Original Article

Impulsivity in multiple sclerosis: A paired case-control study

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Abstract

Aim: The presence of neuropsychiatric disorders in patients with multiple sclerosis (MS) has been recognized since Charcot first described the disease and reported at rates reaching 60%. However, knowledge about impulsivity which can significantly affect the quality of life of patients and their relatives is limited. In this study, we aimed to determine whether there is a relationship between MS and impulsivity.

Material and Methods: MS patients and healthy controls were included in this paired case-control study. The clinical (disability rate, duration of disease, clinical course) of MS patients and demographics (age, gender, income status, marital status, educational status) characteristics of the whole population were questioned. Beck depression scale and Barrat's impulsivity scale were applied to all participants. The patient and control groups were compared in terms of impulsivity. Considering that depression is frequently observed in MS patients and depression may affect impulsivity, the groups were compared again with covariance analysis.

Results: The study included 60 MS patients of whom 41 was female and 51 healthy controls of whom 40 was female. Cognitive impulsivity was significantly higher in the MS group, and the MS group was significantly depressive than the controls. This difference in cognitive impulsivity continued after the effect of depression stabilized.

Conclusion: Impulsivity was significantly higher in MS patients than in normal controls. Approaches that take into account impulsivity may be useful in the treatment of MS.

Keywords: Multiple sclerosis; impulsivity; neuropsychiatric symptom

INTRODUCTION

Multiple sclerosis (MS) is a chronic autoimmune disease of the central nervous system (CNS) caused by neuroinflammation and neurodegeneration (1). MS is accepted to be the leading cause of disability in young adults, affecting more than two million people worldwide. The presence of neuropsychiatric disorders in patients with MS has been recognized since Charcot first described the disease. There is a growing body of literature highlighting the significant impact of neuropsychiatric disorders on the daily functioning and quality of life of MS patients (2). These disorders can be even the first clinical sign of MS (3-4). Results from earlier studies demonstrated that depression is the most common neuropsychiatric disorder in MS. The annual prevalence rate of depression in MS patients ranges from 10% to 25%, which is about 5 times higher than that of the general population (5). Approximately one in two MS patients suffers from depressive episodes after the diagnosis of MS (6). However, depressive symptoms such as fatigue, loss of appetite and difficulty in concentration are thought to be related to the biological process associated with MS and the diagnosis of depression can be underdiagnosed. The under diagnosis of depression may result in suicide. The suicide rate in MS patients is 7 times the general population. Factors found to be influencing suicide in the general population have been explored in several studies; depression and impulsivity are reported as main factors (7-10).

The prevalence of depression and the underlying mechanisms in MS are well documented, however, there is limited data regarding the prevalence of impulsivity in MS. Impulsivity is defined as the tendency to show fast and unplanned responses to internal and external stimuli, without taking into account the negative consequences for the individual or others (11). Patton grouped impulsivity into three main categories; (1) motor impulsivity, (2) cognitive impulsivity, and (3) unplanned impulsivity (12). Motor impulsivity is defined as acting without inhibition, cognitive impulsivity is defined as the inability to focus on the ongoing task, and unplanning impulsivity is defined as in the ability to plan. Limbic structures such as the

orbitofrontal cortex, anterior cingulate gyrus, amygdala, and insula have been reported in the neurobiology of impulsivity. Besides, neurotransmitters such as dopamine, noradrenaline, glutamate, and GABA have been reported to be effective in this process (13).

Although neuroanatomical structures that may affect impulsivity are affected during MS, there is a notable paucity of studies focusing specifically on the impulsivity in MS patients. This study, therefore, was set out to determine whether there is an association between MS and impulsivity by conducting a paired case-control study. We hypothesized that patients with MS have higher levels of impulsivity than the general population. The present study may contribute a better understanding of impulsive behaviors seen in MS and may fill a gap in the literature.

MATERIAL and METHODS

Study Populatıon and Data Collectıon

This paired case-control study was conducted in a University Hospital. Clinically definite MS patients who were admitted to our demyelinating disease outpatient clinic between March 2019 and June 2019 were included in the study. Inclusion criteria for the patient group were as follows:

1. Being diagnosed with MS according to 2017 revision of Mc Donald criteria
2. Having a relapsing-remitting or secondary progressive course

Simultaneously age and gender-matched control group was created from hospital staff or relatives.

The exclusion criteria for both groups were as follows:

1. Cognitive impairment equivalent to a Mini-Mental Status score of 24 or less
2. The presence of any confirmed psychiatric disorder including substance abuse
3. Previous diagnosis of depression

The sample size was calculated using the Lemeshow formula (14).

Study Design

Demographical characteristics (i.e. age at disease onset, sex) and clinical characteristics (i.e. treatment, MS type) were obtained from Imed software. Disease duration was defined as the time from the first attack to the last control date. Participants completed the questionnaires designed to assess depression and impulsivity under the same physical conditions. In the first analysis, the patient and control groups were compared in terms of impulsivity. In the second analysis the groups were recompared in terms of impulsivity after the effect of depression stabilized by covariance analysis. Interferons, Glatiremar asetat, Dimetil Fumarat, Teriflunamid was defined as first step therapy; Fingolimod, Ocrelizumab, Natalizumab was defined as second step therapy; rituximab was defined as third step therapy.

Measures

Barrat Impulsıvıty Scale

Impulsivity was assessed by BIS which was developed by Ernest S. Barrat in 1959 and then revised several times. BIS-11 was used in the current study. The Turkish reliability and validity of BIS were performed by Güleç et al. 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 the 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 (15).

Beck Depressıon Scale

Beck depression scale consists of 21 items. The score of each item ranges from 0 to 3, and the total score is between 0 and 63. 0 to 9 points indicate minimal depression, 10 to 16 points mild depression, 17 to 29 moderate depressions, and 30-63 points to severe depression. Turkish validity and reliability study was carried out by Hisli (16-17).

Statistical Analysis

SPSS 23 was used as the statistical analysis program. Quantitative data were given as mean, standard deviation and categorical data were given as frequency and percentages. The normal distribution of the variables was determined using the Shapiro-Wilk test. For comparisons of the variables distributed normally between the groups, student t-test was used. For comparisons of the variables not distributed normally between the groups, the Mann Whitney U test was used. Categorical data were compared using the chi-square test or Fisher exact test. A p-value less than 0.05 were considered statistically significant. Depression scores were included in the covariance analysis (ANCOVA).

RESULTS

A total of 60 patients and 51 age and sex-matched controls were included in the study. The average age of the patient population was 38.43±11.34 and 81.6% were female. 11 of the control group were male and the average age was 37.12±11.67. There was no statistical difference between the groups in terms of age and gender. Clinical and demographic data of the study population are given in table 1. The mean EDSS of the patient population was 2.3 and the mean disease duration was 4.7 years.

There was no significant difference between the groups in terms of total impulsivity, unplanning and motor impulsivity score. Cognitive impulsivity was significantly higher in the patient group (Table 2).

Beck depression scores of the groups were statistically significantly different. (p: 0.001) MS group had higher depressive scores. Analysis was repeated after adjusting for BEck score. As a result of the covariance analysis, the total impulsivity scores and cognitive impulsivity scores of the patient group were significantly higher (Table 3).

Table 1. Demographic and Clinical Features of the Study Population

	Patients Group (n: 60)	Control Group (n: 51)	p
Female/Male (n)	49/11	40/11	0.67
Age (years)	38.43±11.34	37.12±11.67	0.55
Duration of disease (years)	4.7±5.5		
EDSS	2.3±1.4		
Alcohol Users (n)	9	8	0.92
Smokers (n)	10	11	0.51
Education Status			
Illiterate	1	0	.
Primary school	28	18	.
High school	12	19	.
University	7	14	
Clinical Phenotype			
RRMS	39	-	
SPMS	21	-	
Treatment Usage			
No Drug Use (n)	9	-	
1 Step Therapy Users (n)	25	-	
2 Step Therapy Users (n)	23	-	
3 Step Therapy Users (n)	3	-	
Depressive Scores (Mean SS)	18.11±8.5	13.18±4.6	0.001

RRMS: Relapsing Remitting Multiple sclerosis, SPMS: Sekonder Progressive Multiple Sclerosis
1 Step Therapy: Interferons, Glatiremar asetat, Dimetil Fumarat, Teriflunamid
2 Step Therapy: Fingolimod, Ocrelizumab, Natalizumab
2 Step Therapy: Rituximab
#Statistical evaluation could not performed due to small numbers

Table 2. Impulsivity Scores of the Study Population

	Grup		
	Patients Group (n: 60)	Control Group (n: 51)	p
Total Impulsivity (mean±SS)	26.78±5.86	25.82±5.32	0.37
Motor Impulsivity (mean±SS)	9.13±2.84	8.13±2.75	0.06
Nonplanning Impulsivity (mean±SS)	9.71±3.38	8.76±1.82	0.06
Cognitive Impulsivity (mean±SS)	9.16±2.68	7.92±1.73	0.005

Table 3. Impulsivity Scores of the Patient and Control Groups (ANCOVA)

	p	R^2
Total Impulsivity	0.02	0.05
Motor Impulsivity	0.15	0.05
Nonplanning Impulsivity	0.2	0.03
Attention Impulsivity	0.01	0.19

DISCUSSION

The present study was designed to determine whether there is a relationship between MS and impulsivity. The results of this study indicate that cognitive impulsivity is higher in MS patients. Since the effect of depression on impulsivity have been reported in previous studies, we evaluated impulsivity by fixing the effect of depression, as a result, the cognitive impulsivity was still high in MS patients. Considering all these, it can be said that

MS disease affects impulsivity and especially affects cognitive impulsivity. This effect seems to be independent of depression.

Euphoria and impulsivity can be observed during MS, have been known since Charcot's first description of the disease (18). So far, however, there has been little discussion about this relationship. Lopez-Meza reported a patient presenting with severe impulsivity symptoms as an initial MS attack presentation (19). A few years later, Fishman reported that euphoria and disinhibition are observed in 9% of MS, and these symptoms are consistent with a progressive course, impaired cognition, and high caregiver stress (20). In 2009, Smith et al published an FMRI study and reported that MS patients with cognitive impairment have disinhibition (21). Recently, Toro et al. published a study comparing MS and healthy people in terms of impulsivity (22). As a result of the study, total impulsivity, motor impulsivity, and cognitive impulsivity were found higher in the patient group. However, since the depression scores were significantly higher in the patient group, the author divided both groups into two subgroups according to the presence of depression. Cognitive impulsivity was found to be higher in patients without depression and the controls without depression. But there was no difference in terms of impulsivity between patents with depression group and controls with depression group. A possible explanation for these results may be the lack of an adequate number of controls with depression. So there were only 5 controls with depression. Our results are keeping with the study of Toro, cognitive impulsivity was higher even after considering the effect of depression.

The relationship between depression and impulsivity has not been clarified. Higher impulsivity levels at the onset of major depression and decreasing impulsivity after the drug treatment suggest that this condition might be a state-related effect rather than a personality trait (23).

Several limitations to this study needed to be acknowledged. The most important limitation lies in the fact that the effect of cognitive impairment on impulsivity is not considered. Therefore to control for bias, patients with cognitive impairment equivalent to a Mini-Mental Status score of 24 or less excluded from the study. However, demyelination, atrophy and neurodegenerative process observed in MS can cause cognition impairment even if it is not clinically detected (24). Another limitation in our study is that symptoms such as energy loss and fatigue observed in MS may coincide with the items on the scale of depression. It should be kept in mind that depression scores may not fully reflect the clinic. For this reason, we re-evaluated the groups by fixing the effect of depression. However, a key strength of the current study is the adequate number of the study population.

These findings suggest that cognitive impulsivity is high in MS disease. Although speculative, we think that the observed impulsivity is more related to neurobiological processes than the personality trait. When impulsivity is underdiagnosed, it significantly affects the quality of life of patients and relatives and can even cause suicide when it is accompanied by depression. Our work has created awareness of a topic that has such an important effect. Moreover as mentioned before there is a notable paucity of studies focusing on impulsivity. Our results also contribute a better understanding of impulsive behaviors seen in MS and fill a gap in the literature. 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 impulsive patients with MS.

CONCLUSION

In this study, we found that MS patients scored significantly higher on the cognitive impulsivity domain. Impulsivity is common in patients with MS, and patients need to be screened from this angle. Our findings support that MS and psychiatry specialists working collaboratively may help to overcome the impulsivity of the patients.

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