several study limitations should be noted. First, we were not able to determine symptom severity or whether participants actually met diagnostic criteria for an ICD or related disorder based on the methodology of the PPMI project, and it is important to note that a significant percentage of patients who screen positive with the QUIP do not meet diagnostic criteria for an actual disorder. Future research studies need to use formal diagnostic criteria for each disorder to extend our findings. Clinically, it is important that all patients with a positive QUIP undergo a detailed clinical interview to determine whether diagnostic criteria for an ICD or related disorder are met. Second, the PPMI cohort is made up of volunteers and is not necessarily representative of the underlying population of newly diagnosed PD patients. This limitation is balanced by the fact that it is a large cohort, very well characterized, and that the same selection factors probably existed for both cases and controls. Third, many of the clinical and demographic correlates of ICDs reported in previous studies were not available in this database. Finally, PD patients and HCs were not matched on some common characteristics (e.g., gender and global cognition), which necessitated the use of multivariable analyses.

The results of this study provide additional support to the idea that factors other than PD itself lead to the development of ICDs and related behaviors in PD. Long-term follow-up of patients newly diagnosed with PD is needed to determine whether self-reported symptoms at the time of PD onset predict, along with other demographic, clinical, cognitive, or neurobiological characteristics, the development of ICDs and related behaviors after initiation of PD pharmacotherapy.

AUTHOR CONTRIBUTIONS

Drs. Weintraub and Siderowf were involved with study concept and design, analysis and interpretation of the data, and drafting/revising the manuscript for content, including medical writing for content. Miss Papay was involved with analysis and interpretation of data, and drafting/revising the manuscript for content.

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