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# İdiopatik Parkinson Hastalığında Dürtüsellik: Eşleştirilmiş Vaka Kontrol Çalışması

## Impulsivity in Idiopathic Parkinson Disease: Paired Case Control Study

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### Öz

**GİRİŞ ve AMAÇ**: Çalışmanın amacı İdiopatik parkinson hastalarında (IPH) dürtü kontrol bozukluğu (DKB) prevelansını saptamak ve dürtü kontrol bozukluğunun dürtüsellik üzerine etkisine bakmak.

**YÖNTEM ve GEREÇLER**: 40 IPH ve 40 sağlıklı kontrol dahil edildi. Tüm katılımcılar Minnesota Dürtü Kontrol Bozukluğu testi ve Barret dürtüsellik ölçeği ile değerlendirildi

**BULGULAR**: 7 IPH ve 1 sağlıklı kontrolde dürtü kontrol bozukluğu saptandı. Dopamin agonist kullanımı DKB için risk oluşturuyordu. Hasta grupta motor dürtüslellik harici tüm dürtüsellik parametreleri daha fazlaydı. Hasta grupta kllinik olarak DKB varlığında motor dürtüsellik harici tüm dürtüsellik parametreleri artıyordu.

**TARTIŞMA ve SONUÇ**: IPD'deki motor olmayan bulgular sorgulanmadığı takdirde göz ardı edilebilir. İPD hastalarında artan dürtüsellik dikkatlice izlenmelidir. ICD'si olmayan IPD hastalarının bile, özellikle planlama dışı ve bilişsel alanlarda, dürtüsellik eğilimlerini arttırdığı unutulmamalıdır. Ayrıca, yalnızca motor dürtüsellik ölçen testler yeterli olmayabilir.

**Anahtar Kelimeler:** Parkinson Hastalığı, Dürtü Kontrol Bozuklukları, Dürtüsellik, Dopamin Agonisti, Dopamin Replasman Tedavisi

### Abstract

**INTRODUCTION:** The aim of the current study was to estimate the frequency of Impulse Control Disorder (ICD) in patients with Idiopathic Parkinson's Disease (IPD) and to investigate impulsivity in IPD patients.

**METHODS**: 40 IPD patients (24 female, 16 male) treated with dopamine replacement therapy (DRT) and age and sex similar 40 healthy controls (HC) (23 female, 17 male) were included in this paired case-control study. Minnesota Impulsive Disorder Interview (MIDI) and the Turkish version of the Barratt Impulsiveness Scale (BIS-11) were applied to all participants. The patient and control groups were compared in terms of impulsivity and ICD. The effect of dopamine agonist (DA) usage on the presence of impulse control disorder was evaluated in the patient group.

**RESULTS**: 7 patients with IPD (17.5%) and 1 healthy control (2.5%) reported at least one ICD in MIDI. Multiple ICDs were reported in 2 of 7 patients (28.57%) with IPD.

ICD was significantly more frequent in IPD patient group (p=0.002) and DA was found to be a significant risk for ICD. IPD patients had higher scores in total impulsivity, non-planning, and cognitive impulsivity but interestingly lower scores in motor impulsivity as compared with controls. Except for motor impulsivity, the other domains of impulsivity including nonplanning and cognitive impulsivity were found to be increased in the presence of ICD in patients group.

**DISCUSSION AND CONCLUSION**: Non-motor findings in IPD can be overlooked if they are not questioned. Increased impulsivity should be carefully followed in patients with IPD. It should be kept in mind that even IPD patients who had no ICD have increased tendencies for impulsivity, especially in non-planning and cognitive areas. In addition, the tests which only measures motor impulsivity may not be sufficient.

**Keywords:** Parkinson's Disease, Impulse Control Disorders, Impulsiveness, Dopamine Agonist, Dopamine Replacement Therapy

## INTRODUCTION

Idiopathic Parkinson Disease (IPD) is a neurodegenerative disorder associated with progressive degeneration of nigrostriatal dopaminergic pathway (1). IPD is clinically characterized by motor symptoms such as bradykinesia, rigidity, postural instability and resting tremor (2). IPD is a movement disorder and existing treatment strategies focus on the replacement of dopamine to improve motor symptoms; however, non-motor aspects of the

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disease, including impulse control disorders (ICD) also have a major impact on the quality of life (3-4). ICD is defined as a psychiatric condition characterized by the failure to resist an impulsive act or behavior that may be harmful to an individual or others. ICD is conceptualized as 'behavioral' addictions including compulsive sexual behavior (CSB), compulsive buying (CB), pathological gambling (PG) and intermittent explosive disorder (IED) as well as compulsive behaviors such as punding and compulsive use of medication. (5)

ICD has been widely described in IPD and it is known that ICD can be observed in one of seven patients with IPD (6). ICD is strongly associated with dopamine use and other risk factors associated with ICD have been well defined in previous studies (7). However, less attention has been given to the relationship between IPD and impulsivity. Impulsivity has been defined as the tendency of actions to show rapid and unplanned reactions to internal and external stimuli without taking into account the negative consequences for the individual or others (8). Impulsivity has been thought to be a multidimensional construct including three main behaviors; motor (behavioral disinhibition), cognitive (risk-taking without thinking) and temporal (delay of gratification) impulsivity. It is reported that different psychopharmacological dissociations affect different forms of impulsivity and also critical brain lesions have been identified for different forms of impulsivity (9,10). There is a limited number of studies on impulsivity in IPD.

Previous studies have reported a general inhibitory deficit. It is known that response restriction and cancellation and pathological gambling may increase in IPD (11). The aim of the current study was to estimate the frequency of Impulse Control Disorder (ICD) in patients with Idiopathic Parkinson's Disease (IPD) and to investigate impulsivity in IPD patients.

## METHODS

This prospective, paired, case-control study was carried out at the movement disorder center in Bakirkoy Research and Training Hospital. 40 IPD patients (24 female, 16 male) who were followed-up between March 2012- August 2013 were included in the study. 40 (23 female, 17 male) healthy individuals with similar age and gender were included as the control group. The purpose and content of the study were clearly explained and written approval was obtained from the participants before the study. The study was approved by the institutional ethics committee and conducted in complete accordance with the Declaration of Helsinki.

### Patients

All subjects were evaluated by a movement disorders specialist. All the data including routine neurological exam, Mini-mental state examination score (MMSE) and all the questionnaires were obtained during the clinical visits of the patients (12,13,14.15). All patients with IPD were treated with either a dopamine agonist or levodopa (L-dopa) or a combination of these. Besides, none of the patients was using antidepressants or antipsychotics. Sex, age, age at onset of disease, duration, and severity of the disease, drug types and doses were recorded in all patients.

The inclusion criteria for patient groups were diagnosis of IPD (according to UK Brain Bank Criteria) and dopaminergic treatment for at least a year with no dose change for 6 months. Presence of dementia (scoring less than 25 points in MMSE) and additional comorbidities including other neurological or neurodegenerative diseases other than IPD (including atypical IPD and Parkinson plus syndromes) and prior psychiatric disease history were exclusion criteria's for the patient group.

40 healthy individuals with similar in gender and age who had no history of neurological or

psychiatric disease or substance abuse were included in the control group. Healthy controls were randomly selected from relatives of hospital employees and relatives of IPD patients were not selected as controls.

40 IPD patients and 40 healthy controls were asked to complete the following semi-structured diagnostic instruments: 1- Minnesota Impulse Disorder Interview (MIDI) for CB, CSB, intermittent explosive disorder (IED) and PG and Turkish version of Barratt Impulsiveness Scale (BIS-11) for impulsivity.

**Questionnaires**

**1) Minnesota Impulsive Disorders Interview (MIDI).**

MIDI is a semistructured clinical interview which is demonstrated classification accuracy based on the subsequent structured clinical interviews as follows: CB (sensitivity 100%, specificity 96.2%), IED (sensitivity 100%, specificity 97.4%), CSB (sensitivity 80.0%, specificity 96.9%) and PG (sensitivity 100%, specificity 98.4%) (16).

**2) Barratt Impulsiveness Scale (BIS-11)**

Impulsivity was assessed by BIS which was developed by Ernest S. Barrat in 1959 and then revised several times (17). BIS-11 was used in the current study. The Turkish reliability and validity of BIS were performed by Güleç et al. (18) The scale consists of 30 items in which each item is evaluated with a 4-point Likert-type scale. A total score of the scale ranges from 0 to 120 and an increase in score indicates increased levels of impulsivity. The BIS-11 provides both total impulsivity score and scores for subscales including motor impulsivity, cognitive impulsivity, and non-planning impulsivity

**Statistical analyses**

All statistical analyses were performed using the Statistical Package for Social Sciences 18.0 (SPSS). Numerical values were compared with Student's t-test, non-parametric comparisons were carried out with the Mann-Whitney U test and categorical values were compared with Chi-square and. The threshold level for statistical significance was established at $p < 0.05$.

## RESULTS

There were 24 females (60%) and 16 (40%) males, a total of 40 patients in the IPD group whose mean age was 59.4±9.38 and mean duration for the neurological disease was 6.1±1.73 years. The control group consisted of 23 females (57.5%) and 17 males (42.5%), a total of 40 patients whose mean age was 59.9 ± 5.98. There were no significant differences between the groups regarding age and gender. (p: 0.240, p: 0.202, respectively).

Seven (17.5%) patients with IPD and 1 (2.5%) healthy control were screened for at least one ICD. Multiple ICDs were reported in 2 of 7 patients (28.57%) with IPD.

ICD was significantly more frequent in IPD patient group (p=0.002). All IPD patients with ICD were using the dopamine agonists (DA). 5 patients were taking pramipexole and 2 patients were taking ropinirole among ICD positive IPD patients. 20 of the 33 patients who had no ICD were using DA. DA was found to be a significant risk for ICD ($p = 0.043$).

There was a significant difference between the IPD and control groups according to total BIS-11 scores. IPD patients had higher impulsivity scores than controls. According to the subgroup analyses, cognitive and non-planning impulsivity were higher in IPD patients whereas motor impulsivity was higher in controls (Table 1).

When we compare ICD positive and negative IPD patients in terms of impulsivity, scores of total impulsivity and cognitive impulsivity and non-planning impulsivity were higher in ICD positive IPD patients whereas scores for motor impulsivity were similar (Table 2).

**Tablo 1**. IPD patients and controls

| Scores | IPD patients | Controls | p |
|---|---|---|---|
| BIS-11 (total) | 62.37±9.55 | 56.1±5.93 | 0.001 |
| Motor impulsivity | 16.9±3.95 | 22.24±3.64 | 0.001 |
| Non-planning impulsivity | 27.37±6.29 | 21.51±4.69 | 0.001 |
| Cognitive impulsivity | 18.47±3.67 | 12.62±2.34 | 0.001 |

IPD: Idiopathic Parkinson Disease, BIS: Barrat Impulsivity Scale

**Tablo 2**. IPD with and without ICD

| Scores | IPD patients with ICD | IPD patients without ICD | p |
|---|---|---|---|
| BIS-11 (total) | 74.8±4.8 | 59.7±8.09 | 0.001 |
| Motor ımpulsivity | 18.2±4.15 | 16.6±3.8 | 0.3 |
| Non-planning impulsivity | 33.8±2.8 | 26±6.02 | 0.002 |
| Cognitive impulsivity | 21.42±1.0 | 17.8±2.06 | 0.01 |

IPD: Idiopathic Parkinson Disease, ICD: Impulse control disorders, BIS: Barrat Impulsivity Scale

## DISCUSSION

The present study designed to estimate the frequency of Impulse Control Disorder (ICD) in patients with Idiopathic Parkinson's Disease (IPD) and to investigate impulsivity in IPD patients. ICD was detected in approximately one of six IPD patients. These results are keeping with the previous studies. (19) In our study, DA use found to be a risk factor for the development of ICD. This result agrees with the findings of other studies, in which DA usage was reported as the major risk factor for ICD in IPD patients. It has been demonstrated that DA mostly binds to D3 receptors located in the nucleus accumbens which controls reward and emotions. (20) Moreover, according to Trippmann the use of DA for different diseases such as restless leg syndrome also carries the risk for ICD. (21) Other risk factors identified for ICDs include male gender, young age, depression, smoking, drug abuse, Parkin mutation, and family history of ICD. (22-23)

The most common behavioral problem in our patients was CSB, followed by CB and PG, similar to previous studies (24). One unanticipated finding was that the frequency of PG was 5%, which was less than previous studies (25). It seems possible that these results are due to cultural norms and restrictions in gambling in Turkey. Thus, Kenangil et al who made a similar study in Turkey also failed to show a relationship between PG and IPD (26).

With respect to the second research question, the most clinically relevant finding is IPD patients had higher scores in total impulsivity, non-planning, and cognitive impulsivity but interestingly lower scores in motor impulsivity as compared with controls. As mentioned before, there is a notable paucity of case-control studies investigating the simultaneous impulsivity domains in IPD patients. Impulsivity is defined as a multidimensional structure and various psychopharmacological agents are thought to influence different stages of impulsivity. Patton grouped impulsivity into three main categories; (1) motor impulsivity, (2) attentive impulsivity, and (3) unplanned impulsivity. (27) Motor impulsivity is defined as acting without inhibition, attentive impulsivity is defined as the inability to focus on the ongoing task, and unplanning impulsivity is defined as in the ability to plan. (28) IPD treatment which includes the intake of levodopa and DA has been identified as potentially contributing to especially cognitive impulsivity. Behaviors like compulsive shopping and pathological gambling have been suggested to present evidence of disrupted cognitive impulsivity. Several studies reported the effect of dopamine replacement therapy in the cognitive and attention impulsivity and reported that these

domains were impaired in the patient group. (29-33) In contrast to this, a few studies addressed the motor impulsivity domain in IPD patients. In previous studies, motor impulsivity divided into two categories as reactive and proactive impulsivity. (34) Reactive impulsivity was defined as an inability to inhibit a motor program in the presence of a specific stop-signal, where the need to stop is considered to be irrevocable. Proactive impulsivity was defined as an impairment in withholding a response, where the stop-signal is motivated by external contextual cues, which helps to anticipate the inhibitory. (35) S Gauggel et al. evaluated proactive impulsivity by the Stroop signal test in 32 orthopedic patients and 32 IPD patients and they determined prolonged stop-signal reaction time in the IPD patients, independent of the severity of the disease and cognitive damage. (36) However, in the well-designed study of Antonelli, pramipexol was found to increase cognitive impulsivity but not influence motor impulsivity. The author suggested that different types of impulsivity were differentially sensitive to dopamine treatment and reported that DA influence neural networks underlying impulsive choices but not impulsive action. (37) Our results are According to these studies and indicate that İn IPD patients different domains of impulsivity are implicated in different ways.

The mesolimbic-frontal pathway is thought to be involved in the pathogenesis of risk-taking tasks. (38) Striatal outputs to the globus pallidus external and internal are thought to be involved in the pathogenesis of motor impulsivity. (39) Motor impulsivity has found to be associated with serotonergic and noradrenergic function respectively, whereas cognitive and attention impulsivity has found to be associated with dopamine function. (40-43)

Several limitations to this study needed to be acknowledged. Firstly these findings are limited by the small sample size. These findings suggest that non-motor aspects of the IPD may be overlooked if not questioned. Many patients with neuropsychiatric complaints are at risk of under-diagnosis and under-treatment. Behavioral neurologists must question these diseases to be able to manage the potential harms of these behaviors. According to our study, patients with IPD should be carefully monitored for increased impulsivity. It should be kept in mind that even IPD patients without ICD tend to have increased non-planning and cognitive impulsivity. Tests that only measures motor impulsivity may not be sufficient. Further studies might explore the underlying neurobiology if impulsivity seen in MS. Another possible area of future research would be to investigate how to treat patients with high impulsivity scores.

**Statement of Ethics:** This research was conducted in accordance with the World Medical Association Declaration of Helsinki. The local ethics committee approved the study.

**Informed Consent:** Written consent was obtained from the participants.

**Conflict of Interest:** Authors declared no conflict of interest.

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