Original Article

Impulsivity in Parkinson's Disease

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ABSTRACT

Introduction/Aims: Parkinson's disease (PD) is a neurodegenerative disease characterized by cardinal motor and nonmotor symptoms. Impulse control disorders are common neuropsychiatric manifestations in patients with PD (pwPD) under dopaminergic therapy. However, impulsivity is an underestimated symptom. Hence, the present study aimed to evaluate the impulsivity in pwPD. **Methods:** Forty-seven adults who were diagnosed with having PD according to the Queen Square Brain Bank criteria for PD diagnosis and 30 age-matched healthy controls were enrolled in the study. The sociodemographic data of the study participants and disease characteristics of the patients were recorded. All participants completed the Barratt impulsiveness scale (BIS). BIS scores were statistically analyzed between the groups. **Results:** The results revealed no significant differences between the patients and controls in terms of age ($P > 0.05$) or sex ($P > 0.05$). The total BIS scores were higher in the PD group than in the healthy controls ($t = 2.1$, $P = 0.038$). The items of BIS and attentional impulsivity scores were higher in the pwPD than in the controls ($t = 2.8$, $P = 0.005$), but there were no statistically significant differences between the groups in terms of motor and nonplanning impulsivity (z = 1.8, $P = 0.07$; and $t = 1.1$, $P = 0.31$, respectively). **Discussion:** Our results indicate that attentional impulsivity is an important clinical characteristic of pwPD, even in the absence of impulse control disorders. **Conclusion:** Further studies are required to confirm these findings in view of personalized PD treatment.

Keywords: *Barratt impulsiveness scale, impulse control disorders, impulsivity, Parkinson's disease*

Introduction

Parkinson's disease (PD) is a progressive brain aging disease with a vast spectrum of motor/nonmotor symptoms consisting of neuropsychiatric disorders, such as depression, anxiety, psychosis, and impulse control disorders (ICDs), which are relatively common in patients with PD (pwPD), with a frequency of 17%–20% as a complication of dopaminergic treatment.[1,2] ICDs are most likely to occur due to dopaminergic agonists, but can also be observed with levodopa (LD) treatment.[3] However, the history of premorbid ICD, depression, apathy, rapid eye movement sleep behavior disorder, male sex, and younger age can be summarized as risk factors for the development of ICDs.[3-7] The most common ICDs in pwPD are known as compulsive shopping, hypersexual behavior, and compulsive eating, as well as pathological gambling.[8]

According to the definition of the American Psychiatric Association, ICDs are defined as a category of psychiatric disorders with a characteristic deficiency to resist an inclination, urge, or impulse that may hurt oneself or others.[9] The underlying mechanism is considered to be the dysregulation of mesocorticolimbic circuits and dopamine receptors, leading to the clinical manifestation of ICDs in the presence of premorbid personality traits and risk factors, as described previously.[10] Because ICDs manifest as clinical presentations of psychiatric symptoms, and more pwPD are believed to experience

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subclinical symptoms of impulsivity, it is crucial to determine the behavioral pattern of impulsivity, which can be described as a personality trait or a complex symptomatology that manifests as a result of neurobiological deficits. The term "impulsivity" can be detailed as an inability to inhibit unwanted actions or an inability to stop a progressing action, which are called waiting and stopping impulsivity, respectively.[11,12] On the other hand, a recent meta-analysis revealed that impulsivity as a personality trait signalized pwPD even without ICDs.[13] Thus, the multifactorial association between impulsive traits and ICDs in PD warrants a more in-depth analysis.

On this aspect, the objective of our study was to evaluate impulsivity in pwPD and its possible associations with sociodemographic and disease characteristics of pwPD, which is an underestimated entity in clinical trials because it may be a possible step toward the manifestation of ICDs.

Methods

Study participants and patient data

A total of 47 adults who were diagnosed with idiopathic PD at the outpatient neurology clinic of our university (2016/75 18.10.2016) and 30 age-matched healthy controls were enrolled in the study between October 2018 and February 2019. The healthy age-matched controls were in the same age range as the patient population who had no chronic illnesses, no neurologic diseases, were taking no medications due to any type of reported illness, and who volunteered to participate in the study. This "healthy age-matched control" population consisted of relatives or friends of the patients who had accompanied the patients or the individuals working in the hospital.

Age over 18 years and motor symptoms lasting up to 3 years were prerequisites for inclusion. Individuals with dementia diagnoses or clinical characteristics suggestive of primary atypical Parkinsonism were not included. All participants provided their written informed consent, and the study was approved by the Local Ethics Committee of our university.

The sociodemographic data of all study participants and disease characteristics, such as disease duration, basic symptoms, current medications, and modified Hoehn and Yahr (HY) scores in the patient group, were set down via face-to-face interviews.

All participants completed the Barratt impulsiveness scale (BIS).[14] The Turkish validation and reliability of the questionnaire were performed by Güleç *et al*. in 2008.[15] The BIS is a 30-item self-report questionnaire that was designed to evaluate impulsiveness, the propensity to seek adventure, or take chances without thinking about the consequences. It includes 30 items that are scored to yield six first-order factors (attention, motor, self-control, cognitive complexity, perseverance, and cognitive instability impulsiveness) and three second-order factors (attentional, motor, and nonplanning impulsiveness). All items are graded on a 4-point Likert scale as follows: (1) rarely or never; (2) occasionally; (3) often; and (4) almost. The sum of the items indicates the overall levels of impulsivity. Higher scores indicate higher degrees of impulsivity; values range from 30 to 120.[11]

Statistical analysis

The data were analyzed using the Statistical Package for the Social Sciences for Windows Version 23 software (SPSS, IBM Corp.). The normality of data distribution was graphically explored using Q–Q plots. Categorical variables are summarized as absolute numbers and percentages. Continuous variables are presented as mean ± statistical deviation. Statistical analyses were performed using descriptive statistics, the Chi-square (χ^2) test (for categorical variables), Student's *t*-test, and the Mann–Whitney *U* test (for nonnormally distributed continuous variables). Spearman (rho) and Pearson (*r*) correlation analyses were also performed. $P < 0.05$ were considered to indicate statistical significant differences.

Results

Sociodemographic and clinical characteristics of the study groups

The study group consisted of 47 pwPD and 30 age-matched healthy controls. All participants were right-handed. Two-thirds of the population in the PD group were male ($n = 31$, 66%), and more than half of the control group were female ($n = 16$, 53.3%). However, no statistically significant difference was found between the PD and control groups in terms of sex ($\chi^2 = 2.81$, $P = 0.09$).

The mean age of the pwPD and control group was 67.98 ± 10.26 years and 63.13 ± 10.88 years, respectively. There were no statistically significant differences between the groups in terms of age ($t = 1.98$, $P = 0.51$).

All pwPD were receiving pharmacologic treatment for PD; one patient was treated with additional device-aided therapy, which involved bilateral deep-brain stimulation of the subthalamic nucleus. The disease characteristics of the pwPD are summarized in Table 1.

The mean disease duration of pwPD was 5 (range = 1–15) years. Dopamine dysregulation

syndrome occurred as a complication of treatment with LD + dopamine agonist + monoamine oxidase B inhibitor in a male patient with a disease duration of 72 months (6 years).

Among the pwPD, 7 (14.9%) patients were experiencing complications due to dopaminergic treatment. In addition, 6 (12.7) patients had LD-induced dyskinesia, and 1 (2.2%) had dopamine dysregulation syndrome presenting with excessive shopping.

Correlation analysis of the study group

The mean BIS score in the PD group was 27.83 ± 6.17 and 24.87 ± 5.77 in the control group. This comparison revealed that the BIS total score was significantly higher in pwPD than in the controls ($t = 2.14$, $P = 0.036$). When the items of BIS were evaluated, increased attentional impulsivity scores were also noted in pwPD compared with the controls ($t = 2.8$, $P = 0.005$); there were no marked differences between the groups in terms of motor impulsivity and nonplanning impulsivity ($z = 1.8$, $P = 0.07$; and $t = 1.1$, $P = 0.31$, respectively) [Table 2].

Furthermore, an assessment was made of whether there were any sex-related differences between the PD group in terms of total BIS scores and BIS items, including attentional impulsivity, and motor and nonmotor planning. It was found that the nonmotor planning impulsivity was slightly higher among females when compared with males, although this difference was not statistically significant (11.75 ± 3.35 and 10.03 ± 2.60, respectively, $P = 0.059$).

Correlation analysis in the PD group revealed that there was a positive Pearson correlation between age and attentional ($r = 0.34$, $P = 0.02$), motor ($r = 0.49$, $P = 0.001$), nonplanning ($r = 0.35$, $P = 0.02$), and total BIS impulsivity scores ($r = 0.49$, $P < 0.001$). However, no association was found between age and impulsivity scores in the control group.

In addition, when Spearman correlation analysis was performed for the BIS total, BIS subscale scores, as well as the HY scores of the pwPD, it was found that the HY scores only correlated with nonplanning impulsivity scores (Rho = 0.33, $P = 0.02$).

Table 1: Disease characteristics of the patients with Parkinson's disease Hoehn and Yahr score

Parameters	Value
Disease duration (months), mean±SD (range)	65.65±35.72 (12–180)
Modified HY score	
Median, range	2 (1–4), moderate stage
Side of onset, *n* (%)	
Right	28 (59.6)
Left	19 (40.4)
Symptom of onset, *n* (%)	
Tremor	32 (68.1)
Bradykinesia	15 (31.9)
Treatment regimens, *n* (%)	
LD	2 (4.2)
LD + DA	8 (17)
LD + MAOBI	2 (4.2)
DA + MAOBI	4 (8.5)
LD + DA + MAOBI	17 (36.2)
LD + DA + amantadine	1 (2.2)
DA + MAOBI + anticholinergic agents	1 (2.2)
LD + MAOBI + amantadine	3 (6.4)
LD + DA + MAOBI + amantadine	7 (14.9)
LD + DA + MAOBI + anticholinergic agents	2 (4.2)

HY Score: Hoehn And Yahr Score, SD: Standard derivation, LD: Levodopa, DA: Dopamine agonist, MAOBI: Monoamine oxidase B inhibitor

Table 2: Comparison of impulsivity scores between the groups

Variable	PD (mean±SD)	Control (mean±SD)	*t/z*	*P*
BIS total score	27.8±6.2	24.9±5.8	2.1	0.036
Attentional impulsivity	9.3±2.8	7.8±1.8	2.9	0.005[a]
Nonplanning impulsivity	10.6±2.9	9.8±3.7	1.0	0.31
Motor impulsivity	7.9±2.1	7.2±2.3	1.8	0.07

[a]Indicates a statistically significant difference ($P<0.05$). BIS: Barrat impulsiveness scale, SD: Standard deviation, PD: Parkinson's disease

Discussion

The link between the dopaminergic system and impulse control has been studied in recent years. The role of dopamine in the reward-punishment process linked to behavioral control has been indicated.[16,17] In line with this association, the present study found that impulsivity was higher in pwPD than in the healthy controls, considering PD as a dopamine-related disease. Impulsivity can be explained as a tendency to act immediately or without prediction of negative impact related to the behavior.[18] It is a dimensional phenomenon that represents the lack of inhibitory control over a behavior and is reported to be related to different psychiatric disorders, such as substance addiction, attention deficit disorder, hyperactivity disorder, and borderline personality disorder.[19,20] Despite the multifactorial complex mechanisms reported to be responsible for inhibitory control of the behavior, impulsivity in PD is attributed to cortico-nigrostriatal dopaminergic degeneration and dopamine replacement treatment.[21]

Impulsivity has been proposed to be related to several factors, such as alcohol and substance use or smoking.

However, none of these factors has been confirmed in different studies.[22] Impulsive behaviors in PD have been defined as nonmotor symptoms that may cause economic, legal, or psychosocially disruptive issues.[23] In the present study, age was the only sociodemographic factor that was found to be positively associated with the BIS total scores in the PD group; there was no such association in the healthy controls. A possible explanation for this may be attributed to disease severity, considering the positive correlation between the HY and BIS scores. Moreover, no correlations were found between sex and BIS total scores. The results regarding this issue are conflicting in the literature, and there is no validation of the impact of sex on ICDs.[24-26]

Notably, we revealed no association between anti-Parkinsonian drugs and BIS scores. The use of dopaminergic medications acting on D2 and D3 receptors is one of the crucial factors in the evolution of ICDs. There may be an association with the regulation of the reward network in pwPD; however, the clear mechanism of this procedure remains obscure.[27] Previous studies have proposed second-generation dopamine agonists to provoke, mainly in genetically susceptible patients, an uncontrolled activation of the mesolimbic pathway, which is relatively preserved in PD, and thus arouse the ICDs.[28,29] This genetic susceptibility is associated with the Ser9Gly single-nucleotide polymorphism (rs6280) of the dopamine receptor D3.[30,31] Moreover, ICDs frequently arise in patients who use a combination of L-DOPA and dopamine agonists, which appears to further affirm its impact on the evolution of ICDs.[32] No effect of other dopaminergic drugs, such as amantadine, catechol-O-methyltransferase inhibitors, and monoamine oxidase B inhibitors, was revealed on the onset of ICDs.[32] By contrast, in other studies, a possible effect of amantadine has been reported on the progress of ICDs due to its dopaminergic effects. Nonetheless, other studies have not demonstrated such an association and, in some cases, have even reported an amelioration of the severity of ICDs following amantadine therapy.[33,34]

Given the relatively small sample size and cross-sectional design, these factors should be acknowledged as limitations of our study. The observed lack of difference between the patient and control groups in both motor planning and nonmotor planning impulsivity may be attributable to these constraints. Furthermore, the impact of dopaminergic treatments on impulsivity could not be discriminated against because all of the patients in the present study sample were taking a dopaminergic agent. Thus, further research comparing the impulsivity levels of patients on or off dopaminergic treatment is required.

Even though there is a strong association between trait impulsivity and PD, there is still a growing need for identifying specific predictors of impulsivity in PD. Therefore, we believe that our findings may provide insight into a link between impulsivity, age, and disease severity. This phenomenon may be caused by dysfunction of a brain network that includes the prefrontal cortex, striatum, and possibly the cerebellum. This network is essential for decision-making and inhibitory control.

The results of this study reveal that attentional impulsivity is an important neuropsychiatric symptom of pwPD, even though impulse control disorders are not present.[22,27]

The major limitations of our study are the relatively small sample size of patients with Parkinson's disease with a single-center experience. Thus, we believe that further multicenter international studies are required to examine larger study groups in order to clarify the pathophysiologic sequelae of ICDs.

Conclusions

ICDs are common nonmotor complications of pwPD under dopaminergic treatment, in particular. However, their presence may be neglected in routine clinical visits if the clinical assessments do not address the symptoms of ICDs, which frequently have a negative impact on the quality of life of patients and their family members. The risk factors for ICDs in PD are coming to light and have been proven in recent studies.[25-28] However, there is limited knowledge on the impulsivity as a footstep of ICDs in pwPD.

Further research would be helpful to investigate the complex phenomenology of trait impulsivity in pwPD in a multidisciplinary approach in larger and diverse cohorts.

Author contributions

Conceptualization, Y. D; methodology, K. A and H. K.; software, K. A and H. K.; validation, K. A and H. K.; formal analysis, K. A, H. K. P. G., R., İ; investigation, Y. D; A. B.; resources, Y. D.; data curation, Y. D and A. B.; writing–original draft preparation, Y. D, A. B., RI; writing—review and editing; supervision P. G.

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Conflicts of interest

There are no conflicts of interest.

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