ORIGINAL CONTRIBUTION

Impulse Control Disorders in Parkinson Disease

A Cross-Sectional Study of 3090 Patients

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Context: An association between dopamine-replacement therapies and impulse control disorders (ICDs) in Parkinson disease (PD) has been suggested in preliminary studies.

Objectives: To ascertain point prevalence estimates of 4 ICDs in PD and examine their associations with dopamine-replacement therapies and other clinical characteristics.

Design: Cross-sectional study using an a priori established sampling procedure for subject recruitment and raters blinded to PD medication status.

Patients: Three thousand ninety patients with treated idiopathic PD receiving routine clinical care at 46 movement disorder centers in the United States and Canada.

Main Outcome Measures: The Massachusetts Gambling Screen score for current problem/pathological gambling, the Minnesota Impulsive Disorders Interview score for compulsive sexual behavior and buying, and Diagnostic and Statistical Manual of Mental Disorders research criteria for binge-eating disorder.

Results: An ICD was identified in 13.6% of patients (gambling in 5.0%, compulsive sexual behavior in 3.5%, compulsive buying in 5.7%, and binge-eating disorder in 4.3%), and 3.9% had 2 or more ICDs. Impulse control disorders were more common in patients treated with a dopamine agonist than in patients not taking a dopamine agonist (17.1% vs 6.9%; odds ratio [OR], 2.72; 95% confidence interval [CI], 2.08-3.54; $P<.001$). Impulse control disorder frequency was similar for pramipexole and ropinirole (17.7% vs 15.5%; OR, 1.22; 95% CI, 0.94-1.57; $P=.14$). Additional variables independently associated with ICDs were levodopa use, living in the United States, younger age, being unmarried, current cigarette smoking, and a family history of gambling problems.

Conclusions: Dopamine agonist treatment in PD is associated with 2- to 3.5-fold increased odds of having an ICD. This association represents a drug class relationship across ICDs. The association of other demographic and clinical variables with ICDs suggests a complex relationship that requires additional investigation to optimize prevention and treatment strategies.

Trial Registration: clinicaltrials.gov Identifier: NCT00617019

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IMPULSE CONTROL DISORDERS (ICDs), including problem or pathological gambling, compulsive buying, compulsive sexual behavior, and binge or compulsive eating, have been reported in Parkinson disease (PD).[1] Preliminary cross-sectional prevalence estimates of ICDs in this population range from 1.7% to 6.1% for gambling,[2-5] 2.0% to 4.0% for compulsive sexual behavior,[2,4,6] and 0.4% to 3.0% for compulsive buying[2,4,6]; there has been no formal prevalence estimate for eating disorders in PD.

Case reporting and cross-sectional studies suggest an association between dopamine agonist treatment and ICDs in PD.[2-4,6] Impulse control disorders in PD have also been reported in the context of levodopa treatment[7] and after deep-brain stimulation surgery.[8] However, studies to date have typically assessed convenience samples of patients at single sites, had relatively small sample sizes, assessed only a subset of commonly reported ICDs in PD, and have not broadly assessed clinical or demographic correlates.

Given the clinical significance of ICDs in PD and persisting questions concerning the association with dopamine-replacement therapies and other clinical correlates, a cross-sectional study (the DOMINION Study) of approximately 3000 patients was undertaken to assess the point frequency of ICDs in PD and their association with dopamine-replacement thera-

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pies and other clinical measures. We hypothesized that ICDs would be more common in patients treated with dopamine agonists than those not, with no differences among dopamine agonists.

METHODS

STUDY DESIGN AND PARTICIPANTS

A semi-structured interview using formal diagnostic criteria assessed current (anytime in the past 6 months) frequency of 4 ICDs (problem/pathological gambling, compulsive sexual behavior, compulsive buying, and binge-eating disorder) in treated patients with idiopathic PD. All participants were informed that the primary purpose of the study was to examine the frequency of ICDs in PD and their association with PD medications. Participants answered study questions individually, but corroborative information from informants was included when available. Prior to study initiation, each site developed a fixed subject recruitment strategy designed to minimize selection bias (eg, recruiting or excluding patients on the basis of known ICD or dopamine agonist treatment status). Specifically, patients with PD were recruited during regularly scheduled clinic visits, based on a set selection process individualized for each site (eg, attempting to assess every third scheduled patient during a particular half-day clinic) and by a member of the research staff with no knowledge of patients' current ICD or PD medication status. Each site obtained independent institutional review board approval.

Subjects were diagnosed as having idiopathic PD by a movement disorder specialist, aged 30 to 75 years, and recruited from 46 movement disorders centers in the United States (n=33) and Canada (n=13). Inclusion criteria required treatment with a PD medication for at least 1 year with demonstrated response, and dopamine agonist treatment could not have been initiated or terminated in the 6 months prior to evaluation. Changes in other PD medications and adjustments to dopamine agonist dosage in the 6 months prior to evaluation were allowed. The recorded PD medications and dosages were those being taken at the time of assessment. Written informed consent was provided by each patient prior to study participation.

PROCEDURES AND MEASUREMENTS

The following semi-structured diagnostic instruments were administered by trained research staff to capture clinically significant symptoms: (1) the Massachusetts Gambling Screen,[9] for problem or pathological gambling (pathological gambling, ≥5 criteria endorsed; problem gambling, 3-4 criteria endorsed); (2) the Minnesota Impulsive Disorders Interview[10] for compulsive buying and sexual behavior (both disorders, positive response to gateway question plus ≥1 secondary question for that subsection); and (3) the *Diagnostic and Statistical Manual of Mental Disorders* (Fourth Edition, Text Revision)[11] proposed research criteria for binge-eating disorder (positive response to both gateway questions and ≥3 secondary questions). Demographic and clinical data were obtained from patients in a semistructured interview and verified by medical record review when necessary. Modified Hoehn and Yahr staging[12] was obtained from a movement disorders clinician or by medical record review.

STATISTICAL ANALYSIS

A Cochran-Mantel-Haenszel test with country stratification was performed and odds ratios (ORs) with 95% confidence intervals (CIs) were calculated for between-group comparisons in ICD frequencies. Breslow-Day tests were applied for homogeneity of odds. Other between-group patient characteristics were compared using the Cochran-Mantel-Haenszel test or Wilcoxon-Mann-Whitney test.

As initial analyses identified between-country differences in ICD frequencies and dopamine agonist prescribing, all additional analyses were stratified by country. Because nearly all patients treated with dopamine agonists were taking either pramipexole or ropinirole, the within–dopamine agonist class statistical comparison was made for patients taking pramipexole vs ropinirole as their sole dopamine agonist. For secondary analyses, variables associated with the presence of an ICD on univariate analysis at $P<.10$ were entered into stepwise logistic regression models to determine the independent effects of different correlates.

The 2 primary hypotheses were hierarchically ordered (a noninferiority hypothesis of no difference in overall ICD frequency for different dopamine agonists, followed by the hypothesis that overall ICD frequency would be higher in patients treated with dopamine agonists than those not treated with them), so an α adjustment was not required. Sample size calculation for the first hypothesis was based on the assumption that 50% of PD patients would be taking a dopamine agonist, of whom one-third would be taking pramipexole. Given a noninferiority margin of 5% (ie, an OR of 2) as the accepted limit in signal detection required to establish noninferiority with a type I error probability of 0.025 (1-sided) and a power of 80%, approximately 1500 patients treated with dopamine agonists and 3000 patients overall were required.

The following values were used to calculate levodopa equivalent daily dosages (LEDDs) for dopamine agonist, levodopa, and total (dopamine agonist + levodopa) dosages: 100 mg of regular levodopa=133.3 mg of controlled-release levodopa=80 mg of levodopa + catechol *O*-methyltransferase inhibitor=1 mg of pergolide=1 mg of pramipexole=4 mg of ropinirole. Dopamine agonist and LEDDs were divided into quartiles to examine dosing effects (dopamine agonist, >0-≤150 mg, >150-≤300 mg, >300-≤450 mg, and >450 mg; and levodopa, >0-≤300 mg, >300-≤600 mg, >600-≤900 mg, and >900 mg). Analyses were performed using SAS software, release 8.02 (SAS Institute, Cary, North Carolina). $P<.05$ was considered significant.

RESULTS

DESCRIPTION OF STUDY POPULATION

Three thousand ninety patients participated in this study (**Table 1**). Nearly all (n=3031 [98.1%]) were taking either levodopa or a dopamine agonist. Two-thirds (n=2040 [66.0%]) were taking 1 or more DAs, and 86.8% (n=2682) were taking levodopa, including 37.0% (n=991) not taking a dopamine agonist. For the 59 (1.9%) patients taking neither a dopamine agonist nor levodopa, they took the following PD medications: a monoamine oxidase B inhibitor (n=35), amantadine (n=20), and/or an anticholinergic medication (n=9).

For patients taking a dopamine agonist, the mean daily dosages and LEDDs, respectively, were 3.1 mg (SD, 1.7 mg) and 306.9 mg (SD, 168.2 mg) of pramipexole; 11.1 mg (SD, 6.6 mg) and 277.9 mg (SD, 164.9 mg) of ropinirole; and 2.9 mg (SD, 1.7 mg) and 286.6 mg (SD, 169.3 mg) of pergolide. On pairwise comparison, patients taking pramipexole had a higher dopamine agonist LEDD than those taking ropinirole ($z=-4.1$, $P<.001$).

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Table 1. Demographic and Clinical Correlates of ICDs

Characteristic	No. (%) Total (N=3090)	Current ICD (n=420)	No Current ICD (n=2670)	*P* Value[a]
Male sex	1981 (64.1)	267 (63.6)	1714 (64.2)	.71
Age, mean (SD), y	63.8 (8.0)	60.2 (8.1)	64.4 (7.8)	<.001
Age ≤65 y	1624 (52.6)	302 (71.9)	1322 (49.5)	
White race	2969 (96.1)	402 (95.7)	2567 (96.1)	.67
Married	2448 (79.2)	308 (73.3)	2140 (80.1)	<.001
PD duration, median (IQR), y	6.5 (3.8-10.6)	7.1 (3.8-10.8)	6.5 (3.7-10.6)	.25
Hoehn and Yahr stage, median (IQR)[b]	2.0 (2.0-2.5)	2.0 (2.0-2.5)	2.0 (2.0-2.5)	.93
History of deep-brain stimulation	300 (9.7)	36 (8.6)	264 (9.9)	.18
Living in the United States	2247 (72.7)	337 (80.2)	1910 (71.5)	<.001
Education, partial college or higher	2163 (70.0)	316 (75.2)	1847 (69.2)	.05
Current smoking	118 (3.8)	28 (6.7)	90 (3.4)	<.001
Current alcohol use	1272 (41.2)	184 (43.8)	1088 (40.7)	.14
Family history of gambling problems[c]	126 (4.1)	30 (7.1)	96 (3.6)	<.001
Current family gambling problems	34 (1.1)	9 (2.1)	25 (0.9)	.02
Family history of alcohol abuse	726 (23.5)	119 (28.3)	607 (22.7)	.01

Abbreviations: ICD, impulse control disorder; IQR, interquartile range; PD, Parkinson disease.
[a] Between-group comparison of current ICD with no current ICD; Cochran-Mantel-Haenszel test (stratified by country), *t* test, or Mann-Whitney test.
[b] n=3083.
[c] n=3089.

CURRENT ICD FREQUENCIES AND DEMOGRAPHIC AND CLINICAL CHARACTERISTICS

At least 1 active ICD was identified in 13.6% of patients, with 3.9% of patients overall (or 28.7% of patients with an ICD) experiencing 2 or more ICDs. Five percent experienced problem/pathological gambling, 3.5% compulsive sexual behavior, 5.7% compulsive buying, and 4.3% binge-eating disorder.

DEMOGRAPHIC AND CLINICAL CHARACTERISTICS BY ICD STATUS

Compared with patients without an ICD, those with an active ICD were younger and more likely to be unmarried, reside in the United States, have more formal education, smoke cigarettes, report familial gambling problems (both historical and current), and acknowledge alcohol abuse in first-degree relatives (Table 1). Men were more likely than women to have diagnosed compulsive sexual behavior (5.2% vs 0.5%; OR, 11.98; 95% CI, 4.87-29.48; $P<.001$) and less likely to be diagnosed with compulsive buying (4.5% vs 7.8%; OR, 0.55; 95% CI, 0.40-0.74; $P<.001$) and binge-eating disorder (3.4% vs 5.8%; OR, 0.57; 95% CI, 0.40-0.81; $P=.002$). Compared with Canadian patients, US patients had increased frequencies of 2 ICDs: 5.5% vs 3.6% for problem/pathological gambling (OR, 1.58; 95% CI, 1.05-2.38; $P=.03$) and 6.7% vs 3.2% for compulsive buying (OR, 2.16; 95% CI, 1.42-3.28; $P<.001$). Patients with a history of gambling problems in a first-degree relative compared with patients without such a history had higher rates of problem/pathological gambling (12.7% vs 4.7%; OR, 2.97; 95% CI, 1.71-5.17; $P<.001$), compulsive buying (10.3% vs 5.5%, OR, 1.97; 95% CI, 1.08-3.58; $P=.02$), and binge-eating disorder (9.5% vs 4.0%; OR, 2.49; 95% CI, 1.34-4.64; $P=.003$).

CURRENT ICD FREQUENCIES IN THOSE TREATED AND NOT TREATED WITH DOPAMINE AGONISTS

Patients treated with dopamine agonists had a higher frequency of ICDs compared with those not treated with dopamine agonists (17.1% vs 6.9%, $P<.001$) (**Table 2**), a pattern observed across all 4 ICDs. An ICD was present in 17.7% of patients taking both a dopamine agonist and levodopa, 14.0% taking a dopamine agonist without levodopa, and 7.2% taking levodopa without a dopamine agonist. On multivariate analysis, the odds of having an ICD was higher in patients treated with a dopamine agonist than in levodopa-treated patients not taking a dopamine agonist (OR, 2.60; 95% CI, 1.97-3.43; $P<.001$). The combination of dopamine agonist and levodopa use, compared with dopamine agonist use alone, increased the odds of having an ICD (OR, 1.42; 95% CI, 1.02-1.98; $P<.001$). Of the 59 patients not taking a dopamine agonist or levodopa, 1 (1.7%) was diagnosed with an ICD.

CURRENT ICD FREQUENCIES BY DOPAMINE AGONIST TYPE

There was no statistically significant difference in overall ICD frequency between pramipexole- (n=1286 [17.7%]) and ropinirole- (n=651 [15.5%]) treated patients (OR, 1.22; 95% CI, 0.94-1.57; $P=.14$). This finding remained after controlling for either dopamine agonist LEDD or total LEDD, and was observed across all 4 ICD types. The overall ICD frequency in pergolide-treated patients (n=50) was 22.0%.

MULTIVARIABLE ANALYSIS OF ICD CORRELATES

Examining the entire study population (N=3090), demographic and clinical variables associated with a current

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Table 2. ICD Frequencies by Dopamine Agonist Treatment Status

ICD Type	Treatment Status (N=3090)[a]	No. (%)		OR (95% CI)[b]	*P* Value[c]
		Current ICD	No Current ICD		
Any ICD	No dopamine agonist	72 (6.9)	978 (93.1)	2.72 (2.08-3.54)	<.001
	Dopamine agonist	348 (17.1)	1692 (82.9)		
Problem/pathological gambling	No dopamine agonist	24 (2.3)	1026 (97.7)	2.82 (1.81-4.39)	<.001
	Dopamine agonist	130 (6.4)	1910 (93.6)		
Pathological gambling only	No dopamine agonist	17 (1.6)	1033 (98.4)	2.15 (1.26-3.66)	.004
	Dopamine agonist	72 (3.5)	1968 (96.5)		
Compulsive sexual behavior	No dopamine agonist	18 (1.7)	1032 (98.3)	2.59 (1.55-4.33)	<.001
	Dopamine agonist	90 (4.4)	1950 (95.6)		
Compulsive buying	No dopamine agonist	30 (2.9)	1020 (97.1)	2.53 (1.69-3.78)	<.001
	Dopamine agonist	147 (7.2)	1893 (92.8)		
Binge-eating disorder	No dopamine agonist	18 (1.7)	1032 (98.3)	3.34 (2.01-5.53)	<.001
	Dopamine agonist	114 (5.6)	1926 (94.4)		

Abbreviations: CI, confidence interval; ICD, impulse control disorder; OR, odds ratio.
[a] No dopamine agonist, n=1050; dopamine agonist, n=2040.
[b] Stratified by country.
[c] Cochran-Mantel-Haenszel test.

Table 3. Multivariable Analyses of ICD Correlates in Entire Study Population

Variable[a]	All Subjects (N=3090)	
	OR (95% CI)	*P* Value
Age, ≤65 vs >65 y	2.50 (1.98-3.15)	<.001
Not married vs married	1.48 (1.16-1.89)	.002
Living in the United States	1.62 (1.25-2.10)	<.001
Current smoking	1.70 (1.07-2.70)	.02
Family history gambling problems	2.08 (1.33-3.25)	.001
Dopamine agonist treatment	2.72 (2.07-3.57)	<.001
Levodopa treatment	1.51 (1.09-2.09)	.01

Abbreviations: CI, confidence interval; ICD, impulse control disorder; OR, odds ratio.
[a] Clinical and demographic variables included were those with $P<.10$ on univariate analysis; only data for significant results are presented.

ICD on multivariable analysis were younger age (≤65 years), being unmarried, living in the United States, current cigarette smoking, and a family history of gambling problems (**Table 3**). Both dopamine agonist and levodopa use were independently associated with an active ICD, with the OR nearly twice as high for dopamine agonist use.

Examining only patients taking a dopamine agonist (n=2040), on univariate analysis the median dopamine agonist LEDD in ICD and non-ICD patients was numerically the same (300 mg), but the interquartile range was higher for ICD patients (200-450 mg vs 150-400 mg, overall $P=.002$). The median levodopa LEDD was higher in patients with an ICD (450 mg vs 375 mg, $P<.001$). On multivariable analysis, there was no dopamine agonist dosage effect, but any levodopa use (OR, 1.43; 95% CI, 1.03-2.00; $P=.03$) and higher levodopa dosages ($P=.008$) were associated with a current ICD.

On univariate analysis, the median levodopa LEDD was higher in the ICD than the non-ICD group in patients taking levodopa but not a dopamine agonist (n=991) (621 mg vs 461 mg, $P=.003$). On multivariable analysis, higher levodopa dosages were associated with a current ICD ($P=.002$).

COMMENT

This is the largest and most detailed study of the frequency and correlates of ICDs in PD. Specific strengths of the study include systematic evaluation of a very large number of PD patients in routine clinical care; concurrent evaluation of gambling, sex, shopping, and eating ICDs using standardized assessment instruments; use of a priori–defined recruitment procedure to minimize sampling bias; and blinding of ICD raters to PD medication status. Important new findings demonstrate (1) that nongambling ICDs occur at a similar frequency as compulsive gambling in PD; (2) a strong class association between dopamine agonist use and all ICDs; (3) an association between levodopa use and ICDs; (4) an association between higher levodopa dosages, but not dopamine agonist dosages, and ICDs; and (5) an independent association between numerous clinical and demographic variables and ICDs.

Although initial ICD case reporting in PD focused on pathological gambling,[13] the 4 ICDs examined in this study occurred at similar frequencies, ranging from 3.5% (compulsive sexual behavior) to 5.7% (compulsive buying). Overall, the results suggest that ICDs as a group are not uncommon in PD. As some patients either did not acknowledge symptoms or had an ICD history during PD but were currently in remission, the cumulative prevalence of ICDs sometime during PD is likely higher than point prevalence reported here. In addition, this protocol did not assess the frequency of other compulsive behaviors reported to occur in this population, such as punding[14] and dopamine dysregulation syndrome,[15] which may differ from ICDs in terms of their phenomenology and association with PD medications.

More than one-fourth of ICD patients had 2 or more ICDs, which is consistent with previous case reporting that comorbid ICDs commonly occur in patients with

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PD.[16,17] This highlights the importance of inquiring about multiple ICDs when assessing patients with PD.

Although ICD frequency was similar for men and women, between-sex differences for individual ICDs existed. Men were both more (compulsive sexual behavior) and less (compulsive buying and binge eating) likely than women to have particular ICDs. These findings mirror patterns in the general population.[18-20] Gender effects may explain the relatively low overall rate of compulsive sexual behavior, given its low frequency in women in this study (0.5%).

Impulse control disorders as a group, and compulsive gambling and buying specifically, were significantly more common in US than Canadian patients, even after controlling for possible confounding variables. These findings differ from earlier non-PD studies showing no consistent between-country differences in problem/pathological gambling prevalence estimates.[21] It is possible that new environmental factors (eg, increased availability of casino gambling in the United States) or differences between PD populations in the United States and Canada contributed to the observed differences.

Consistent with previous case reporting and smaller cross-sectional studies,[2,3,6] the odds of having an individual ICD were 2 to 3.3 times higher in patients treated with dopamine agonists compared with patients not treated with them, ranging from 2.53 (compulsive buying) to 3.34 (binge-eating disorder), which is also consistent with previous case reporting and smaller cross-sectional studies.[2,3,6] Overall and individual ICD frequencies were similar for pramipexole- and ropinirole-treated patients. These results, similar to those reported previously,[2,16,17,22] suggest that dopamine agonists as a class are associated with ICDs. In this study, after controlling for levodopa exposure and other covariates, no dopamine agonist dosing effect was found, though there are reports to the contrary.[2,16] As the study was cross-sectional, a selection bias for current dopamine agonist dosage may have existed that obscured a dosing effect (eg, patients with an ICD history on higher dopamine agonist dosages may have become asymptomatic after decreasing their dopamine agonist dosage).

A possible neurobiological explanation for the association between dopamine agonist treatment and ICDs centers around dopamine-receptor binding profiles. Dopamine$_2$ (D_2) and D_1 receptors, abundant in the dorsal striatum,[23] may mediate the motor effects of dopamine-replacement therapies, whereas D_3 receptors are abundant in the ventral striatum,[23] a brain region associated with both behavioral addictions[24] and substance use disorders.[25] Second generation nonergot dopamine agonists (eg, pramipexole and ropinirole) demonstrate relative selectivity for D_3 receptors compared with D_2 and D_1 receptors.[26]

The independent association between levodopa treatment and ICDs has not been reported in previous cross-sectional studies. In patients taking a dopamine agonist, concurrent levodopa use increased the odds of an ICD by approximately 50%. In contrast to dopamine agonist treatment, higher levodopa dosages were also associated with ICDs. This observation of a significant, but less robust, association between levodopa treatment and ICDs is consistent with the dopamine-receptor binding profile of dopamine (the physiologically active metabolite of levodopa), which demonstrates greater selectivity for D_1 and D_2 receptors than the D_3 receptor compared with nonergot dopamine agonists.[26]

There were multiple demographic and clinical correlates of ICDs. Although younger patients are more likely to be treated with a dopamine agonist, the age effect remained after controlling for dopamine agonist exposure. Both younger age and being unmarried have been associated with ICDs in the general population.[18,27,28] Elevated frequencies of tobacco smoking have been reported in association with ICDs in the general population.[29] This finding, in conjunction with the association of a family history of gambling problems, is consistent with the proposition that there are shared neurobiological, genetic, or environmental contributions to the development of ICDs.[30-32] These findings, together with sex differences for individual disorders, suggest that multiple factors may contribute to ICD development in patients with PD. This may be used in clinical settings to help identify individuals at increased risk.

Use of movement disorder centers as study sites limits the generalizability of our results. In addition, the study was not designed to define the etiological risk factors of ICDs in PD, as it was not a prospective randomized study of different dopamine-replacement therapies. Given that there may be a significant lag time between initiation of dopamine-replacement therapies and onset of ICD behaviors and that PD patients frequently undergo changes in dopamine-replacement therapies over time, conducting a prospective study was not feasible and might have produced data that were difficult to interpret. Lack of inclusion of an early untreated PD group and a non-PD control group prevents comparison of prevalence estimates for ICDs in untreated and treated PD patients and the general population. Most studies of ICDs in treated PD patients that have included a matched non-PD control group or used comparative data from epidemiological studies reported cross-sectional[5,33] or cumulative[34] frequencies that were significantly higher in the PD group than in the general population. Also, structured diagnostic interviews were not used to diagnose ICDs, and the severity of ICD symptoms was not rated. Finally, because PD patients typically undergo long-term changes in treatment and we used a 6-month time frame for an ICD diagnosis, it was not possible to accurately ascertain the impact of the duration of dopamine agonist treatment or recent changes in non–dopamine agonist treatment on ICD status.

This study demonstrates that 4 clinically significant ICDs occur in PD, they are associated with dopamine replacement-therapies (both dopamine agonists and levodopa), and they have other clinical and demographic correlates that may represent risk factors. Dopamine agonists are increasingly used in clinical settings to treat disorders other than PD, and initial case reporting suggests that ICDs may occur with dopamine agonist treatment in patients with restless legs syndrome[16] and fibromyalgia.[35] Larger epidemiologic studies in these other populations are needed to examine the possible relationships between dopamine agonist treatment, other clinical features, and ICDs.

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