RESEARCH ARTICLE

Impulsivity and Compulsivity in Drug-Naïve Patients with Parkinson's Disease

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ABSTRACT:

Background: Abnormal repetitive behaviors have been reported in Parkinson's disease (PD) during dopamine replacement therapy (DRT) and associated with individual predisposing features, including impulsivity. However, impulsivity and compulsive symptoms have never been explored in PD patients before initiation of DRT. We previously reported a 20% of impulse control disorders (ICD) in an Italian cohort.

Methods: 103 consecutive newly diagnosed drug-naïve PD patients (means: age = 60.5 ± 9.2 years; duration = 15.4 ± 15.3 months) were screened for compulsive sexual behavior, compulsive buying, intermittent explosive disorder (Minnesota Impulsive Disorders Interview, MIDI), and pathological gambling (South Oaks Gambling Screen, SOGS). Barratt Impulsiveness Scale (BIS-11) and Maudsley Obsessional-Compulsive Questionnaire (MOCQ/R) assessed impulsivity, obsessive-compulsive symptoms, respectively. Depression (GDS-15) and general cognitive status were additionally assessed. We also compared ICDs frequency with our healthy controls.

Results: 17.5% of PD patients screened positive for at least one ICD at MIDI (17/103) and SOGS (1/103), though none had a disorder based on DSM-IV criteria. These frequencies were similar to healthy controls. There was a trend toward higher scores in BIS-11 attentive-impulsivity subscale (15.2 ± 4.8 vs. 18.7 ± 4.9; $P = 0.007$) and in MOCQ/R-Doubting subscale (0.67 ± 1.1 vs. 1.5 ± 1.2; $P = 0.007$) in PD with ICD. We also observed a positive correlation between GDS-15 and BIS-11.

Conclusions: Similar to our healthy control population, we found a significant proportion of early PD patients positive for ICDs before starting treatment. We also found a relationship between impulsivity and depression. A detailed behavioral assessment before starting dopaminergic therapy is recommended.

Key Words: Parkinson's disease; drug naïve; impulse control disorders; impulsivity; compulsivity

A range of impulse control disorders (ICDs) and compulsive behaviors have been reported in clinical practice and became relevant in the management of Parkinson's disease (PD). However, the relationship between dopamine replacement therapy (DRT), underlying individual predisposing factors and the occurrence of behavioral disturbances is still debated.[1]

Though some authors reported that high doses of dopaminergic medications were associated with increased risk to develop ICDs,[2,3] recent findings

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suggest that ICDs may occur even in patients on standard daily dosage of medications underlining the prominent role of individual predisposing factors.[1,4,5] So far, personality traits such as high novelty seeking[1] and impulsivity[5] have been associated to the occurrence of ICDs in PD.

We recently reported in a large survey that 28% of PD subjects on DRT versus 20% of healthy controls had at least one ICD at the Minnesota Impulsive Disorder Inteview (MIDI) or a pathological score at the South Oaks Gambling Scale (SOGS) while PD had an overall higher impulsivity score at Barratt Impulsiveness Scale (BIS) than controls.[5] More recently, a cross-sectional study in over 3,000 PD patients showed a prevalence of ICDs of 14%.[6] It has thus been speculated that DRT might trigger ICDs in individuals with specific impulsivity traits.[5] However, currently available data about ICDs regards only PD patients undergoing DRT while the prevalence of impulsivity and compulsive behaviors in de novo PD has never been assessed so far.[1,3,5] The aim of the present multicenter study was to investigate behavioral features in a large cohort of consecutive PD patients before starting dopaminergic therapy.

Patients and Methods

One hundred and three consecutive newly diagnosed PD patients (mean age = 60.5 ± 9.2 years, range 36–79; mean disease duration = 15 ± 15 months, range 1–72) were screened for impulsive and compulsive behaviors, cognitive status and depression, before the initiation of any anti-parkinsonian therapy. Patients were enrolled in four Italian movement disorders tertiary clinics from October 2007 to January 2009.

In details, we assessed compulsive sexual behavior, compulsive buying, and intermittent explosive disorders using the Minnesota Impulsive Disorders Interview (MIDI)[7]; pathological gambling was screened using the South Oaks Gambling Screen (SOGS),[8] impulsivity using the validated Italian version of the Barratt Impulsiveness Scale (BIS-11),[9] obsessive-compulsive symptoms with the reduced form of the Maudsley Obsessional-Compulsive questionnaire, Italian version (MOCQ-R),[10] and depression with the Geriatric Depression Scale 15 items (GDS-15).[11] General cognitive status was assessed using the Mini Mental State Examination (MMSE),[12] and the validated Italian version of the Frontal Assessment Battery (FAB).[13] Corrections by age and education were applied to MMSE and FAB scores.

All subjects were clinically interviewed by trained neuropsychologists with clinical expertise in ICDs (C.S., G.S., M.P., A.C.), and DSM-IV-TR criteria for the diagnosis of ICDs and ICDs NOS were additionally applied.[14]

The MIDI is a scale that is largely used to screen for pathological gambling, trichotillomania, kleptomania, pyromania, intermittent explosive disorder, compulsive buying, and compulsive sexual behavior. It evaluates these disorders beginning with a general question, which, if answered affirmatively, allows the interviewer to ask a series of questions mirroring DSM criteria for ICDs.[3,6,15,16] ICDs were defined positive in the presence of problem/pathological SOGS (cut-off score >3) or answering affirmatively at the MIDI scale to one gateway question plus an affirmative answer to one or more of the remaining questions.[3,5]

The BIS-11 is a commonly used scale to assess three different dimensions of impulsiveness, such as motor impulsiveness, non-planning, and attentional impulsiveness.[17] For comparison, we used age-matched normative values (n = 40; M:F = 19:21; mean age = 56.5 ± 4.7 years, range 51–68) obtained from a large sample of healthy subjects used to validate the Italian version of the BIS-11 (n = 1856, mean age 25.7 ± 7.6 years, range 15–68).[9] These values were as follows: total score 67.8 ± 8.6 (range 48–84); attention factor = 25.5 ± 4.1 (range 17–34); motor factor = 22.2 ± 4.15 (range 16–31); non-planning factor = 28.3 ± 4.3 (range 19–38); the attention factor of the BIS-11 was the only one correlated with age (Pearson's coefficient $r = 0.282$. The Pearson's coefficient ranges from −0.03 to 0.08 in the other subscales). Cut off scores for MOCQ/R were obtained from the CBA manual[18] which indicates as pathological scores equal to or greater than 95° percentile (for both genders: ≥13 for the total score, ≥8 checking scale, ≥6 cleaning scale, ≥3 doubting scale).

Inclusion criteria for PD patients were diagnosis of idiopathic PD (according to UK Brain Bank Criteria). We did not include patients who had clinical features consistent with diagnosis of primary atypical parkinsonism, such as multiple system atrophy, progressive supranuclear palsy and corticobasal degeneration[19] and those with diagnosis of dementia according to DSM-IV criteria. Magnetic resonance imaging exclusion criteria were imaging signs suggestive of atypical parkinsonism, normal pressure hydrocephalus, moderate-to-severe vascular abnormalities, and tumors. None of them had ever been treated with antiparkinsonian drugs.

In all subjects, we recorded gender, age, years of education, disease duration (months from the onset of first motor symptoms), side of symptoms onset, and family history of PD. Severity of motor symptoms was measured by means of the activity-of-daily-living and motor subscales of the Unified Parkinson's Disease Rating Scale (UPDRS Part II and III, respectively)[20] and staging was assessed by the Hoehn and Yahr (HY) scale.[21] In all subjects, the UPDRS III scores were recorded in the morning.

Informed consent was obtained from all subjects according to the Declaration of Helsinki. The Hospital Ethic Committee approved the study and all PD patients provided written informed consent.

Furthermore, we considered data from a group of 100 healthy subjects evaluated with MIDI and SOGS described elsewhere[5] to compare ICDs frequencies.

TABLE 1. Demographic, clinical, and general cognitive features of PD patients with and without impulse control disorders

Features	Total patients (n = 103)	ICD positive (n = 18)	ICD negative (n = 85)	*P* value
Men, n (%)	67 (65%)	15 (83%)	52 (61%)	0.06
Age	60.5 (9.2)	58.3 (9.7)	60.9 (9.1)	0.40
Education	11.5 (4.6)	13.4 (4.7)	11.1 (4.5)	0.06
Disease duration (mm)	15.4 (15.3)	19.3 (16.5)	14.6 (15.0)	0.25
UPDRS II	6.9 (4.1)	7.1 (3.5)	6.9 (4.4)	0.89
UPDRS III	16.4 (8.7)	16.5 (8.1)	16.4 (8.9)	0.95
H&Y stage	1.5 (0.5)	1.4 (0.5)	1.6 (0.5)	0.14
MMSEc	28 (1.9)	27.4 (1.5)	28.3 (1.9)	0.07
FABc	15.6 (2.1)	15.2 (2.1)	15.7 (2.1)	0.36
GDS-15	4.4 (3.5)	5 (4)	4.3 (3.5)	0.50

Values are given as mean (SD).
P values between ICD positive versus negative are calculated using 2-tailed *t*-test, while men prevalence using Chi-square test.
MMSEc, mini mental state examination corrected score; FABc, frontal assessment battery corrected score.

Data Analysis

We compared ICD positive and negative PD. Moreover, we compared PD patients with a cohort of historical healthy controls (HC).

Testing scores and normally distributed variables were compared by means of *t*-test. Correlations were assessed by means of Spearman's correlation test. Frequencies were compared by means of $\chi 2$ test or Fisher's Exact Test, as appropriate with respect to the frequency of events.

Statistical Analysis was carried out using SPSS for Windows Release 10.0 (SPSS, Chicago, IL). Results are reported with significance set at $P < 0.006$ with Bonferroni correction for multiple comparisons. Results with $P < 0.05$ but not reaching significance level are reported as trends.

Results

Demographic and clinical features of PD patients have been detailed in Table 1. Using the screening scales eighteen PD subjects (17.5%) resulted positive for at least one abnormal behavior at the MIDI (17 patients) or SOGS (1 patient), with compulsive buying and compulsive sexual behavior most commonly recorded (10.7%). The remaining subjects were classified as ICDs negative (n = 85). However by means of clinical interview based on DSM-IV criteria, none of the patients had a clinically significant disorder.

Differences in gender did not reach significance ($P = 0.06$).

Intermittent explosive disorder showed a trend for higher frequency in men (8/67 vs. 0/36, $P = 0.03$). Three PD subjects were positive at more than one ICD, and none of ICDs was more prevalent than the others, with PG as the least frequent (Table 2).

The two PD groups had similar age, age at onset and disease severity, according to UPDRS scores and H&Y stage; groups did not show any difference in other clinical features such as side of onset and onset symptoms (tremor or rigidity). As shown by *t*-test analysis, no difference was found also in the global cognitive performance, frontal-lobe functions, and depression, according to the MMSE, FAB, and GDS-15 scores, respectively. In detail, after applying correction for age and education, MMSE was found within the range of normal values (established cut-off = 24) in all PD patients but one (MMSEc score 23.7; ICD negative group), while FABc scores below the established cut-off (13.4) was recorded in sixteen patients (mean score 12.2 ± 1.3; 20% in ICD negative group vs. 11% in ICD positive group). Mild to moderate depression (GDS-15 score 6–10) was found in 25 PD subjects (24%), and severe depression (GDS-15 > 10) was reported in 6 PD (6%), equally distributed in the two subgroups.

We found a positive significant correlation between GDS-15 scores and BIS 11 total score ($r = 0.27$; $P = 0.005$) and a trend toward significance for the correlation between GDS-15 and lack of planning subscale ($r = 0.28$; $P = 0.01$). When considering the two subgroups, the same trend between GDS-15 and BIS 11 total score was found (ICD positive $r = 0.48$ $P = 0.04$; ICD negative $r = 0.28$; $P = 0.03$).

TABLE 2. Number (%) of PD patients with ICDs and domain distribution

ICDs scales	N total
SOGS	1 (0.9%)
MIDI tot	17 (17.5%)
Compulsive buying	11 (11%)
Compulsive sexual behavior	11 (11%)
Intermittent explosive disorder	8 (7%)

MIDI, minnesota impulsive disorders interview; SOGS, South Oaks gambling screen: pathological gambling.

TABLE 3. Mean scores of behavioral and psychiatric screening scales of PD patients with and without impulse control disorders

Scales	Total patients (n = 103)	ICD positive (n = 18)	ICD negative (n = 85)	*P* value*
BIS-11 total	63.7 (9.5)	65.6 (12.4)	63.3 (8.8)	0.34
Attention	15,8 (5.0)	18.7 (4.9)	15.2 (4.8)	0.007
Motor	25.0 (4.7)	25.4 (5.9)	24.9 (4.4)	0.69
Lack of planning	26.1 (4.8)	28.1 (4.6)	25.7 (4.8)	0.14
MOCQ/R total	4.7 (3.4)	6.3 (3.6)	4.4 (3.3)	0.03
Checking	2.2 (2.2)	2.9 (2.4)	2.1 (2.1)	0.12
Cleaning	2.0 (1.5)	2.3 (1.4)	1.9 (1.4)	0.31
Doubting	0.8 (1.1)	1.5 (1.2)	0.7 (1.1)	0.007
SOGS	0.2 (0.7)	0.50 (1.5)	0.16 (0.7)	0.04

Values are given as mean (SD).
*P values after Bonferroni correction are set at $P > 0.006$. None of the comparisons reaches significance.

Overall PD patients showed mean BIS-11 total scores of 63.7 ± 9.5 (range 45–91), below the normative mean values in the age-matched healthy population (67.8 ± 8.6, range 48–84). The "attentional" factor was the one showing the larger difference between the two groups (PD = 15.8 ± 5.2, range 8–30 vs. normative values 25.5 ± 4.1, range 17–34). In the whole PD sample, the MOCQ/R scores were within the normal range either in the total score or in any of the subscales (4.7 ± 3.4, cut-off > 13).

As shown in Table 3, the PD subgroups of patients ICD positive vs. negative had similar BIS-11 total scores; however, ICD positive subgroup scored higher than ICD negative subjects in the attention impulsiveness subscale of BIS-11 ($P = 0.007$). The two subgroups differed in MOCQ/R total score ($P = 0.03$) and in the doubting subscale of MOCQ/R ($P = 0.007$); SOGS total scores were also different ($P = 0.04$).

PD and HC group had similar age and education; women were less represented in PD than in controls (53 F/47 M).

The frequency of ICDs did not differ between PD and HC. Due to the higher frequency of men in PD, we additionally compared PD men with HC men but found no difference (Fisher's exact test).

Discussion

This is the first screening of ICDs, impulsivity and compulsive behaviors in a large cohort of consecutive PD patients before the initiation of DRT. The prevalence of ICDs may also vary according to the population studied and depend on different cultural background.[6,22,23] In a previous study, we reported 28% presence of ICD in treated PD versus 20% in controls examined at our institution.[5] In this study, PD patients were surveyed in multiple movement disorders clinics throughout Italy to embrace different clinical and socio-cultural settings.

ICD positive PD showed higher scores in the "attentional impulsiveness" component of the BIS-11 and "doubting" subscale of the MOCQ/R compared to negative ICD even if the overall measures of impulsivity and compulsive behaviors did not differ. The elevation of attention impulsiveness scores in PD screening positive for ICDs may suggest a subclinical pattern characterized by a relatively reduced ability to focus on the task at hand.[9] Relatively high scores in the MOCQ/R doubting subscale have been associated with anxiety and/or depressive thoughts,[17] and in our cases may reflect a reduced self-confidence in presence of compulsive behavior. More importantly, we found in these drug-naïve patients a positive correlation between GDS-15 and BIS-11, which is in line with the association between impulsivity and depression we had found in treated PD.[5] Overall, depression was frequent in this cohort of drug-naïve PD patients consistently with other epidemiological studies.[24]

Mean impulsivity scores were overall similar and slightly lower in our de novo PD patients compared to the age-matched healthy normative sample. In a previous study, we found higher scores in the impulsivity scale in PD subjects on dopaminergic therapy compared to matched healthy controls[5] suggesting that medications may increase this trait.

Our data are in line with other reports suggesting that impulsivity is modulated by dopamine[25] and that its deficiency in PD may underlay specific personality features.[26–28]

Interestingly, a relatively high frequency (up to 17.5%) of patients reported at least one ICD at MIDI or SOGS, mainly compulsive sexual behavior and compulsive buying although individual clinical interviews performed by the neuropsychologist before testing showed that these behaviors were not considered unusual by patients. Moreover, frequency of ICD did not differ with HC (see Isaias[5] for details), where 20% (20 of 100) reported at least one abnormal behavior at MIDI (11% compulsive buying; 9% intermittent explosive disorder; 3% abnormal sexual behavior; 3 subjects reported more than one ICD) or pathological SOGS score (1%). We therefore speculate that the frequency of ICDs as assessed by MIDI and

SOGS in Italy is higher than rates reported in literature, possibly because of cultural factors; furthermore it should be taken into account that the scales we used are screening instruments that may overestimate the rate of compulsive behaviors.

We did not consider binge eating disorder that is also reported in PD[6] but it is not included in MIDI. However, we included intermittent explosive disorder that is poorly investigated in PD and was rather frequent (6%) in our previous study.[5]

According to the MOCQ/R scale, de novo PD subjects do not show a significant increment in compulsive behaviors compared to normative healthy population. These results confirm and further expand previous findings in early-stage PD subjects on DRT.[5,29]

Taken together, these results suggest that subclinical behavioral abnormalities are common in PD even before the initiation of dopaminergic medication and they are as frequent as in non-PD controls. Therefore careful investigation is needed in routine clinical setting, as these behaviors are not spontaneously reported to the neurologist.

This study has been conceptualized as the first step of a prospective assessment of individual predisposing factors to ICDs that should be carefully assessed before the initiation of DRT. It is conceivable that DRT may turn a personality trait and/or subclinical abnormal behaviors into a clinically relevant disorder. We speculate that those patients with high scores in screening scales may be more prone to develop clinically relevant ICDs. Prospective assessment of these subjects will help clarifying these issues. Since ICDs often develop in individuals who apparently have unremarkable psychiatric history and no cognitive impairment, their identification and management is complex. We believe that these results encourage active screening to identify at-risk subjects and follow close their behavioral response to DRT.

In conclusion, we found a significant number of ICD in de novo PD with similar frequency as in HC. These results support the use of specific scales even before dopaminergic therapy is initiated. ■

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