Affective Temperament Profiles in Patients with Multiple Sclerosis: Association with Mood Disorders

Multiple Skleroz Hastalarında Afektif Mizaç Özellikleri: Duygu Durum Bozukluklarıyla İlişkisi

Adile ÖZKAN¹, Kürşat ALTINBAŞ², Emine Rabia KOÇ³, Halil Murat ŞEN¹, Handan Işın ÖZIŞIK KARAMAN¹

¹Department of Neurology, Çanakkale Onsekiz Mart University Faculty of Medicine, Çanakkale, Turkey
²Department of Psychiatry, Çanakkale Onsekiz Mart University Faculty of Medicine, Çanakkale, Turkey
³Department of Neurology, Balıkesir University Faculty of Medicine, Balıkesir, Turkey

ABSTRACT

Introduction: The aim of this study was to screen for bipolarity and to investigate the affective temperaments of patients with Multiple Sclerosis (MS) and the possible association between clinical and demographic characteristics of MS patients and temperament profiles.

Methods: A total of 65 patients with MS and 66 healthy volunteers completed the HCl-32, the Mood Disorder Questionnaire (MDQ) and The Temperament Evaluation of Memphis, Pisa, Paris and San Diego-Autoquestionnaire version (TEMPS-A) tests. HCl-32, MDQ and TEMPS-A scores were compared between patients and healthy volunteers.

Results: MS patients had significantly higher scores for depressive, cyclothymic, irritable and anxious domains of the TEMPS-A scale compared to the control group. Relapsing remitting MS patients had higher MDQ and TEMPS-A hyperthymia scores compared to secondary progressive patients. MS patients who were being treated with interferon beta 1-b therapy had significantly higher MDQ scores than those being treated with interferon beta 1-a, glitamer acetate or who were without medication. Expanded Disability Status Scale (EDSS) scores were positively correlated with Temps-A depressive and hyperthymic temperaments.

Conclusion: Our results suggest that higher scores for affective temperament in MS patients may indicate subclinical manifestations of mood disorders. Higher hyperthymia scores and manic symptoms detected in the RRMS group could shed light on the relationship between bipolarity and multiple sclerosis. Thus, screening of bipolarity and affective temperament profiles in MS patients could help clinicians predict future mood episodes and decrease their impact on disease severity.

Keywords: Affective temperament, bipolarity, multiple sclerosis

ÖZET

Amaç: Bu çalışmanın amacı bipolarite taramak ve Multipl Skleroz (MS) hastalarında afektif mizaç özellikleri ve MS hastalarının klinik ve demografik özellikleri arasındaki olası ilişkiye ve mizaç profillerini araştırmaktır.


Bulgular: MS hastalarında afektif mizaç profilleri ve üstüne kategorik özelliklerde önemli bir fark vardır. RRMS grubunda görülen hiperthymia ve depresif mizaçlar,;textually impossible to transcribe.
laughing and crying, psychosis and personality disorders (PD) also reported among patients with MS (6,7,8,9). Hence, early diagnosis and treatment of these psychiatric symptoms have an important role in the prognosis and quality of life in MS, considering that psychiatric symptoms are more common than other neurological disorders (10,11). However, few studies have been reported to evaluate personality and temperament dimensions or the co-occurrence of bipolar disorders with MS (12,13,14,15,16).

There are a few studies that focused on personality characteristics in MS patients using different screening tools for mood disorders. Several chronic medical disorders are associated with mood disorders, and it has also been hypothesized that immune and neurodegenerative diseases may cause increased neuronal oxidative stress, which can lead to pathological processes in the brain area that affect the emotions in bipolar disorders (BD) (17). Carta et al. (18) evaluated the risk of bipolar disorders for MS patients and stated that a lifetime prevalence of manic/hypomanic episodes, DSM-IV bipolar and major depressive disorders was higher in MS patients than healthy controls. Previous studies have also emphasized that a lifetime prevalence of BD is more frequently seen in MS patients, but still the association between these two disorders is not fully determined (19,20).

Temperament as a heritable phenomenon describes the underlying biological and genetic tendencies of personality and provides to the automatic emotional response to events as establishing individual’s activity level, rhythms, mood and related cognitions types. Affective temperaments are thought to be subclinical forms of bipolar disorders (21). Akiskal et al. (22) identified five types of affective temperaments: depressive, hyperthymic, cyclothymic, irritable, and an anxious type known as The Temperament Evaluation of Memphis, Pisa, Paris and San Diego Autoquestionnaire (TEMPS-A).

The aim of this study was to evaluate (hypo)manic symptoms and affective temperaments and their relation with the clinical and demographic characteristics in patients with MS. Our main hypothesis was (hypo)manic symptoms are more common in MS and that mood disorder questionnaires and affective temperament scores would be higher than in a control group. Besides, there is a relation between bipolarity and affective temperament that has an impact on disease severity in MS.

METHODS

Subjects
Sixty-five clinically definite MS patients were recruited into the study that diagnosed with the McDonald criteria (23). Patients with hepatic disorders, renal disorders or who received corticosteroid therapy within three months prior to testing were excluded. The demographic and clinical data of the patients were documented.

Sixty-six age and sex matched volunteers were enrolled as control subjects who have no medical or psychiatric disorders. HCl-32, MDQ and TEMPS-A tests were applied to all subjects.

Measures

HCl-32
The hypomania checklist (HCL-32) including 32 yes/no questions to identify hypomanic symptoms with depressive episodes for diagnosing bipolar disorders. The standard cut-off points have been reported to be a score of 14 or higher for HCl-32 (24).

Mood Disorder Questionnaire (MDQ)
The MDQ was identified by Hirschfeld et al. (25) to assess the history of hypomanic or manic symptoms, and to screen for bipolar disorders. The first part consists of 13 (yes/no) questions that screen for lifetime history of hypomanic symptoms. The second part evaluates if two or more symptoms have been at the same time and the last part asks for the results of the symptoms reported in the first part. Konuk et al. (26) performed the validity and reliability of the Turkish version of the MDQ. The optimal cut-off points have been reported to be a score of 7 or higher for MDQ and 14 or higher for HCl-32. “Positive scores” that show high probability of a mood disorder are considered if scores are higher than the cut-off point (≥14) of the HCL-32 and MDQ (≥7 positive answers on the first item and yes answer for the second item) (27).

Temperament Evaluation of Memphis, Pisa, Paris, San Diego Autoquestionnaire (TEMPS-A)
The TEMPS-A is a self-report questionnaire consists 110 items to measure five affective temperament that define depressive, cyclothymic, hyperthymic, irritable and anxious (5). Vahip et al. (28) performed the validity and reliability of the Turkish version of TEMPS-A.

Statistical Analysis
All data were analyzed using the Statistical Package for Social Sciences version 19.0 (SPSS for IBM, Armonk, NY, USA). Normality of distribution in the groups was determined by Kolmogorov-Smirnov test. Datas were shown as mean ± SD (standard deviation). Differences between groups were performed with Mann-Whitney U and Student’s t-test for non-parametric or parametric values. Correlations between datas were analyzed using Pearson and Spearman correlation tests. P value <0.05 was considered statistically significant.

RESULTS

Demographic and Clinical Data of the Patient Group
70.8% (n=46) of the patients were female and most were married (78.5%, n=51). The mean age was 37.8±7.7 years. Their educational status was classified as: primary, high school or college, which were 26.7% (n=17), 38.5% (n=25), and 35.4% (n=23), respectively. Mean duration of the disease was 6.52±5.1 years. When we looked at the clinical subtype of MS, the sample consisted of two different groups: relapsing remitting (75.4%, n=49) and secondary progressive (24.6%, n=16). The mean EDSS score was 2.07±2.3. There was statistically significant differences between EDSS score of relapsing remitting MS patients and secondary progressive MS patients (the mean EDSS scores for RRMS:1.04±1.31; for SPMS 5.25±1.80; p<.001). When the patients were evaluated with regard to treatment: 14 (21.5%) patients were on interferon beta 1-a 30 µg/0.5 mL once a week, 16 (24.6%) patients were on interferon beta 1-a with a dosage of 44 µg three times per week, 18 (27.6%) patients were on interferon beta 1-b 9.6 MIU every other day, 12 (18.5%) patients were on glatiramer acetate 20 mg/mL once a day and 5 (7.7%) patients were medication free.

Comparison of the Mood Disorder Questionnaire and Temperament Scores between Patients and Control Groups
There were no statistically significant differences between groups both in gender (p=.49) and age (p=.69).

The proportion of patients with positive MDQ score was 18.5% (n=12) and 63.1% (n=41) for HCl-32 score. 12.3% (n=8) of the patients had positive scores for both MDQ and HCl-32.

The mean Temps-A scores of the patients were 8.9±4.3, 8.4±4.8, 7.9±4.8, 5.0±4.3, 8.4±5.8 for depressive, cyclothymic, hyperthymic, irritable and anxious temperament domains, respectively.
Comparison of the Temps-A scores between the groups revealed significantly higher scores for depressive, cyclothymic, irritable and anxious domains in MS patients than the control group (p=.002, p=.011, p=.033, p=.002, respectively). There were no significant differences for MDQ, HCl-32 and Temps-A hyperthymic scores between the groups (p=.2, p=.6, p=.8) (Table 1.2).

Comparison of the Mood Disorder Questionnaire and Temperament Scores According to Clinical Factors in the Patient Group

For the MS patients, there was a significant difference in MDQ and Temps-A hyperthymic scores in the relapsing remitting type compared to the secondary progressive type (p=.035, p=.036) (Table 3).

Comparisons due to treatment of MS patients for all scales indicated that patients who were on interferon beta 1-b had significantly higher MDQ scores than those who were on interferon beta 1-a and glitamer acetate or who were without medication, but not the interferon beta 1-a 3 group (p=.023, p=.006, p=.27, p=.198, respectively).

EDSS scores were found to be positively correlated with Temps-A depressive and hyperthymic scores (p=.046, r=.249; p=.011, r=-.312 respectively) (Table 4).

No correlation was found between disease duration and scores.

**DISCUSSION**

This is the first study screening both the affective temperament and bipolarity of MS patients using TEMPS-A-HCI-32 and MDQ. We found higher scores for TEMPS-A depressive, cyclothymic, irritable and anxious scores in MS patients compared to the control group. Higher MDQ and Temps-A hyperthymic scores were found in MS patients for the relapsing remitting type compared to the secondary progressive type. In addition, patients who were on interferon beta 1-b treatment had significantly higher MDQ scores than those taking interferon beta 1-a or glitamer acetate or who were without medication.

There are a few studies on personality characteristics of MS patients. Benedict et al. (28) have evaluated personality traits in MS patients using both the NEO Personality Inventory (NEO-PI) and the Hogan Empathy Scale (HES) and they also investigated the relationship between cognitive dysfunction and personality change. MS patients presented slightly higher neuroticism and lower extraversion and conscientiousness compared to healthy controls. They also indicated that low conscientiousness was a risk factor for cognitive impairment in MS patients.

In another study, Fazekas et al. (30) investigated temperament characteristics of MS patients with clinically isolated syndrome (CIS) and relapsing remitting MS (RRMS) patient scores using the Temperament and Character Inventory (TCI-125) scale. They found that higher scores of harm avoidance temperament was significantly associated with the increased lesion load per year of disease duration in their study. Another study was performed by Gazigolu et al. (31) to determine personality traits of MS patients using the TCI-125 scale, and they found increased harm avoidance and decreased self-directedness (SD) scores among MS patients compared to controls. Previous studies indicated that higher HA and lower SD scores are associated with neuroticism and depression (32).

Although depression is one of the most common psychiatric manifestation in MS, there is still limited data concerning bipolar disorder and MS coexistence. There are some hypothesis concerning the comorbidty of MS and BD, and one hypothesis is that the disease itself may cause psychiatric manifestations while another hypothesis suggests that both diseases have a common underlying pathophysiological process (33). Increased oxidative stress play an important role in the pathogenesis of multiple sclerosis which leads to lipid peroxidation and inflammation (18). Similarly, previous studies have shown oxidative damage in the pathophysiology of bipolar disorder (34) where some researchers indicated that the demyelinating lesions of MS patients occurs in special areas of the brain which regulates the affective functioning, emotions and pleasure involved in BD (35). Another hypothesis is genetic relationship between MS and bipolar disorder. It has been thought that there was a genetic link between MS and BD (36,37). Schiffer et al. (38) have demonstrated that human leukocyte antigen (HLA) genes were associated with both MS and bipolar disorder.

Taking these into account, it is important to diagnose the co-occurrence of BP in MS patients and clinicians should pay particular attention to treatment and the effects on quality of life in managing both diseases. On the other
Approximately ten years later, Relapsing remitting MS that characterised by episodic relapses and remission is the most seen type of the disease. Approximately ten years later, interferon beta 1-b and mood symptoms needs to be specifically related to RRMS. In our study, an interesting finding was that the patients who were on interferon beta 1-b treatment had significantly higher MDQ scores than those taking interferon beta 1-a or glitamer acetate or who were without medication. These higher scores might also indicate manic symptoms, not only depression. Thus, a causal relationship between interferon beta 1-b and mood symptoms needs to be clarified with further longitudinal studies.

Relapsing remitting MS that characterised by episodic relapses and remission is the most seen type of the disease. Approximately ten years later, most of the RRMS patients develops secondary progressive MS where symptoms get worse without any remission (44). Secondary progressive MS patients are more disabled and EDSS scores tend to be higher than relapsing remitting ones (45). Previous studies stated that there was a positive correlation between EDSS scores and disease severity or progression (46). Tsivgoulis et al. (47) indicated that higher EDSS was strongly associated with depression and anxiety in MS patients. Recently, Askari et al. (48) reported that both MS patients with higher EDSS scores and secondary progressive type MS sufferers had significantly higher BDI scores in their study. Consisted with these studies we found statistically higher EDSS scores in SPMS patients than relapsing remitting ones and also a positive correlation was determined between EDSS scores and TEMPS-A depressive and hyperthymic scores.

Many studies reported that affective temperament subtypes were associated with mood disorders, and higher temperament scores might indicate a liability toward specific mood syndrome (49). In the light of this evidence, the correlation of EDSS and hyperthymic-depressive temperament scores could be explained as an impact of the comorbidity of MS and mood disorder liability on disease severity.

There are some limitations of this study. First, our sample size was relatively small and the study was of cross sectional design. Second, there was an absence of psychiatric evaluation of the patients. Third, the heterogeneity of the sample limits the generalizability of our findings.

In conclusion, our study is the first to evaluate both bipolarity and affective temperament of MS patients. The high scores of affective temperaments, in which we found greater scores for RRMS patients with known subclinical manifestations of mood disorders, supports the high comorbidity rates of mood disorders in MS. The diagnosis and treatment of psychiatric disorders in MS patients is important, because they affects quality of life, prognosis and also treatment adherence of MS patients. Thus, screening of bipolarity and affective temperament profiles in MS patients could help clinicians predict future mood episodes and decrease their impact on disease severity.

**Conflict of Interest:** No conflict of interest was declared by the authors.

**Financial Disclosure:** The authors declared that this study has received no financial support.

**Çıkış弥sma:** Yazarlar çikar çatışması bildirmemişlerdir.

**Finansal Destek:** Yazarlar bu çalışma için finansal destek almadıkları beyan etmişlerdir.

**REFERENCES**


