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Prevalence of Impulsive-Compulsive Symptoms in Elderly Parkinson's Disease Patients:
A Case-Control Study

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ABSTRACT

Background: Impulse-control disorders (ICDs) are frequently described in patients with Parkinson's disease (PD), particularly among those treated with dopaminergic medications, but data on the prevalence of ICDs in elderly populations are lacking.

Objective: The aim of this study was to estimate the prevalence of ICDs by using an Italian validation of the Questionnaire for Impulsive-Compulsive Disorders in Parkinson's Disease (QUIP) and to identify associated sociodemographic and clinical factors in a sample of elderly PD patients and in a control group of similarly aged healthy volunteers.

Methods: Using the United Kingdom Parkinson's Disease Society Brain Bank diagnostic criteria, we included 115 consecutive PD and 105 healthy controls. They were recruited from June 2014 to December 2015. All participants completed the self-administered QUIP-Anytime for assessment of ICDs occurring any time during the course of PD.

Results: Mean ± SD age was 75.7 ± 7.0 years in the PD patients and 76.1 ± 7.0 years in the control group. The mean disease duration was 6.8 years (range, 1–26 years). Among the PD patients, 44.7% (n = 51) had at least 1 ICD or related disorder compared to 25.2% (n = 26) in the control group (between-group difference: $P = .003$). Hypersexuality and compulsive shopping were significantly more common in the PD group than in the control group ($P < .05$). The prevalence of other compulsive behaviors was 42.5% in the PD group and 38.9% in the control group (P = NS). The Italian version of the QUIP-Anytime showed high test-retest reliability (κ > 0.70 for all items).

Conclusions: Our data confirm a high prevalence of ICD symptoms in elderly PD patients, approximately twice that seen in the general population.

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Parkinson's disease (PD) is a neurodegenerative disorder characterized by progressive depletion of nigrostriatal dopamine, causing abnormalities in movement, behavior, cognition, and emotion. Since 2003, dopaminergic medications, particularly dopamine agonists, have been found to be associated with the development of impulse-control disorders (ICDs) and related behaviors in patients with PD.[1,2] The *DSM-5* defines ICDs as a category of behavioral disorders characterized by recurrent maladaptive disinhibited behavior despite adverse personal and relationship consequences.[3] ICDs associated with PD include pathological gambling, hypersexuality, compulsive shopping, and binge eating, and related compulsive behaviors include punding (ie, repetitive, purposeless behaviors), hobbyism (ie, intense fascination with specific activities or hobbies such as writing, repairing or dismantling things, or computer use), and walkabout (ie, excessive, aimless wandering).[4,5]

Compulsion to excessive consumption of dopaminergic therapy, defined as dopamine dysregulation syndrome (DDS), is a distinct clinical entity that is more commonly related to levodopa therapy.[6] The reported prevalence[7,8] of ICD among adult PD patients is 14%, and association between dopamine agonists and ICD risk is well documented. According to the DOMINION study,[8] ICDs affect 17.1% of patients who are receiving dopamine agonists and 6.9% of those who are not.

Epidemiologic data on the prevalence of ICDs in the elderly population are lacking. Tamam et al[9] have reported a 17% lifetime prevalence of ICDs among individuals over 60 years of age.

The Questionnaire for Impulsive-Compulsive Disorders in Parkinson's Disease (QUIP) and the QUIP-Rating Scale (QUIP-RS) have emerged as the most widely used screening instrument and rating scale, respectively, for clinical assessment of ICD in patients with PD.[10,11] We conducted an observational, cross-sectional study to estimate the prevalence of ICD in a sample of elderly PD patients compared with a group of healthy controls

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Clinical Points

- Impulse-control disorders (ICDs) are frequently described in patients with Parkinson's disease (PD), particularly among those treated with dopaminergic medications, yet data on the prevalence of ICDs in elderly populations are lacking.
- The prevalence of ICDs is high both in PD patients and in healthy elderly individuals; however, among PD patients it is twice that in the general elderly population.
- ICDs are common in elderly populations and need close surveillance, at least equal to that used for younger patients.

and sought to identify the sociodemographic and clinical factors associated with ICD in elderly PD patients.

METHODS

Study Design

ICD prevalence and clinical patterns were assessed in a sample of elderly PD patients and compared with those in a control group of healthy volunteers. We used the current World Health Organization (WHO) definition of elderly (≥ 65 years of age), although there has been debate about using this age as a cutoff.[12]

All study participants self-completed the QUIP-Anytime for ICD symptoms occurring any time during the course of PD.

Study Sample

All PD patients were recruited from June 2014 to January 2016 among those attending the outpatient Geriatric Day Hospital and Movement Disorder Clinic of the Catholic University Hospital in Rome, Italy. The age-matched healthy volunteers were recruited among subjects attending the fitness center for elderly people at the same hospital.

PD patients were enrolled if all of the following inclusion criteria were fulfilled: (*a*) diagnosis of PD according to United Kingdom Brain Bank criteria,[13] (*b*) stable dopaminergic treatment for at least 1 month prior to study enrollment, (*c*) Mini-Mental State Examination (MMSE)[14] score > 24/30, (*d*) age ≥ 65 years, and (*e*) signed informed consent.

The inclusion criteria for the control group were as follows: (*a*) clinical exclusion of parkinsonism, (*b*) MMSE score > 24/30, (*c*) age ≥ 65 years, and (*d*) signed informed consent. For PD patients and the control group, exclusion criteria were any psychiatric problems other than substance use disorders and depression.

The study protocol was reviewed and approved by the Ethics Committee of the Catholic University, Fondazione Policlinico Universitario A. Gemelli, Rome. The study was carried out in agreement with legal requirements and international norms (Declaration of Helsinki, 1964).

Study Procedures

The following data were recorded for all study participants: age, sex, education level, marital status, living situation, smoking history, abilities in activities of daily living as assessed by the Activities of Daily Living (ADL) and Instrumental Activities of Daily Living (IADL) scales,[15] cognitive abilities according to the MMSE, depression severity according to the 15-item Geriatric Depression Scale (GDS-15) with a cutoff score of 5 for clinically significant depressive symptoms,[16] and clinical characteristics including age at PD onset and disease duration, comorbid medical conditions, and concomitant medications.

Clinical characteristics of PD were assessed by the Unified Parkinson's Disease Rating Scale (UPDRS)[17] and Hoehn and Yahr Staging Scale[18] during the "on" state, and the levodopa equivalent daily dose (LEDD, mg) was calculated according to the published conversion factors for individual antiparkinsonian drugs.[19] The LEDD is defined as the levodopa equivalent dose of a drug that produces the same symptomatic relief as 100 mg of immediate-release levodopa (combined with a dopa decarboxylase inhibitor).

Linguistic Validation of the Questionnaire

The QUIP was developed and validated to detect the presence of clinically significant ICD, DDS, and other compulsive behaviors (punding, hobbyism, and walkabout).[10] The QUIP consists of 3 sections: section 1 assesses 4 primary ICDs (gambling, sexual, buying, and eating behaviors); section 2 queries other compulsive behaviors (punding, hobbyism, and walkabout); and section 3 examines compulsive medication use.[20] The linguistic validation of the Italian version of the QUIP-Anytime was performed for the purpose of this study.

The linguistic validation process included the following steps: (1) 2 forward translations of the English QUIP-Anytime into Italian were produced by 2 independent professional translators who are native Italian speakers; (2) a preliminary combined version (reconciled version) was produced by consensus among the translators and the study investigators; (3) a backward translation of the reconciled Italian version was produced by a professional translator (native English speaker) who had no access to the original version of the instrument; and (4) the backward translation and the original English version were compared, mistranslations and inaccuracies were noted, and the preliminary Italian version was revised accordingly in a consensus meeting between the backward translator and the investigators. The test-retest reliability of the final Italian version of the QUIP-Anytime was then assessed in a separate sample (n = 20) of PD patients who completed the survey twice with a mean time between tests of 15 days (range, 7 to 30 days).

Statistical Analyses

Descriptive statistics were used to report on the sociodemographic and clinical characteristics of the study participants. The prevalence of ICD symptoms in each group was estimated. Descriptive statistics included mean and standard deviation to summarize continuous variables

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Table 1. Main Characteristics of Participants According to the Presence or Absence of Parkinson's Disease (PD)[a]

Characteristic	PD Patients (n = 115)	Controls (n = 105)	*P* Value[b]
Age, mean ± SD, y	75.7 ± 7.0	76.1 ± 7.0	.6000
Age at PD onset, y			
Mean ± SD	67.8 ± 8.3	…	
IQR	(43–83)	…	
Male	73 (63.5)	42 (40.0)	**.0005**
Disease duration, median (IQR), mo	68 (43–83)	…	
Marital status			.3774
Married	90 (78.3)	72 (68.6)	
Single	4 (3.5)	7 (6.7)	
Divorced	4 (3.5)	4 (3.8)	
Widower/widow	17 (14.7)	22 (21.0)	
Living alone	9 (7.8)	8 (7.6)	.9815
Education[c]			.0545
None	3 (2.6)	8 (7.6)	
Primary school	16 (13.9)	24 (22.8)	
Middle school	29 (25.2)	17 (16.2)	
Secondary school	33 (28.7)	36 (34.3)	
Degree	33 (28.7)	19 (18.1)	
Smoking			.1941
Never smoker	82 (71.3)	85 (80.9)	
Smoker	10 (8.7)	8 (7.6)	
Ex-smoker	23 (20.0)	12 (11.4)	
Mini-Mental State Examination score, mean ± SD	26.7 ± 2.0	27.6 ± 2.0	**.0031**
Activities of Daily Living score, mean ± SD	4 ± 2	5 ± 1	**< .0001**
Instrumental Activities of Daily Living score, mean ± SD	5 ± 2	7 ± 1	**< .0001**
UPDRS-III score, median (IQR)	20 (12–30)	…	
Depression	59 (51.3)	29 (27.6)	**.0005**
No. of diseases, median (IQR)	2 (1–3)	3 (2–5)	**.0047**
No. of drugs, median (IQR)	5 (4–7)	4 (2–6)	**.0088**
Drugs			
Antidepressants	20 (17.4)	8 (7.6)	**.0298**
Benzodiazepines	18 (15.7)	5 (4.8)	**.0128**
Antipsychotics	2 (1.7)	1 (1.0)	.5666
Anticholinergics	9 (7.8)	0	**.0039**
Dopamine agonists	49 (42.6)	0	**< .0001**
Dopamine agonists in monotherapy	10 (8.7)	0	**< .0001**
Levodopa	97 (84.3)	0	**< .0001**
Levodopa + dopamine agonists	34 (29.6)	0	**< .0001**
Levodopa in monotherapy	52 (45.2)	0	**< .0001**
Total levodopa equivalent daily dose, median (IQR), mg	350 (59–700)	0	**< .0001**
Impulse-control disorders	51 (44.3)	26 (24.8)	**.0031**
Other compulsive behaviors	49 (42.6)	41 (39.0)	.6059
Additional dopaminergic medication usage	6 (5.2)	0	.0670

[a]Values are shown as n (%) unless otherwise noted.
[b]*P* value was calculated by means of *t* test and χ^2 test, respectively, for continuous and categorical data. Significance (values shown in boldface) was set as $P < .05$.
[c]Data missing for 1 PD patient.
Abbreviations: IQR = interquartile range, UPDRS-III = part III of the Unified Parkinson's Disease Rating Scale.

and proportions for categorical variables. PD patients and controls were compared with respect to sociodemographic and clinical characteristics, as were PD patients with and without ICDs.

Normally distributed continuous variables were compared using the Student *t* test for independent samples, while the nonparametric Mann-Whitney *U* test was used to compare variables with abnormal distribution, as detected by the Kolmogorov-Smirnov test. Categorical variables were compared using the χ^2 test. The Cohen κ was calculated to assess the test-retest reliability of the Italian version of the QUIP-Anytime. A *P* value < .05 was chosen to define statistical significance. All analyses were conducted with SAS version 8.2 (SAS Institute Inc., Cary, North Carolina).[21]

RESULTS

The study included a total of 220 participants: 115 PD patients (63.5% male; mean age = 75.7 years [range, 65–94 years]; mean duration of disease = 6.8 years [range, 1–26 years]) and 105 healthy controls (60.9% male; mean age = 76.1 years [range, 37–90 years]). Clinical and sociodemographic data of the study population are depicted in Table 1. Compared to the members of the control group, PD patients had a higher level of education (see Table 1; $P = .05$), higher frequency of depressive symptoms (50.9% vs 27.4%, $P < .05$), greater mean ± SD impairment in ADLs (score = 4.5 ± 1.7 vs 5.4 ± 0.9, $P < .05$) and IADLs (score = 5.2 ± 2.3 vs 6.8 ± 1.7, $P < .05$), a higher number of prescribed medications (5.2 ± 2.2 vs 4.0 ± 3.8, $P < .05$), and a higher prevalence of psychotropic

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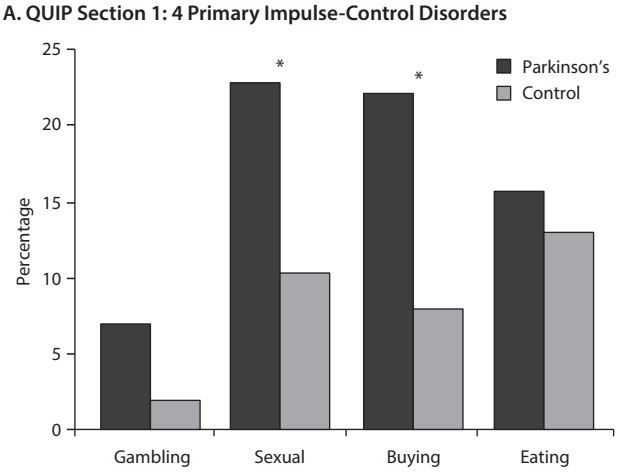
Figure 1. Prevalence of Individual Impulse-Control Disorders Among Patients With Parkinson's Disease and Healthy Controls[a]



[a]Presence of individual impulse-control disorders was assessed with the Questionnaire for Impulsive-Compulsive Disorders in Parkinson's Disease for impulse-control disorder symptoms occurring anytime during the course of Parkinson's disease (QUIP-Anytime).
*$P < .05$.

drug use, including antidepressants (17.4% vs 7.6%, $P = .03$) and benzodiazepines (15.7% vs 5.0%, $P < .05$). Levodopa was the most frequently prescribed anti-PD medication (84.3%), with 45.2% of patients receiving levodopa in monotherapy.

According to the QUIP-Anytime, 44.7% of the PD patients and 25.2% of the healthy controls had an ICD ($P < .05$). Among the individual ICDs, hypersexuality and compulsive shopping were significantly more common in PD patients than in the control group (Figure 1). The prevalence of other compulsive behaviors was 42.5% in PD patients and 38.9% in the control group; this difference was not significant.

Among PD patients only (Table 2), those with ICDs were slightly younger than those without ICDs (mean age = 74.5 vs 76.6 years, $P = .05$) and had fewer comorbid medical conditions (median = 2 vs 3, $P = .01$), lower UPDRS part III (UPDRS-III) scores (24.5 vs 26, P = NS), a higher prevalence of other compulsive behaviors (60.0% vs 28.6%, $P < .05$) and compulsive medication use (8.0% vs 3.2%, P = NS), and numerically higher use of antidepressants (23.5% vs 12.7%, P = NS), benzodiazepines (20.8% vs 11.1%, P = NS), and dopamine agonists (52.1% vs 35.2%, $P = .08$). Patients with no ICDs were more likely to receive levodopa, in combination or as monotherapy, and median LEDD values were similar between the 2 groups (460 vs 450 mg/d, P = NS).

A significantly higher number of PD patients with other compulsive behaviors (Table 3) lived alone, and PD patients were more likely to take levodopa in combination with dopamine agonists compared to PD patients without compulsive behaviors (39.6% vs 23.1%, $P = .0586$). PD patients with other compulsive behaviors had similar median LEDD (450 vs 450 mg/d, P = NS) and median UPDRS-III score (25.5 vs 25, P = NS).

As a secondary result, the Italian version of the QUIP-Anytime showed high test-retest reliability ($\kappa > 0.70$ for all items).

DISCUSSION

Our data confirm a relevant prevalence of ICD symptoms in both PD and healthy elderly subjects. In particular, the prevalence of ICD symptoms among PD patients was approximately 2-fold higher than the prevalence in the general population.

ICDs, initially reported in sporadic cases of PD,[1,6] have been systematically investigated in PD patients since 2005, and they are now widely recognized as a side effect of dopaminergic treatment.[8,22]

The evidence from early epidemiologic studies showed a marked variability in ICD prevalence, albeit with some well-established evidence for risk factors or correlates including young age at onset, disease severity, male sex, sleep disorders, novelty-seeking personality trait, and treatment with dopamine agonists.[23]

Less consistent correlations have been observed when assessing ICDs and drug treatment, including lifetime dopaminergic load, current dose of dopamine agonist, prevention and treatment efforts, and neuropsychological factors such as the loss of ability to inhibit automatic reaction when needed. ICD may occur in childhood (at 11 years of age according to Dell'Osso et al[24]) and has an estimated lifetime prevalence of 24.8% in the general population.[8]

At present, scant data are available on the prevalence of ICD in the general elderly population. A study of 200 Turkish elderly individuals in a rural area indicated that 20% had an ICD.[9] To our best knowledge, there are no data on ICDs that are specific to elderly PD patients. Old age has been regarded as a deterrent to ICD, but, in contrast to this assumption, our results indicate a prevalence of ICD of 25.2% in a geriatric population and of 44.7% in PD patients.

In our series, dopamine agonist treatment was associated with ICD behaviors in 52% of participants. This finding was confirmed for dopamine agonists taken both alone and in combination with levodopa and is in agreement with previous studies.[2]

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Table 2. Main Characteristics of Parkinson's Disease Patients According to the Presence of Impulse Control Disorders (ICDs)[a]

Characteristic	Patients With ICDs (n = 51)	Patients Without ICDs (n = 64)	*P* Value[b]
Age, mean ± SD, y	74.5 ± 5.1	76.6 ± 6.1	.0548
Male	35 (68.6)	38 (59.4)	.3579
Marital status			.7648
Married	42 (82.3)	48 (75.0)	
Single	1 (2.0)	3 (4.7)	
Divorced	2 (3.9)	2 (3.1)	
Widower/widow	6 (11.8)	11 (17.2)	
Living alone	3 (5.9)	6 (9.4)	.0744
Education[c]			.8143
None	1 (2.0)	2 (3.1)	
Primary school	9 (17.6)	7 (10.9)	
Middle school	13 (25.5)	16 (25.0)	
Secondary school	13 (25.5)	20 (31.3)	
Degree	14 (27.4)	19 (29.7)	
Smoking			.9416
Never smoker	36 (70.6)	46 (71.9)	
Smoker	4 (7.8)	6 (9.4)	
Ex-smoker	11 (21.6)	12 (18.8)	
Mini-Mental State Examination score, mean ± SD	26.1 ± 2.1	26.1 ± 1.9	.7775
Activities of Daily Living score, mean ± SD	5 ± 1	4 ± 2	.2097
Instrumental Activities of Daily Living score, mean ± SD	5 ± 2	5 ± 3	.4461
UPDRS-III score, median (IQR)	24.5 (17–33)	26 (15–33)	.1610
Depression	27 (52.9)	32 (50.0)	.9020
No. of diseases, median (IQR)	2 (1–3)	3 (2–4)	**.0143**
No. of drugs, median (IQR)	5 (3–7)	5 (4–7)	.3168
Drugs			
Antidepressants	12 (23.5)	8 (12.5)	.1306
Benzodiazepines	11 (21.5)	7 (10.9)	.1778
Antipsychotics	1 (2.0)	1 (1.6)	.9436
Anticholinergics	4 (7.8)	5 (7.8)	.8814
Dopamine agonists	27 (52.9)	22 (34.4)	.0854
Dopamine agonists in monotherapy	6 (11.8)	4 (6.3)	.3386
Levodopa	40 (78.4)	57 (89.0)	.1778
Levodopa in monotherapy	19 (37.2)	33 (51.6)	.1069
Levodopa + dopamine agonists	19 (37.2)	15 (23.4)	.1504
Total levodopa equivalent daily dose, median (IQR), mg	460 (300–779)	450 (300–757)	.3630
Compulsive behaviors	31 (60.8)	18/ (28.1)	**.0008**
Additional dopaminergic medication usage	4 (7.8)	2/ (3.1)	.2559

[a]Values are shown as n (%) unless otherwise noted.
[b]*P* value was calculated by means of *t* test and χ^2 test, respectively, for continuous and categorical data. Significance (values shown in boldface) was set as $P < .05$.
[c]Data missing for 1 patient with an ICD.
Abbreviations: IQR = interquartile range, UPDRS-III = part III of the Unified Parkinson's Disease Rating Scale.

The relevant prevalence of ICDs reported in this study, both in PD and in healthy subjects, should be interpreted in light of 3 major considerations. First, ICDs were detected using the QUIP, which is a screening tool; no further standard diagnostic interview for ICD identification was used. Therefore, a possibility of an overestimation of ICD prevalence cannot be disregarded. Furthermore, approximately 40% of patients without diagnosis of ICDs had a QUIP-Anytime score that showed positive for ICD, suggesting that many PD patients may experience subsyndromal ICD symptoms that require ongoing monitoring.[25] Second, the presence of subsyndromal depression or mild cognitive impairment might contribute to impulsive and compulsive symptoms, although fairly cognitively impaired patients were excluded from the study. Finally, increased impulsivity in the elderly compared to younger individuals may also reflect age-related functional alterations in the neural mechanisms underlying decision-making ability and reward circuits. Individuals undergoing cognitive examination such as the Iowa gambling test showed normal activation of cortical and striatal circuits related to the anticipation of social or monetary rewards while exhibiting a deficit in the mechanisms of anticipation of losses.[26]

Moreover, the ability of getting new information (ie, learning) about losses and gains is reduced in older age, especially when this knowledge is fluid or unrelated to past experience. These age-related changes in decision-making processes could be explained at least in part by the depletion of monoamines, in particular dopamine, serotonin, and norepinephrine, that has been observed in the aging brain.

It must be acknowledged that our results are difficult to compare with data from younger populations. As a matter of fact, dopamine agonists may not be an option for most elderly PD patients, who, unlike younger PD patients, are often treated only with levodopa. In line with previous observations in younger PD patients, we documented the association of ICDs with male sex and depressive symptoms,

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Table 3. Main Characteristics of Parkinson's Disease Patients According to the Presence of Other Compulsive Behaviors (CBs)[a]

Characteristic	Patients With CBs (n = 49)	Patients Without CBs (n = 66)	*P* Value[b]
Age, mean ± SD, y	75.6 ± 6.2	75.8 ± 5.5	.8746
Male	30 (61.2)	43 (65.2)	.5307
Marital status			.4921
Married	40 (81.6)	49 (74.2)	
Single	2 (4.1)	2 (3.0)	
Divorced	1 (2.0)	3 (4.5)	
Widower/widow	6 (12.2)	11 (16.6)	
Living alone	1 (2.0)	8 (12.1)	**.0286**
Education[c]			.8201
None	1 (2.0)	2 (3.0)	
Primary school	9 (18.4)	7 (10.6)	
Middle school	12 (24.5)	17 (25.7)	
Secondary school	13 (26.5)	21 (31.8)	
Degree	13 (26.5)	19 (28.7)	
Smoking			.1391
Never smoker	37 (75.5)	45 (68.2)	
Smoker	2 (4.1)	8 (12.1)	
Ex-smoker	10 (20.4)	13 (19.7)	
Mini-Mental State Examination score, mean ± SD	26.4 ± 2.1	26.9 ± 1.9	.2600
Activities of Daily Living score, mean ± SD	4 ± 2	5 ± 1	.4306
Instrumental Activities of Daily Living score, mean ± SD	5 ± 2	5 ± 3	.3951
UPDRS-III score, median (IQR)	25.5 (17–38)	25 (19–28)	.4206
Depression	27 (55.1)	32 (48.5)	.4059
No. of diseases, median (IQR)	2 (1–4)	2 (2–4)	.1549
No. of drugs, median (IQR)	5 (3–7)	5 (4–7)	.2772
Drugs			
Antidepressants	11 (22.4)	9 (13.6)	.2117
Benzodiazepines	10 (20.4)	8 (12.1)	.2646
Antipsychotics	1 (2.0)	1 (1.5)	.8399
Anticholinergics	4 (8.2)	5 (7.5)	.7158
Dopamine agonists	25 (51.0)	24 (36.4)	.1210
Dopamine agonists in monotherapy	4 (8.2)	6 (9.1)	.8681
Levodopa	41 (83.7)	55 (83.3)	.5938
Levodopa in monotherapy	20 (40.8)	32 (48.5)	.3083
Levodopa + dopamine agonists	19 (38.7)	15 (22.7)	.0586
Total levodopa equivalent daily dose, median (IQR), mg	450 (300–700)	450 (300–800)	.4789

[a]Values are shown as n (%) unless otherwise noted.
[b]*P* value was calculated by means of *t* test and χ^2 test, respectively, for continuous and categorical data. Significance (values shown in boldface) was set as $P < .05$.
[c]Data missing for 1 patient with CBs.
Abbreviations: IQR = interquartile range, UPDRS-III = part III of the Unified Parkinson's Disease Rating Scale.

although we did not observe the significant role of smoking status that has been reported in other studies.[4,8,23] The degree of functional impairment among our ICD patients was also lower than has been previously reported.[27] It might be hypothesized that older people with better physical status have greater capability to act out their ICDs.

In the largest observational study on ICD to date,[8] the prevalence of ICD as determined by the QUIP was 13.6%. Other studies,[4] using different assessment tools and study designs have reported prevalence rates ranging from 8.1% to 13.6%, and the prevalence reached 35.9% by QUIP-Anytime in a Danish population of 490 PD patients and was 14.9% by QUIP-Current in the same group.[28]

These variations can be related to the combination of disease course, psychiatric comorbidities, and environment.[23] In a recent Indian study,[29] the QUIP was administered to 299 PD patients, and the point prevalence of ICD and ICD-related behaviors was 42.8%, with 24.8% exhibiting at least 1 ICD.

Regarding the association between depressive symptoms and ICDs, the prevalence of depression is 5% to 10% among older members of the general population.[30] Depression in the elderly may manifest with nonspecific symptoms including lack of appetite, fatigue, and sleep disturbances,[26] and, according to Blanchard et al,[31] it is almost invariably associated with anxiety disorders (95%). ICD may be a component of this distinctive phenomenology.

Aging is also associated with a progressive and substantial reduction, 5% to 10% per decade on average, of specific binding of dopamine to D_1 and D_2 receptors in the nigrostriatal, mesolimbic, and mesocortical systems.[32–35] This imbalance among the dopaminergic pathways has been examined by analyses of brain connectivity at both the structural and the functional levels that have detected a progressive segregation and isolation among the 3 systems that might further explain the cognitive and behavioral changes in the aging brain.[34]

The information gleaned about dopaminergic therapy, particularly dopamine agonist therapy alone or in combination with levodopa, is consistent with several studies.[2,7] The expression of dopamine D_1 and D_2 receptors is largely segregated in direct (D_1) and indirect (D_2) pathway

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neurons in the dorsal striatum.[32] Both D_1 and D_2 receptors mediate the motor effects of dopaminergic therapy. The D_3 receptors are preferentially expressed in the ventral striatum[33] and are linked to compulsive seeking behaviors and substance abuse. The second-generation, nonergot dopamine agonists bind selectively to the D_3 receptor.[34]

According to recent hypotheses, ICDs may present in the early stages of PD because of the reduction of dopamine in the dorsal striatum. The ventral striatum is less affected. Thus, dopaminergic therapy restores homeostasis at the level of the dorsal striatum while at the same time inducing an "overdose" at the level of the ventral striatum that can potentially favor the occurrence of mood disorders and ICDs. Accordingly, ICDs have also been described in patients who are treated with dopamine agonists for restless legs syndrome or fibromyalgia.

Study Limitations

The study population is relatively small, and future research in larger populations will be required to confirm our findings. In addition, completing the QUIP may be a challenging task for older PD patients in terms of both the length of the questionnaire (30 questions, each with 2 response options) and the possible overestimation of some behavioral disorders, as has been suggested previously.[5] Finally, the correlation of ICDs and depression must be considered carefully, as no structured diagnostic interview was used to confirm the diagnosis of depression according to *DSM* criteria.

CONCLUSIONS

Although several epidemiologic studies have investigated ICDs in the last decade, there is a paucity of data about the incidence and prevalence of ICDs in elderly populations. Previous data have suggested reductions in impulsivity with aging, but we found a high prevalence of ICDs in our healthy geriatric population, with approximately 1 in 4 participants reporting an ICD.[9]

Our study further indicates that the prevalence of ICDs among elderly PD patients is significantly higher than in the general elderly population. The estimated prevalence of ICDs is higher in our study than in previous studies,[2,8] but the distribution and associated factors are similar.

Chronic exposure to dopaminergic therapy in association with dysregulation of the nigrostriatal, mesolimbic, and mesocortical dopaminergic pathways and loss of inhibitory control over motor function and behavior that can accompany aging clearly lend support to this finding.

Further studies are needed to confirm these data and to evaluate their clinical relevance in geriatric populations and older PD patients, with integration of these data with psychiatric and cognitive assessment of impulsivity trait, inhibitory control, mood disorders, and apathy.

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