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ORIGINAL ARTICLE

Impulse control disorders related cognitive and behavioral features in Parkinson's disease

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ABSTRACT

Objectives: This study aimed to investigate cognitive and behavioral distinctions in patients with Parkinson's disease (PD) with impulse control disorders (ICDs).

Patients and methods: A total of 72 patients (52 males, 20 females; mean age: 60.8±9.2 years; range, 41 to 77 years) with PD (31 with ICD features [PDwIC] and 41 without ICD [PDwoICD]) and 67 healthy controls (35 males, 32 females; mean age: 60.4±10.4 years; range, 36 to 79 years) were included in this prospective cross-sectional study between April 2018 and January 2020. All participants underwent a comprehensive neuropsychometric assessment, including a battery of cognitive and psychiatric tests. Furthermore, the Iowa Gambling Task was employed to evaluate risky decision-making capacities, and the UPPS (Urgency, Premeditation [lack of], Perseverance [lack of], Sensation Seeking) Impulsive Behavior Scale was utilized to assess impulsive personality traits. The Beck Depression Inventory (BDI) was used to assess the presence and severity of depression.

Results: The PDwICD, PDwoICD, and healthy control groups showed comparable characteristics in terms of age and education level. Male sex was more prevalent in the PDwICD group than in the control group (p=0.01). The PDwICD group exhibited significantly higher MDS UPDRS I scores and total LEDD compared to the PDwoICD group (p=0.027 and p=0.003, respectively). The PDwICD group also had higher BDI scores and UPPS-Sensation Seeking subscores than the PDwoICD group (p=0.001 and p=0.044, respectively). The multivariate analyses demonstrated an independent association between higher scores of BDI and presence of ICD in PD (p=0.006).

Conclusion: In conclusion, comprehensive screening for affective characteristics can help clinicians identify those at higher risk for impulsive behaviors in PD. Prospective studies are needed to better understand the factors leading to ICDs and explore the roles of personality traits, cognitive and behavioral features, and dopaminergic medications.

Keywords: Impulse control disorders, impulsivity, Parkinson's disease.

Impulse control disorders (ICDs) are defined as repetitive, excessive, and compulsive hedonistic behaviors that interfere with major areas of life functioning.[1] Extensive research consistently indicates a heightened prevalence of ICDs in individuals with Parkinson's disease (PD) compared to the general population, with estimated frequencies ranging from approximately 3.5 to 43%.[2-4] In recent times, there has been a notable increase in awareness regarding the susceptibility of patients with PD to develop ICDs, leading to an increase in reported cases. A longitudinal study revealed a five-year cumulative incidence of ICDs in PD at approximately 46%.[5] Among the prevalent ICDs in this cohort were pathological gambling, hypersexuality, compulsive eating, and compulsive shopping. Moreover, additional impulsive-compulsive behaviors, such as punding (involving repetitive, purposeless activities like repairs, playing instruments,

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gardening, hoarding, and pacing) and dopamine dysregulation syndrome (involving compulsive use of dopamine medications despite adequate motor benefits and associated negative consequences), were documented in the literature.[2,6,7]

The precise mechanisms underlying ICDs remain incompletely understood; nonetheless, it was established that dopamine reward and inhibition systems play a pivotal role.[2] Numerous studies investigating factors related to ICDs in patients with PD demonstrated the influence of neurobiological, environmental, and genetic factors on susceptibility to ICDs.[2,8-11] Dopamine replacement therapies, particularly dopamine receptor agonists, stand out as prominent risk factors. The overactivity of the mesocorticolimbic dopaminergic system induced by dopaminergic treatment is frequently implicated in the onset of ICDs. Other factors linked to ICDs include younger age, earlier onset of PD, longer disease duration, male sex, smoking habits, education, and personal or family history of addictions preceding the diagnosis of PD, as delineated in prior research.[4,7,10] While cognitive impairments, comorbid psychiatric conditions, and high novelty-seeking personalities have been posited as potential risk factors for ICDs in various studies, the findings in this regard have been notably inconclusive.[12-20]

Impulse control disorders can exert a substantial impact on functioning, diminish the quality of life, and increase caregiver burden.[21] Hence, it is crucial to identify risk factors associated with ICDs in PD for a better understanding, prevention, and early management of these disorders. The identification of cognitive and behavioral attributes that predispose individuals to ICDs holds the potential to contribute valuable insights into the incompletely elucidated pathophysiological mechanisms. Furthermore, it assumes significance in recognizing patients with a heightened risk profile for ICD development and tailoring their treatment regimen accordingly. However, studies on this topic have yielded inconsistent results.

The primary objective of this study was to investigate potential cognitive and behavioral distinctions among patients with PD with and without ICDs. Moreover, the study aimed to determine distinct characteristics that could serve as markers for identifying patients with a predisposition to ICDs. The ultimate goal was to enhance the strategic planning and tailored treatment interventions for patients with PD at risk of developing ICDs by acquiring a thorough understanding of the associated cognitive and behavioral features.

PATIENTS AND METHODS

In the prospective cross-sectional study, patients diagnosed with PD were recruited from the movement disorders outpatient clinic of Gazi University Faculty of Medicine, Department of Neurology between April 2018 and January 2020. Inclusion criteria encompassed an age range between 30 and 80 years, a diagnosis of idiopathic PD by the UK Parkinson's Disease Society Brain Bank Clinical Diagnostic Criteria, mild-to-moderate PD status (Hoehn and Yahr Stage 1-3 in the ON state), cognitive normalcy as evidenced by Montreal Cognitive Assessment (MoCA) scores ≥21 out of 30, in addition to clinical interview and maintenance of stable medication with anti-PD agents for a minimum duration of three months. Exclusion criteria were the presence of neurological disorders other than PD, a family history of PD, psychosis, a documented history of ICDs predating the onset of PD, cognitive impairment indicated by a MoCA score <21, and using centrally acting anticholinergic or atypical antipsychotic medications.

Out of 137 patients subjected to assessment, a cohort comprising 72 patients (52 males, 20 females; mean age: 60.8±9.2 years; range, 41 to 77 years) with PD meeting all requisite criteria and completing the test protocols was included in the study. Among this cohort, 31 individuals exhibited characteristics indicative of ICDs (PDwICD), as ascertained by a specialist neurologist employing the self-reported Questionnaire for Impulsive-Compulsive Disorders in Parkinson's Disease (QUIP), in addition to a clinical interview.[22] The remaining 41 patients exhibited features of PD without ICD (PDwoICD). Consistent with published recommended cutoff scores, participants providing positive responses to one or more screening questions on the QUIP were categorized as presenting with features of ICDs. The control group comprised 67 healthy volunteers (35 males, 32 females; mean age: 60.4±10.4 years; range, 36 to 79 years) exhibiting a MoCA score ≥21 and possessing no history of neurological or psychiatric disorders.

Participants underwent a thorough evaluation conducted in a single session, with assessments administered to the PD group during their ON state. A specialized neurologist evaluated the PD group, considering factors such as age at PD onset,

PD duration, PD medication type, total L-dopa equivalent daily dose (LEDD), and total dopamine agonist LEDD. The severity of both motor and nonmotor impairment was assessed utilizing the Movement Disorder Society Unified Parkinson's Disease Rating Scale (MDS-UPDRS) I-IV[23] and Hoehn and Yahr stage.[23]

A comprehensive neuropsychometric assessment was administered to all participants encompassing the following battery of tests: MoCA, Beck Depression Inventory (BDI), Frontal Assessment Battery (FAB), Iowa Gambling Task (IGT), and the UPPS (Urgency, Premeditation [lack of], Perseverance [lack of], Sensation Seeking) Impulsive Behavior Scale.

Montreal Cognitive Assessment, a screening test validated for application in Turkish patients with PD, was designed to assess general cognitive functions.[24] The total score ranges from 0 to 30, evaluating visual-spatial perception, executive functions, memory, attention, language, abstract thinking, and orientation skills. As a result of the validation study of the MOCA test for the Turkish population, probably due to cultural differences, the cutoff value for cognitive impairment was determined as 21 out of 30.[25]

Beck Depression Inventory was employed for the assessment of depression presence and severity in PD. This instrument is acknowledged as a valid and reliable tool in the context of PD research.[26]

Frontal Assessment Battery is comprised of subtests focusing on the evaluation of executive functions, including assessments of similarities, word persistence, motor series, conflicting directives, and catching behavior.[27]

Iowa Gambling Task is one of the commonly employed tasks for assessing decision-making abilities in uncertain situations and decisions made under ambiguity. The assessment utilized the IGT format, a standardized computer-administered test as outlined by Bechara et al.[28] In this format, participants were tasked with making 100 selections from a horizontal array of four decks of cards. Following each choice, the computer presented an associated abstract monetary reward and, on occasion, a monetary punishment. Participants were informed in advance about the existence of good and bad decks and were instructed to avoid unfavorable decks while selecting from the advantageous decks to maximize their "money" accumulation. The primary dependent variable measured was the difference between advantageous selections and disadvantageous selections in each block of 20 trials.[28,29]

The UPPS Impulsive Behavior Scale was employed to measure four distinct facets of impulsivity.[30] The instrument was utilized to assess behavioral traits associated with impulsivity, including tendencies toward impulsive behavior, acting thoughtlessly, difficulty maintaining focus, and a propensity for seeking risky, exciting, and dangerous experiences. The scale comprises four subscales, encompassing a total of 45 questions, and employs a Likert-type scoring system ranging from 1 to 4. A higher score indicates an increase in impulsivity, while a lower score implies a decrease in impulsivity.[30,31]

The neuropsychiatric assessment tools utilized in this study possessed Turkish validity and were administered by a specialist neuropsychologist.

Statistical analysis

Statistical analysis was performed using IBM SPSS version 20.0 software (IBM Corp., Armonk, NY, USA). Assessment of the normal distribution of numerical variables was conducted through the Kolmogorov-Smirnov and Shapiro-Wilk tests. In instances where variables exhibited a normal distribution, Student's t-test was employed to scrutinize the mean difference between two independent groups. Conversely, for numerical data lacking normal distribution, the Mann-Whitney U test was applied to analyze the median difference between the two independent groups. Categorical variables were subjected to analysis using the chi-square test under circumstances where the assumptions for this test were met. In cases where these assumptions were not fulfilled, Fisher exact test was utilized. In addition, logistic regression analysis was applied to investigate the independent associations of ICD presence in PD. The analyses were executed with a confidence level of 95%, and statistical significance was determined based on a p-value <0.05.

RESULTS

Twenty-two of the patients with PDwICD manifested one or more active ICD symptoms, while nine of them exhibited two or more distinct ICD features. The PDwICD, PDwoICD, and healthy control groups demonstrated comparable characteristics in age and education level. Sex distribution was also similar between the PDwICD and PDwoICD groups (p=0.165). However, the

TABLE 1
Demographic data of PD and control groups

	PDwICD (n=31)			PDwoICD (n=41)			Healthy control (n=67)			
	n	%	Mean±SD	n	%	Mean±SD	n	%	Mean±SD	*p*
Age (year)			58.4±8.7			62.6±9.2			60.4±10.4	0.179
Sex										**0.022***
Male	25	80.6		27	65.8		35	52.2		
Female	6[x,y]	19.3		14[z]	34.1		32	47.7		
Education (year)			11.1±3.8			10.1±3.8			10.3±3.6	0.454

PDwICD: Parkinson's disease with impulse control disorder; PDwoICD: Parkinson's disease without impulse control disorder; SD: Standard deviation; x: p=0.40 PDwICD *vs.* PDwoICD; y: p=0.01 PDwICD *vs.* Healthy Controls; z: p=0.41 PDwoICD *vs.* Healthy controls; * p<0.05.

proportion of male sex was higher in the PDwICD group than that in healthy controls (p=0.01). Further details about the demographic data of groups are presented in Table 1.

Within the PD group, no statistically significant distinctions were observed between the PDwICD and PDwoICD subgroups concerning disease duration, Hoehn and Yahr Stage, MDS-UPDRS II, III, and IV scores, L-dopa LEDD, and dopamine agonist LEDD. However, significant differences surfaced with a higher prevalence of elevated MDS UPDRS I scores in the PDwICD group (p=0.027). On the other hand, the PDwICD group exhibited a significantly higher total LEDD in comparison to the PDwoICD group (p=0.020). A comprehensive summary of the comparative data about PD groups is presented in Table 2.

In terms of neuropsychiatric and behavioral characteristics, notable distinctions were observed in the BDI scores among the PDwICD, PDwoICD, and control groups (p=0.000). Specifically, the PDwICD group exhibited significantly elevated BDI scores in comparison to both the PDwoICD group and the control group (p=0.001 and p=0.004, respectively). There were no significant differences among the groups regarding MoCA and FAB scores. Similarly, no significant distinctions were observed in terms of IGT scores, which assessed decision-making skills, and UPPS total scores, reflecting personality traits associated with impulsivity. However, upon a detailed examination of UPPS subscores, a significant difference emerged in the UPPS-Excitement Seeking subscores among the groups (p=0.044), with the PDwICD group demonstrating

TABLE 2
Comparative data of PD groups

	PDwICD (n=31)			PDwoICD (n=41)			
	n	%	Mean±SD	n	%	Mean±SD	*p*
PD duration (year)			6.54±4.71			5.01±3.24	0.183
HY Stage 1	9	29		15	36.6		
HY Stage 2	21	67.7		24	58.5		0.720
HY Stage 3	1	3.2		2	4.9		
MDS-UPDRS I			7.45± 3.17			5.83±3.4	0.027*
MDS-UPDRS II			6.00±4.72			5.80±4.79	0.797
MDS-UPDRS III			17.42±8.83			15.24±7.59	0.378
LD LEDD			590.39±370.09			449.34±318.16	0.076
DA LEDD			183.23±167.49			129.63±124.55	0.204
Total LEDD			866.03±409.03			660.68±359.63	0.020*

PD: Parkinson's disease; PDwICD: Parkinson's disease with impulse control disorder; PDwoICD: Parkinson's disease without impulse control disorder; SD: Standard deviation; HY: Hoehn and Yahr; MDS-UPDRS: Movement Disorders Society-Unified Parkinson's Disease Rating Scale; LD: L-dopa; LEDD: L-dopa Equivalent Daily Dose; DA: Dopamine agonist; * p<0.05.

TABLE 3
Neuropsychometric and behavioral test characteristics of groups

	PDwICD (n=31)	PDwoICD (n=41)	Healthy controls (n=67)	
	Mean±SD	Mean±SD	Mean±SD	*p*
Montreal cognitive assessment	24.19±2.40	24.04±2,40	24.34±2.24	>0.05
Frontal battery (max. 18)	15.93±1.48	14.80±2.63	14.91±2.73	>0.05
Beck depression inventory	16.16[a,b]±12.52	6.97[c]±5.50	7.70±8.06	**0.000***
UPPS total (max. 180)	101.61±19.77	95.90±12.98	97.16±14.03	>0.05
UPPS subtest (sensation seeking)	21.58[d,e]±9.39	17.09[f]±6.90	17.59±8.24	**0.044***
Iowa Gambling test	2245.96±1096.70	2220.73±1087.98	2345.14±1145.53	>0.05

PD: Parkinson's disease; PDwICD: Parkinson's disease with impulse control disorder; PDwoICD: Parkinson's disease without impulse control disorder; SD: Standard deviation; UPPS: Urgency-Premeditation-Perseverance-Sensation seeking Impulsive Behaviors Scale; a p=0.001, PD ICD+ *vs.* PD ICD-; b p=0.004, PD ICD+ *vs.* healthy control; c p=0.92, PD ICD- *vs.* healthy control; d p=0.046, PD ICD+ *vs.* PD ICD-; e p=0.137, PD ICD+ *vs.* healthy control; f p=0.982, PD ICD- *vs.* healthy control; * p<0.05.

TABLE 4
Independent associates of ICD in PD

	Univariate analysis			Multivariate analysis		
Variables	Exp (B)	95% CI	*p*	Exp (B)	95% CI	*p*
Sex	2.160	0.719-6.492	0.170	4.056	0.985-16.699	0.053
MDS-UPDRS 1	1.156	1.000-1.337	0.050	1.106	0.914-1.337	0.300
Total LEDD	1.001	1.000-1.003	0.034*	1.001	1.000-1.003	0.115
Beck depression inventory	1.143	1.056-1.238	0.001*	1.131	1.036-1.234	**0.006***
UPPS subtest (sensation seeking)	1.071	1.007-1.139	0.029*	1.054	0.983-1.130	0.141

ICD: Impulse control disorders; PD: Parkinson's disease; MDS-UPDRS: Movement Disorders Society-Unified Parkinson's Disease Rating Scale; LEDD: L-dopa Equivalent Daily Dose; UPPS: Urgency-Premeditation-Perseverance-Sensation seeking Impulsive Behaviors Scale; * p<0.05.

a higher score than PDwoICD (p=0.046). Table 3 provides a comprehensive presentation of the comparative data across the groups concerning neuropsychometric and behavioral assessments.

To further explore the independent associates of ICD presence in PD, logistic regression was applied, including sex, MDS UPDRS I score, total LEDD, BDI score, and UPPS-Sensation Seeking subscore as covariates. Although univariate analyses yielded significance for total LEDD, BDI score, and the UPPS subscore, a multivariate analysis revealed that BDI was the only variable that demonstrated an independent association with ICD in PD (Table 4).

DISCUSSION

In the present study, a detailed examination of cognitive and behavioral features was undertaken within the PD groups with and without characteristics of ICD. Consistent with the previous literature,[2,4,7] pairwise comparisons in the current study demonstrated a higher mean of LEDD and rate of male sex in the PDwICD group than in the PDwoICD group. Our analysis revealed a significant increase in depressive symptoms, as indicated by BDI scores, within the PDwICD group. Additionally, significant traits of impulsivity within the personality characteristics of the PDwICD group were identified.

Our findings on depression, as assessed by BDI scores, are in concordance with prior studies, which, despite variations in depression scales and diagnostic criteria used, have reported similar results.[16,18,32-35] An increase in BDI scores demonstrated an independent association with the presence of ICD in PD. These outcomes suggest a plausible association between depression, anxiety, and susceptibility to ICD. A longitudinal investigation conducted by Marín-Lahoz et al.[16] demonstrated that depression acted as a predisposing factor for the emergence of ICDs in individuals with PD. Depression may manifest as a consequence of impulsive-compulsive behaviors, referred to as reactive depression. It has been proposed that

ventral striatal dopaminergic denervation is a shared mechanism underlying both depression and ICD, with dysfunction in brain regions related to reward and motivation.[18,32,33] Furthermore, individuals exhibiting impulsive-compulsive behaviors and depression often experience a diminished quality of life.[18,21]

In our study, the IGT served as the instrument for assessing reward-related decision-making abilities under risk in individuals with PD. Our investigation indicated that the IGT did not exhibit discriminatory efficacy between PD patients with and without ICD and the control group. Consequently, the presence of ICD does not appear to exert a significant impact on the capacity of risky decision-making. These findings align with previous studies conducted by Biars et al.[15] and Bentivoglio et al.[36] Martini et al.[17] and Ricciardi et al.[37] explored risky decision-making utilizing the Balloon Analog Risk Task (BART) in individuals with PD experiencing ICD, yielding results consistent with our findings. Conversely, a preceding study by Rossi et al.[38] observed worse performance on the IGT in the PDwICD group in comparison to the PDwoICD group. Moreover, Claassen et al.[39] reported increased risk-taking behavior in patients with PDwICD, specifically under dopamine agonist medication. These disparities in outcomes may be attributed to variations in the clinical characteristics of patients with PD, such as age and medication regimens, differences in the tasks employed (e.g., BART or alternative gambling tasks), or methodological variations inherent in the respective study designs. It was suggested that an imbalance between the ventral and dorsal frontostriatal loops could contribute to higher impulsivity and impaired reward-related decision-making in patients with ICD.[36] The absence of significant differences in IGT performance between PD groups with and without ICD may be elucidated by the predominant engagement of frontal lobe activity in this task despite the concurrent involvement of the ventral striatum, as delineated in prior investigations. It was proposed that impaired IGT performance might be observed in PD patients with age-related frontal involvement.[15]

Participants underwent an assessment of impulsive personality traits, recognized as affective factors potentially linked to ICDs. The UPPS Impulsive Behavior Scale was employed as a self-reported questionnaire to gauge personality traits associated with impulsivity. The elevated score in the Sensation Seeking subscale observed in the PDwICD group substantiated the proposition of a predisposition to impulsivity within the context of our study. In previous studies where impulsive personality traits were evaluated using UPPS or different scales, such as the Barrat Impulsivity scale, a relationship between impulsive personality traits and the emergence of ICD in individuals with PD was also reported.[4,20,35,36,40-42] The majority of these studies identified heightened scores in Sensation/Novelty Seeking in the population with PDwICD, similar to our study.[4,40,41,43] However, we should also point out that in our study, the result obtained in comparative analyses did not maintain statistical significance after the application of a regression model. While impulsive personality traits appear to be a risk factor for the development of ICD according to existing literature,[2-4,7,40,42] it does not unequivocally substantiate the notion that PD is characterized by a distinct personality profile before the onset of the disorder.[44] Although the UPPS Impulsive Behavior Scaleproves valuable in examining impulsive personality traits within the population with PD, its utilization has been limited in the existing literature, yielding variable results in the subscales.[20,40,41,43] Future studies incorporating larger sample sizes would be advantageous in further elucidating the UPPS impulsivity model in the context of PDwICD.

Our examination of the cognitive characteristics within the PD cohort revealed no statistically significant differences between the PD and control groups in terms of MoCA and FAB scores. This aligns with several studies reporting comparable findings, wherein no disparities in neuropsychological tests were identified between patients with PD with and without ICDs.[14,36,38] Erga et al.,[45] in a longitudinal study, demonstrated that cognitive changes over time did not exhibit variance between patients with and without impulse control behaviors. A meta-analysis conducted by Santangelo et al.[13] investigating the cognitive profile of individuals with PDwICD in comparison to those without ICD, reported no significant association between ICD and global cognitive ability or global frontal function. This outcome resonates with our study and several others.[14,36,38] However, Santangelo et al.[13] observed greater impairment in specific cognitive functions, such as abstraction/concept formation, set-shifting, and visuospatial/constructive abilities, in individuals with PDwICD compared to those without ICD. Similarly, some previous studies have identified significant impairments in executive

functions and working memory in the PDwICD group compared to the PDwoICD group.[12,44,46-48]

In addition to the evaluation of global cognitive functions using the MoCA, our study also searched executive functions through the frontal battery. Contrary to some studies, we did not identify specific executive dysfunction in the ICD group. Conflicting results among study outcomes may be attributed to variations in patient selection criteria and the specific neuropsychometric batteries employed. For instance, our study only recruited patients with high MoCA scores, excluding those with potential cognitive impairments.

A notable limitation of our study is the relatively small sample size, potentially accounting for the absence of statistically significant differences, despite the presence of statistical trends in neuropsychological variables across our groups. The cross-sectional design of the study represents another limitation. Finally, the cutoff score of the MoCA was taken as <21 during the identification of cognitive impairment, as recommended for the Turkish version of the MoCA; however, keeping this cutoff at <25, as in the original version of the test, could be a more appropriate approach to be on the safe side.

In conclusion, conducting comprehensive screening for mood characteristics, particularly depressive tendencies, may help clinicians distinguish individuals at increased risk of developing clinically significant impulsive behaviors in PD. To further enhance our understanding of predisposing factors for ICDs, there is a critical need for prospective studies investigating the potential contributions of various variables such as personality traits, cognitive or behavioral features, and dopaminergic medications.

Ethics Committee Approval: The study protocol was approved by the Gazi University Clinical Research Ethics Committee (date: 28.05.2018, no: 389). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Patient Consent for Publication: A written informed consent was obtained from each patient.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

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