



Relationship of Number of Depression Episodes with Depression Severity, Treatment Adherence, Stress, Personality, Executive Functions and Decision-Making

Depresyon Atak Sayısının Depresyon Şiddeti, Tedavi Uyumu, Stres, Kişilik, Yürütücü İşlevler ve Karar Verme ile İlişkisi

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ABSTRACT

Major depressive disorder (MDD) is a psychiatric disorder that significantly affects the world population. The aim of this study was to investigate the relationship between the number of episodes and severity of depression, treatment adherence, perceived stress, personality, executive functions and decision making in MDD patients. Measurement tools including Beck Depression Inventory (BDI), Morisky Medication Adherence Scale (MMAS), Perceived Stress Scale (ASO-14), Temperament and Personality Inventory-Revised Form (TCI-R), Wechsler Memory Scale-III/Letter-Number Sequence Subtest (HSD), Wisconsin Card Sorting Test (WCST), Stroop Test TBAG Form (STR) and Iowa Gambling Task (IGT) were used in the study. The findings of the study showed that the severity of depression in MDD was not related to the number of episodes ($r=-0.051$, $p>0.05$) and treatment compliance ($r=-0.082$, $p>0.05$), but there was a significant relationship between the number of episodes and treatment compliance ($r=-0.880$, $p<0.001$). As the number of episodes increased, the perceived stress level and the level of knowledge about treatment decreased, whereas reward addiction and novelty seeking among personality traits increased. Executive functions and decision-making functions were also found to be weaker in MDD patients with recurrent episodes. The severity of depression in MDD was not associated with the number of episodes and medication adherence, suggesting that other variables associated with recurrent episodes should be addressed. In cases of recurrent MDD, in addition to factors such as medication adherence, perceived stress and personality, executive functions and decision-making behavior are also influential and should be closely monitored. Thus, it seems necessary to evaluate cognitive intervention options in the follow-up and treatment process of MDD.

Keywords: Depression severity, number of episodes, stress, personality, medication adherence, executive functions, decision making

ÖZ

Majör depresif bozukluk (MDB) dünya popülasyonunu önemli düzeyde etkileyen psikiyatrik bozukluklardan bir tanesidir. Bu çalışmada MDB hastalarında atak sayısı ile depresyon şiddeti, tedavi uyumu, algılanan stres, kişilik, yürütücü işlevler ve karar verme arasındaki ilişkinin araştırılması amaçlanmıştır. Araştırmanın örneklemini MDB tanısı almış kişilerden oluşmaktadır. Araştırmada Beck Depresyon Envanteri (BDE), Morisky Tedavi Uyum Ölçeği (MTU), Algılanan Stres Ölçeği (ASO-14), Mizaç ve Kişilik Envanteri-Gözden Geçirilmiş Form (MKE-R), Wechsler Bellek Ölçeği-III/Harf-Sayı Dizisi Alt Testi (HSD), Wisconsin Kart Eşleme Testi (WKET), Stroop Testi TBAG Formu (STR) ve Iowa Kumar Testi (IKT) olmak üzere 8 tane ölçme aracı kullanılmıştır. Araştırma bulguları MDB'de depresyon şiddetinin atak sayısı ($r=-0,051$, $p>0,05$) ve tedavi uyumu ile ilişkili olmadığını ($r=-0,082$, $p>0,05$), ancak atak sayısı ile tedavi uyumu arasında anlamlı düzeyde ilişki olduğunu ($r=-0,880$, $p<0,001$) göstermiştir. Atak sayısı arttıkça algılanan stres düzeyinin ve tedaviye dair bilgi düzeyinin azaldığı, kişilik özelliklerinden ödül bağımlılığı ve yenilik arayışının ise arttığı görülmüştür. Yürütücü işlevler ve karar verme işlevlerinin de tekrarlayan atakları olan MDB hastalarında daha zayıf olduğu saptanmıştır. Bu çalışmada MDB'de depresyon şiddetinin atak sayısı ve tedavi uyumu ile ilişkili olmadığı görülmüş ve bu durum tekrarlayan ataklarla ilişkili diğer değişkenlerin ele alınması gerektiğini düşündürmüştür. MDB'nin yineleyici olduğu durumlarda tedaviye uyum, algılanan stres ve kişilik gibi etmenlerin yanı sıra yürütücü fonksiyonların ve karar verme davranışının da etkili olduğu ve önemle takip edilmesi gerektiği düşünülmektedir. Bu durumda MDB'nin takibinde ve tedavi sürecinde bilişsel müdahale seçeneklerinin de değerlendirilmesi gerekli görülmektedir.

Anahtar sözcükler: Depresyon şiddeti, atak sayısı, stres, kişilik, tedavi uyumu, yürütücü işlevler, karar verme

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Introduction

Disorders affecting mental health have become the focus of more attention worldwide with each passing day. Major Depressive Disorder (MDD), one of the mood disorders, is a common disorder among psychiatric disorders and adversely affects the quality of life (Aydemir et al. 2009). The World Health Organization (WHO) stated in its 2017 data that MDD is one of the most prevalent psychiatric disorders and that there was an 18.4% increase in the prevalence of MDD between 2005 and 2015.

The severity of MDD can be different, and this severity is categorized as mild, moderate, and severe based on the quality and quantity of symptoms (Kılınç and Torun 2011). Although MDD is a treatable mental disorder, just like many others, individuals diagnosed with MDD may experience an increase in symptoms after recovery (Anber et al. 2021). A diagnosis of recurrent MDD is indicated in patients with at least two episodes of depression. According to The Diagnostic and Statistical Manual of Mental Disorders (DSM-5), recurrent MDD requires periods separated by at least two months in which the patient does not manifest significant depressive symptoms (Köroğlu 2015). Between 75% and 95% of patients with a depressive episode will have at least one more episode in their lifetime (Hales and Yudofsky 2004). Each subsequent episode is associated with a worse prognosis and less response to pharmacologic treatment (Köroğlu 2015, Torun 2019).

Some studies reported that the severity of depression did not differ significantly by the number of episodes (Lampe et al. 2004, Karabekiroğlu et al. 2008). Other researchers noted that the severity of depression leads to the recurrence of MDD. Furthermore, the severity of depression disrupts treatment adherence (Işık et al. 2013, Köroğlu 2015). Treatment adherence requires the patient to acknowledge and adhere to health-related treatment recommendations, comply with the necessary controls for treatment, use medications regularly, and make recommended behavioral changes (Demirkol and Tamam 2016). Only 10% of patients diagnosed with MDD receive adequate doses and duration of medication, and more than half of the patients receiving treatment discontinue treatment within three weeks (Ervatan et al. 2003, Thase and Rush 1997). There are differing findings in the relevant literature regarding the relationship between the number of episodes, severity of depression, and medication adherence in patients with MDD. In this context, investigating the relationships between these variables will contribute to existing research in the literature.

Many factors affect the course of depression. Stress, which is assumed to be one of these factors, has a significant relationship with mental health in some scientific studies (Çevik and Şentürk 2008). A study comparing stress-coping skills between the control and MDD groups concluded that the MDD group had relatively weaker stress-coping skills and that MDD patients had dysfunctional stress management (Özarslan et al. 2013). Akkaya et al. (2013) found that health problems and family or domestic problems, as stressors, decreased treatment response. Similarly, another study confirmed the role of stress in the development of depression (Helvacı-Çelik and Hocaoğlu 2016). Namely, studies suggest that MDD patients cannot cope with stress or use inappropriate coping methods. Therefore, it is crucial to determine the perceived stress levels of MDD patients and assess the relationship with the number of episodes.

As in many psychiatric disorders, a personality disorder is a predisposing factor for depression (Aslan 2008). When the studies on MDD and personality are considered, high harm avoidance, low cooperation, and self-management scores in depression patients are correlated with depression severity (Hansenne et al. 1999). A different study also showed that patients with depression had high harm avoidance scores and low self-directedness scores, and the harm avoidance sub-dimension was a risk factor for the recurrence of depression (Teraishi et al. 2015). According to Bajraktarov et al. (2017), people with recurrent MDD episodes have different temperaments and personality characteristics. These individuals had low self-directedness and high harm avoidance scores, while high novelty-seeking and reward-dependence subtests were identified as risk factors for depression. Wiegand and Godemann (2017) revealed that the recurrence rate of MDD in the presence of personality disorder was almost twice as high within a year. The depressive symptoms experienced, and the duration of hospitalization were longer. In this context, determining which personality traits have a more prominent role in recurrent MDD cases is critical.

Executive functions are independent, purposeful, self-directed, and self-serving processes that address what a person will do about a task or subject or how to do that task or subject (Lezak et al. 2012). Executive functions (Smith and Kosslyn 2013), summarized as good problem-solving to achieve a goal and maintain the set-up, are responsible for coordinating mental activity (Karakaş and Karakaş 2000). Miyake et al. (2000) classified the tasks of executive functions into three categories: modifying setup, updating (updating and monitoring working memory representations), and inhibition (blocking dominant responses).

Executive functions are acknowledged to be adversely affected by prefrontal cortex dysfunction, and therefore it is expected that MDD patients show impairments in executive function tests (Karabekiroğlu et al. 2010). Although Alexopoulos et al. (2015) reported no significant relationship between low executive function test performances and depression in their study, the limited sample size and the fact that the severity of depression was not measured necessitates a cautious approach to their results. Indeed, many studies have suggested that depression has some neuropsychological effects (Must et al. 2013).

Recent studies indicate that depression is closely related to attention, memory, and higher-order cognitive function changes. In studies comparing MDD and control groups, the MDD group performed lower in executive functions (Lampe et al. 2003, Paelecke-Habermann et al. 2005, Knight and Baune 2012, Kotan et al. 2018, Varghese et al. 2021). Bringer et al. (2005) suggested that the impairment in executive functions of depressed individuals recovered during the remission period. Li et al. (2021) stated that cognitive impairment is primarily manifested by dysfunction between the frontoparietal network and the Default Mode Network. This impairment manifests itself as deficits in attention, memory, and attention maintenance. However, they also stated that these deficits improved during the remission period. Lampe et al. (2003) also reported some impairments in executive functioning in patients with recurrent MDD compared to healthy individuals. A comparison of MDD patients with the first episode and recurrent episodes revealed poorer executive functioning in the MDD group with recurrent episodes (Karabekiroğlu et al. 2010). Aker et al. (2014) detected significantly more negative emotional responses, ruminative behavior and suppression, and less cognitive reappraisal in patients with recurrent MDD. However, an important limitation of that study is that the sample consisted only of women and therefore did not address gender differences. Mackin et al. (2014) found that executive dysfunctions were also impaired with depression in older adults. However, this impairment may also be related to the aging process.

Another study observed differences in cognitive functions between first- and second-episode MDD patients regarding cognitive functions and concluded that impairments in executive functions increased with recurrent episodes (Talarowska et al. 2015). The small sample size and age differences of the participants were considered limitations in this study. Albert et al. (2018) reported that the executive functions of patients weakened as the duration of depression and the number of episodes increased. However, the severity of depression did not affect executive function functions. Likewise, in another study, patients with a lifelong and recurrently progressive MDD diagnosis had lower executive function performance, and the consequences in psychosocial areas were more pronounced (De Nooij 2020). Roca et al. (2019) emphasized that impaired neurocognitive functions (in all stages of depression) in MDD patients may be associated with suicidal behavior and that neurobiological studies may find a marker to define suicidal behavior. There are also studies in which changes in the components of executive functions related to MDD are examined separately. Many researchers have suggested that working memory capacity is weaker in MDD compared to the control group (Stordal et al. 2004, Rose and Ebmeier 2006, Smith et al. 2006, Gohier et al. 2009, Parlar et al. 2016).

Psychomotor retardation in depression was associated with working memory in another study comparing the experimental and control groups (Nikolin et al. 2021). Yüksel et al. (2018) reported abnormal functional changes in the frontoparietal region related to working memory load, particularly in recurrent MDD cases. Abnormal functional connections between frontal and parietal regions in MDD patients have contributed to working memory impairment in MDD (Cao et al. 2021). Inhibition in MDD was also lower than in the control group (Gohier et al. 2008, Karabekiroğlu et al. 2010, Dai and Feng 2011, Rizk et al. 2017). According to Hasler et al. (2004), the attention dimension of executive functions does not fully recover functionally even after the clinical remission of MDD. Paelecke-Habermann et al. (2005) reported that attention processes were impaired in MDD compared to the control group, but there was no significant difference according to the number of episodes. In another study by Stordal et al. (2004), the MDD group with recurrent attacks was less successful in inhibition and set-up switching performances than the control group. As can be seen, there are discrepant findings in the relevant literature for attention and inhibition dimensions. Liu et al. (2021) detected a significant difference between the experimental and control groups in the ability to change the set-up in MDD patients, while no significant difference was noted between the first and recurrent episode patients in the performance for changing the set-up. However, they also stated that the ability to change the set-up, which was impaired in the first episode, did not improve after remission and that there was a progressive deterioration of the skill of changing the set-up with each depressive episode. There are many studies in the literature on the relationship between the number of episodes of depression and executive functions, and differing findings have been obtained from time to time in these studies. In the current study, the researchers aimed to contribute to the literature by reconsidering executive differences according to the number of depression episodes.

Decision-making behavior, defined as the best choice among possibilities and as evaluating a situation and taking action or continuing to remain inactive, is a high-level cognitive process (Brand et al. 2005, Smith and Kosslyn

2010). Must et al. (2006) indicated that patients diagnosed with MDD had poor decision-making skills. However, in their study, participants whose executive functions were largely intact had more healthy decision-making processes if their depression was not severe. In one study on decision-making behavior and depression, MDD has been shown to affect decision-making processes (Rinaldi et al. 2020). Baeza-Velesko et al. (2020) suggested addressing decision-making processes when evaluating MDD. Siqueira et al. (2018) noted that the decision-making processes of young adults diagnosed with MDD and older individuals were more impaired than healthy control groups. In a study of adolescents in which MDD-diagnosed and healthy control groups were compared, depressed adolescents exhibited impaired sustained attention, and depressed males exhibited less advantageous decision-making (Han et al. 2011). In such a case, different findings have been obtained concerning the number of episodes in MDD and decision-making behavior, which is a high-level cognitive process. More research is necessary to explain the relationship in this context.

In previous studies on MDD cases, depression severity, number of episodes, medication adherence, perceived stress, executive functions, and decision-making variables were examined, and conflicting findings were sometimes obtained. In the present study, it is hypothesized that there is a significant relationship between depression severity, medication adherence, and number of episodes. Additionally, the perceived stress levels and personality traits of MDD patients are predicted to differ according to the number of episodes. Finally, the executive function test performances and decision-making performances of MDD patients are predicted to differ depending on the number of episodes.

Method

Sample

The study sample consists of patients diagnosed with MDD with first and recurrent episodes who applied to the Psychiatry Outpatient Clinic of Kartal Dr. Lütfi Kırdar City Hospital in 2020-2021. Participants were selected for the study by convenience sampling. A total of 113 participants were recruited during the data collection process. First of all, as age and educational status are confounding variables for neuropsychological test performances (Karakas 2006), the sample was limited to those between the ages of 30-45 and having a high school education level. In this context, 57 participants were evaluated within the scope of the study. The inclusion criteria included being predominantly right-handed, not having any other psychiatric disorder, personality disorder, mental-developmental retardation, physical disability, neurological disorder, hereditary disease, and not having alcohol, substance, and drug use at a level that would affect cognitive processes. The sample size was calculated as 40 people, 20 for each group in the power analysis (power: 0.80, α : 0.05, d: 0.89). The number of cases in the study was deemed sufficient, with 41 participants who met the inclusion criteria. While 48.8% (n=20) of the participants were admitted to the hospital for the first time with depressive symptoms, 51.2% (n=21) were admitted for recurrent depressive episodes. Of the sample, 85.4% (n=35) were female, and 15.6% (n=6) were male. The mean age of the sample was calculated as mean=37.4 (SD=4.5). The mean depression severity of the participants was mean=22.7 (SD=7.9).

Measures

General Information and History Form, Beck Depression Inventory (BDI), Morisky Treatment Adjustment Scale (MTAS), Perceived Stress Scale (PSS), Temperament and Character Inventory-Revised Form (TCI-R), Wechsler Memory Scale-III, Letter-Number Sequence Subtest (LSS), Wisconsin Card Sorting Test (WCST), Stroop Test TBAG Form (STR) and Iowa Gambling Test (IGT) was applied in the research.

General Information and History Form

A semi-structured history form was developed to determine the sociodemographic characteristics of the participants and to assess the participant's compliance with the inclusion and exclusion criteria of the study. With this form, the participant's contact information, gender, date of birth, educational status, employment and income status, family information, detailed medical history about the course of the disorder, other psychiatric, neurological, and hereditary diseases, mental-developmental retardation and physical disabilities, any visual impairment and hearing difficulties, dominant hand preference, alcohol, substance, and drug use at a level that would affect cognitive processes were obtained. A psychologist administered the form, and the patient's suitability for participation in the study was evaluated in the presence of a psychiatrist.

Beck Depression Inventory (BDI)

The BDI is a 21-item scale developed by Beck (1961) to measure the severity of symptoms of depression in adults. Hisli completed the scale's Turkish adaptation, validity, and reliability study in 1988 and 1989. Hisli (1989) found the item analysis coefficient of the scale to be 0.80 and the two-half reliability coefficient to be 0.74. In the present study, the Cronbach Alpha coefficient of the scale was 0.88. In the Beck Depression Inventory, which is a 21-item self-report scale, there are different verbal expressions in the "a," "b," "c," and "d" options. These items score "0", "1", "2," and "3" respectively. The lowest score on the scale is 0, and the highest is 63.

The Morisky Medication Adherence Scale (MMAS)

The self-report-based scale developed and validated by Morisky et al. (1986) assesses medication adherence. The validity and reliability study in Turkey was conducted by Vural et al. (2012). There was no statistically significant difference ($p > 0.05$) in the answers given to the pre-test and post-test questions, and it was concluded that the scale would help evaluate adherence to long-term drug treatment in chronic diseases in primary care (Vural et al. 2012). The 6-item scale consists of "yes" and "no" answers. In the rating, a yes answer is 1 point, and a no answer is 0 points in questions 2 and 5; in the other questions, a yes answer is 0 points, and a no answer is 1 point. If the participant's total score from questions 1, 2, and 6 is 0 or 1, it indicates a low motivation level; if it is greater than 1, it indicates a high motivation level. If the participant's total score from questions 3, 4, and 5 is 0 or 1, it indicates a low level of knowledge; if it is greater than 1, it indicates a high level of knowledge (Vural et al. 2012).

Perceived Stress Scale (PSS)

The Perceived Stress Scale (PSS) is a 14-item self-report scale developed by Cohen et al. (1983) that measures the extent to which people perceive situations in their lives as stressful. The scale was adapted to Turkish, and its validity and reliability study was conducted by Eskin et al. (2013). The internal consistency coefficient of the scale was 0.86, and the test-retest reliability coefficient was 0.87. In the current study, Cronbach's alpha coefficient was 0.89. There are reverse-scored items in the scale. The total score that can be obtained from the scale is between 0-64, and a high score indicates a high perceived stress level (Eskin et al. 2013).

Turkish Version of the Revised Temperament and Character Inventory (TCI-R)

In the study, the Turkish version of the Revised Temperament and Character Inventory (TCI-R) was used to determine the temperament and personality characteristics of the participants. The English form of the Temperament and Character Inventory ("TCI") (Version 9, 240 items) developed by Cloninger et al. (1993) within the framework of the seven-factor psycho-biological personality model of Cloninger was translated into Turkish by Köse et al. (2004), and validity and reliability analyses of the scale were performed. The revised form of the scale (TCI-R) was carried out by Yalçın (2017). While the internal consistency coefficient of the TCI-R for the whole scale was determined to be 0.85, it was 0.81 in the present study. In the TCI-R, the temperament subscale, Perseverance (SE), was developed and divided into four subscales. In addition, the 5-point Likert scoring type was changed from a true-false response format. In the temperament section, there are Novelty Seeking (NS), Harm Avoidance (HA), Reward Dependence (RD), and Perseverance (P) dimensions. Novelty Seeking (NS) and Harm Avoidance (HA) consist of four subscales, while Reward Dependence (RD) and Perseverance (P) consist of three subscales. In the character dimension, there are Self-Directedness (SD), Cooperativeness(CO), and Self-Transcendence (ST) dimensions. While Self-Directedness (SD) and Cooperativeness(CO) consist of five subscales, Self-Transcendence (ST) consists of three subscales (Köse et al. 2009).

Wechsler Memory Scale-III, Letter-Number Sequence Subtest (LNS)

Turkish adaptation studies for different subtests of the Wechsler Memory Scale-III were conducted by Ant (2005) and Özdemir (2005). The Letter-Number Sequencing Subtest (LNS), one of the subtests of the Wechsler Memory Scale-III, was used to assess working memory, one of the prefrontal cortex functions. The total Cronbach's alpha coefficient of the subtest was .90 (Ant 2005). In the present study, the Cronbach Alpha coefficient of the scale was 0.90. The test consists of 7 items. Each item has three trials. The correct completion of each of these trials is worth 1 point. The test is terminated if the participant fails three attempts at an item. The highest score the participant can get from the test is 21. The administration time is approximately 5-10 minutes.

Wisconsin Card Sorting Test (WCST)

The original version of the WCST was first developed by Berg (1948) to assess abstract thinking skills and cognitive flexibility. Afterward, it was revised and reorganized by Heaton (1981) and expanded and finalized by

Heaton et al. in 1993. Standardization studies were conducted for the Turkish version of the WCST within the scope of the BILNOT Battery, and the standardized instructions and recording form of the test were developed by Karakaş in 2006. The reliability of the WCST cannot be determined due to its nature (Karakaş 2006). In the test, the total number of responses (WCST 1), the total number of errors (WCST 2), the total number of correct responses (WCST 3), the number of completed categories (WCST 4), number of perseverative responses (WCST 5), number of perseverative errors (WCST 6), number of non-perseverative errors (WCST 7), percentage of perseverative errors (WCST 8), A total of 13 points are obtained, including the number of responses used to complete the first category (WCST 9), the conceptual level response number (WCST 10), the conceptual level response percentage (WCST 11), failure to maintain the construction (WCST 12) and learning to learn (WCST 13) (Karakaş 2006). The application takes approximately 15-20 minutes.

Stroop Test TBAG Form (STR)

The first form of the Stroop Test was developed by Stroop (1935) and formed the basis of many forms created later. The Stroop Test-TBAG Form used in the study was prepared by Karakaş et al. (1999), and a standardization study of the Stroop Test-TBAG Form was conducted by Karakaş (2006). Due to the nature of the test, internal consistency could not be calculated; test-retest results were found to be .56 for the fifth section (2nd card), where the Stroop effect was observed. The other sections ranged between 0.26 and 0.88 (Karakaş et al. 1999). The test measures psychomotor speed, the ability to change the perceptual setup in the face of changing demands and disruptive effects, and the ability to suppress a habitual behavior pattern (e.g., inhibit the behavior) and consists of 5 sections. The test is scored in three ways. These are the time from the start command until the last stimulus is read (STR 1, STR 2, STR 3, STR 4, and STR 5), the number of errors in each section (E), and the number of corrections in each section (D) (Karakaş 2006). The administration time is approximately 5-10 minutes.

Iowa Gambling Task (IGT)

The Iowa Gambling Task (IGT), developed by Bechara et al. in 1994, is sensitive to ventromedial prefrontal cortex functions (İçellioglu 2015) and assesses the ability to make appropriate decisions in uncertain situations. The validity and reliability study of the IGT in Turkey was conducted by Güleç et al. (2007), and the norm study was completed by İçellioglu (2015). In the reliability and validity study of the test, the internal consistency coefficient (Cronbach's alpha) was found to be 0.76. While the inter-rater reliability coefficient (rho) was found to be 0.99, the Cronbach Alpha coefficient of the scale was 0.81 in the current study. The task calculates net scores obtained separately in 5 blocks (IGT 1, IGT 2, IGT 3, IGT 4, and IGT 5). Changes in the net scores for blocks indicate how the learning process was throughout the test. At the end of the test, behavioral performance in the task (IGT TP) is evaluated by calculating the values obtained when 100 card selections are completed (Bechara 2007). In addition, the risky card selection score (IGT C-A) is obtained for risky selection behavior. The application takes approximately 15-20 minutes.

Procedure

This quantitative and cross-sectional study was conducted in the Psychiatry Outpatient Clinic of Kartal Dr. Lütfi Kırdar City Hospital between 10.04.2020-30.12.2021. The ethics committee permission for the research was obtained from Kartal Dr. Lütfi Kırdar City Hospital Clinical Research Ethics Committee. The application (Decision No: 2020/514/169/8) was approved by the ethics committee convened on 02.01.2020. In Kartal Dr. Lütfi Kırdar City Hospital Psychiatry Outpatient Clinic, the personal histories and diagnostic criteria of the participants diagnosed with first and recurrent episode MDD by the Psychiatry Specialist were recorded in the information management system of the institution, and these participants were referred to the Psychology Unit to be included in the study. Participants were first asked to read the informed consent form. In the next stage, semi-structured interviews were conducted with the participants who read the informed consent form and agreed to participate in the study. The General Information and History Form created by the researchers was filled out. In line with the information received, participants who met the study's inclusion criteria were asked to fill in the self-report scales. Afterward, appointments were made for neuropsychological test applications. Neuropsychological tests were administered by an institutional psychologist who had acquired test administration competence within the scope of graduate courses. Neuropsychological tests were administered in different orders to minimize the order effect.

Statistical Analysis

SPSS 21 Program (Statistical Package for the Social Sciences) was used for statistical analysis of the data. The researchers performed a statistical analysis of the data. In the first stage, the conformity of the data to the

normal distribution was examined according to the condition that the skewness values were between -2 and +2, and the kurtosis values were between -7 and +7 (Hair et al. 2010, Byrne 2010). Parametric test analyzes were performed with the data that met this condition. Firstly, descriptive statistical analyses (percentage distributions, mean, standard deviation) were used within the study's scope. Subsequently, Pearson correlation analysis was performed to see the relationship between the number of episodes, depression severity, and treatment adherence. Then, a cross-tabular analysis was conducted to examine the relationship between the number of episodes and the treatment adherence scale's motivation and knowledge level sub-dimensions. Finally, Independent Groups t-Test analysis was performed to test whether perceived stress, personality dimensions, executive functions (working memory, set-up maintenance, inhibition), and decision-making functions differed according to the number of episodes.

Results

There was no significant relationship between the number of episodes of depression and depression severity in MDD patients ($r=-.051$, $p>.05$). There was also no significant relationship between depression severity and medication adherence ($r=-.082$, $p>.05$). A strong and negatively significant correlation was determined between the number of depression episodes and medication adherence ($r=-0.88$, $p<0.001$). In this regard, as the number of episodes of depression increased, medication adherence decreased (Table 1).

Table 1. Relationship between number of episodes, depression severity and medication adherence

	Number of episodes	BDI
Number of episodes	1	
BDI	-0.051	1
MMAS	-0.880***	-0.082

BDI: Beck Depression Inventory score, MMAS: Morisky Medication Adherence Scale

According to the results of the analysis performed to examine the relationship between the number of episodes in MDD patients and the motivation level and knowledge level sub-dimensions of the MTU scale, no significant relationship was observed between the motivation levels of depression patients with first and recurrent episodes ($\chi^2=0.016$, $p=0.901$) (Table 2).

Table 2. Cross table analysis regarding the number of depression episodes and treatment motivation level

	High		Low		Total		χ^2	p
	N	%	N	%	N	%		
First episode	12	60	8	40	20	100	0.016	.901
Recurrent episode	13	61.9	8	38.1	21	100		
Total	25	61	16	39	41	100		

MDD patients with recurrent episodes had significantly lower levels of knowledge about treatment than first episode MDD patients ($\chi^2=8.497$, $p=0.004$), (Table 3).

Table 3. Cross table analysis on the number of depression episodes and level of treatment knowledge

	Level of Treatment Knowledge						χ^2	p
	High		Low		Total			
	N	%	N	%	N	%	8.497	0.004
First episode	18	90	2	10	20	100		
Recurrent episode	10	47.6	8	52.4	21	100		
Total	28	68.3	10	31.7	41	100		

According to the research findings, there was a significant difference between the groups concerning the perceived stress level by the number of depression episodes ($t=2.61$, $p=0.013$). In this respect, the mean perceived stress level of first-episode depression patients was higher than that of depression patients with recurrent episodes. This difference implies that patients with recurrent episodes perceive stress less. Help-Seeking (SA) and Reward Dependence (RD) dimensions, which are sub-dimensions of the TCI-R, also differed significantly by the number of depression episodes ($t=-10.34$, $p=0.000$), ($t=-7.29$, $p=0.000$). Thus, the help-seeking and reward-dependence characteristics of MDD patients with recurrent episodes were higher than those of first-episode MDD patients. The dimensions of Harm Avoidance (HA), Perseverance (P), self-directedness (SD), cooperativeness (CO), and self-transcendence (SR) did not differ significantly by the number of depression episodes ($t=0.57$, $p=0.566$), ($t=0.082$, $p=0.414$), ($t=-0.93$, $p=0.356$), ($t=-0.32$, $p=0.750$), ($t=-0.06$, $p=0.951$), (Table 4).

When the results of the analysis of the LNS scores according to the number of depressive episodes were analyzed, a significant difference was detected between the two groups according to the number of episodes by LNS score

($t=5.33$, $p=0.000$). Hence, MDD patients with recurrent depressive episodes showed lower performance in working memory functions.

Table 4. Relationship of the number of depression episodes with perceived stress level and personality factors

	First episode (N:20)		Recurrent episode (N:21)		t-Test	df	p	Cohen's d
	Mean	SD	Mean	SD				
PS	36.05	8.45	28.61	9.65	2.61	39	0.013	0.81
NS	88.00	5.80	105.90	5.28	-10.34	39	0.000	3.22
HA	112.30	18.59	109.04	17.39	.57	39	0.566	0.18
RD	87.95	8.53	105.52	6.83	-7.29	39	0.000	2.27
P	125.40	25.77	119.14	22.74	.82	39	0.414	0.25
SD	116.50	16.79	121.61	18.21	-.93	39	0.356	0.29
CO	127.70	22.46	125.80	13.94	.33	39	0.750	0.10
ST	84.65	16.03	84.95	15.36	-.06	39	0.951	0.01

PS:Perceived Stress, NS:Novelty Seeking, HA:Harm Avoidance, RD:Reward Dependence, P:Perseverance, SD:Self-Directedness, CO:Cooperativeness, ST:Self Transcendence

Table 5. Relationship of the number of depression episodes with executive functions

	First episode (N:20)		Recurrent episode (N:21)		t-Test	df	p	Cohen's d
	Mean	SD	Mean	SD				
LNS	7.90	1.51	4.90	2.04	5.33	37	0.000	1.66
WCST 1	115.05	17.48	128.00	0.00	-3.31	39	0.002	1.06
WCST 2	37.45	14.46	66.28	13.07	-6.70	39	0.000	2.09
WCST 3	77.55	5.39	61.23	12.31	5.37	39	0.000	1.70
WCST 4	4.80	1.10	1.94	1.16	8.03	39	0.000	2.52
WCST 5	16.85	10.86	39.61	15.87	-5.33	39	0.000	1.66
WCST 6	15.35	9.52	32.47	11.90	-5.70	39	0.018	1.58
WCST 7	21.85	7.74	31.57	15.96	-2.49	39	0.000	0.76
WCST 8	13.03	7.67	25.78	8.98	-4.87	39	0.000	1.52
WCST 10	64.50	7.42	37.57	18.58	6.13	39	0.000	1.88
WCST 11	58.42	14.59	29.36	14.34	6.42	39	0.000	2.00
WCST 12	1.70	0.86	1.66	1.35	0.09	39	0.925	0.03
STR 1	9.15	1.49	11.33	2.95	-2.96	39	0.005	1.25
STR 2	10.55	2.06	12.19	4.00	-1.63	39	0.110	0.62
STR 3	12.95	2.16	14.61	3.93	-1.67	39	0.102	0.78
STR 4	16.90	2.95	21.76	7.31	-2.81	26.6	0.009	0.96
STR 5	26.80	3.27	36.90	14.37	-3.13	22.1	0.005	0.97
STR 5 D	0.75	0.85	2.52	2.06	-3.62	26.8	0.001	1.11

LNS: Letter-Number Sequencing Subtest, WCST: Wisconsin Card Sorting Test, STR: Stroop Test TBAG Form, WCST 1: total number of responses, WCST 2: total number of errors, WCST 3: total number of correct response, WCST 4: number of categories completed, WCST 5: number of perseverative responses, WCST 6: number of perseverative errors, WCST 7: number of non-perseverative errors, WCST 8: percentage of perseverative errors, WCST 10: number of conceptual level responses, WCST 11: percentage of conceptual level responses, WCST 12: failure to maintain set-up, STR 1, 2, 3, 4, 5: duration scores (sec) for 5 cards, STR 5 D: Number of error corrections for the 5th card

When the analysis comparing WCST scores by the number of MDD episodes was analyzed, WCST 1 scores significantly differed according to the number of depression episodes ($t=-3.31$, $p=0.002$). First-episode depression patients used fewer cards to complete the test than recurrent-episode patients. WCST 2 scores showed a significant difference according to the number of episodes of depression ($t=6.70$, $p=0.000$). In other words, patients with recurrent depressive episodes made more incorrect choices than patients with first-episode depression. WCST 3 scores significantly differed according to the number of depression episodes ($t=5.37$, $p=0.000$). In this case, patients with first-episode depression made more correct choices than patients with recurrent depressive episodes. WCST 4 scores also showed a significant difference according to the number of episodes ($t=8.03$, $p=0.002$). The number of categories completed in the test by patients with first-episode depression was higher than that of patients with depression with recurrent episodes. WCST 5, WCST 6, WCST 7, and WCST 8 scores also showed a significant difference between the groups ($t=-5.33$, $p=0.000$; $t=-5.70$, $p=0.000$, $t=-2.49$, $p=0.018$, $t=-4.87$, $p=0.000$). These results suggest that patients with recurrent depressive episodes exhibited more perseverative responses than first-episode depression patients, and the number of perseverative errors was higher in patients with recurrent depressive episodes than in patients with first depressive episodes. Non-perseverative errors were also higher in patients with recurrent depressive episodes than in patients with the first episode. The percentage of perseverative errors was also higher in patients with recurrent depressive episodes than in patients with a first depressive episode. WCST 10, which indicates the number of conceptual level responses, and WCST 11, which indicates the percentage of conceptual level

responses, differed significantly between the two groups ($t=6.13, p=.000$; $t=6.742, p=0.000$). In this case, the number of conceptual level responses and percentages of conceptual level responses of patients who had their first episode of depression was higher than the number of conceptual level responses and percentages of conceptual level responses of patients with recurrent depressive episodes. The WCS 12 scores, which measure the failure to maintain the set-up, did not show a significant difference between the groups ($t=0.09, p=0.925$). There is no significant difference between patients with recurrent depressive episodes and patients with first-episode depression for the mean scores of failure to maintain the set-up.

When the results of the analysis were performed to determine whether STR 1, 2, 3, 4, and 5 duration scores and STR 5 correction scores differed significantly according to the number of MDD episodes, STR 1 duration score differed significantly according to the number of MDD episodes ($t=-2.96, p=0.005$). In contrast, STR 2 and STR 3 duration scores did not significantly differ between the groups ($t=-1.63, p=0.110$), ($t=-1.67, p=0.102$). The patients' STR 4 and STR 5 duration scores demonstrated a significant difference between the groups ($t=-2.81, p=0.009$), ($t=-3.13, p=0.005$). When the number of STR 5 corrections was analyzed, a significant difference was observed between the groups according to the number of episodes ($t=-3.62, p=0.001$). The results of the relationship between the number of MDD episodes and executive functions are presented in Table 5.

Table 6. Relationship between the number of depression episodes and decision making

	First episode (N:20)		Recurrent episode (N:21)		t-Test	df	p	Cohen's d
	Mean	SD	Mean	SD				
IGT 1	B	1.99	-3.52	4.28	3.30	29	0.003	1.01
IGT 2	.45	3.72	-3.95	4.58	3.36	39	0.002	1.05
IGT 3	2.00	4.72	-1.33	5.26	2.13	39	0.040	0.66
IGT 4	3.85	5.64	-3.80	4.50	4.81	39	0.000	1.49
IGT 5	5.85	6.25	-4.00	7.48	4.55	39	0.000	1.42
IGT TP	13.90	11.97	-15.57	19.04	2.58	39	0.014	0.80
IGT C-A	11.70	6.91	-1.61	7.71	5.81	39	0.000	1.81

IGT: Iowa Gambling Task, IGT 1-5: Block net scores for 5 sections, IGT TP: Total score for all sections, IGT C-A: risky card selection score

According to the results of the analysis for the comparison of IGT scores according to the number of MDD episodes, IGT 1, IGT 2, IGT 3, IGT 4 and IGT 5 net scores by the number of depression episodes, IGT C-A and IGT TP scores were significantly differed between both groups, ($t=3.30, p=0.003$), ($t=3.36, p=0.002$), ($t=2.13, p=0.040$), ($t=4.81, p=0.000$), ($t=4.55, p=0.000$), ($t=2.58, p=0.014$), ($t=5.81, p=0.000$). The mean scores of IGT 1, IGT 2, IGT 3, IGT 4, IGT 5 and the mean scores of IGT TP and IGT C-A of the patients with recurrent episodes were lower than the mean scores of the patients with first-episode MDD. In other words, depressed patients with recurrent episodes made riskier choices during the test and ended the test with more losses. The results of the relationship between the number of MDD episodes and decision making are presented in Table 6.

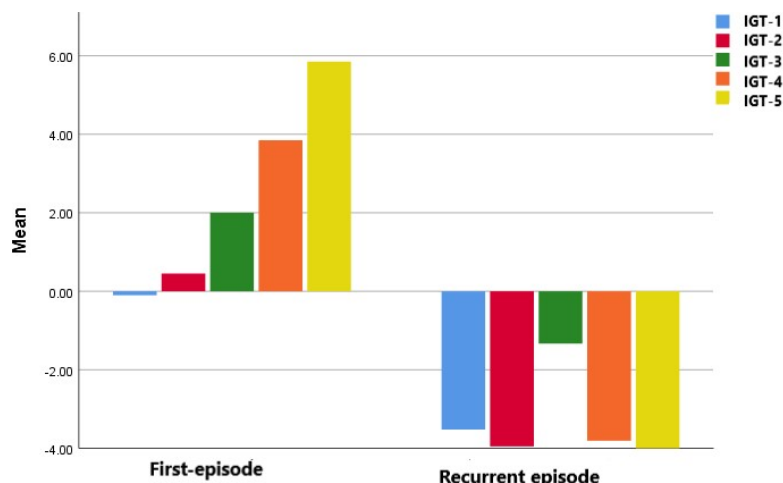


Figure 1. Iowa Gambling Test (IGT) block net scores of major depressive patients with first episode and recurrent episodes

The graph showing that the net scores for each block of the IGT differed according to the episode number is shown in Figure 1. While the graph indicates that learning occurred during the task in first episode depression patients, such learning was not observed in MDD patients with recurrent episodes.

Discussion

In this study, the relationship between the number of episodes in MDD and depression level, treatment adherence, perceived stress level, personality, executive functions, and decision-making was examined. In some previous studies, the number of episodes of depression and treatment adherence were associated with the level of depression. In contrast, in other studies, there was no evidence of this relationship (Thase and Rush 1997, Davidson and Meltzer-Brody 1999, Lampe et al. 2004, Karabekiroğlu et al. 2008, Işık et al. 2013, Köroğlu 2015, Torun 2019). The results of the current study did not reveal a significant relationship between the number of episodes and severity of depression, nor between medication adherence and severity of depression. Besides, the present study showed a strong correlation between the number of episodes and medication adherence in MDD. When the number of episodes increased, medication adherence decreased. When the sub-dimensions of medication adherence were analyzed, the number of episodes was not significantly related to the level of motivation for treatment. However, the knowledge about treatment correlated highly with the number of episodes. These results suggest that the patient group providing adequate information about the medication may be more compliant with the treatment and support the previous findings by demonstrating that possible future episodes can be prevented.

Stress is an important factor in the development of depression, and stress can negatively affect medication adherence in individuals with recurrent episodes (Stefanescu and Ciobica 2012, Helvacı-Çelik and Hocaoğlu 2016, Hong et al. 2021). In the current study, perceived stress decreased as the number of depression episodes increased. In this case, stress could not be perceived due to the loss of executive functions with the increasing number of episodes, and therefore, appropriate coping strategies could not be devised. There is a need for further research to explain this relationship in detail.

Previous studies have reported that personality factors may be a predisposing factor in depression, high harm avoidance, low cooperativeness, and low self-directedness scores may be associated with the severity of depression, high harm-avoidance score may constitute a risk factor for recurrent MDD, and low self-directedness, high novelty seeking and high reward dependence scores may be present in recurrent MDD (Hansenne et al. 1999, Aslan 2008, Teraishi et al. 2015, Bajraktarov et al. 2017). In the present study, patients with recurrent episodes had higher novelty-seeking and reward-dependence scores, and there was no significant difference between the groups in other personality dimensions.

In many studies, the neurocognitive functions of people with MDD were found to be impaired compared to the control group (Lampe et al. 2003, Paelecke-Habermann et al. 2005, Knight and Baune 2012, Must et al. 2013, Salık 2017, Kotan et al. 2018, Varghese et al. 2021). Furthermore, studies comparing the executive function performance of first-episode and recurrent-episode MDD patients have revealed that the executive function performance of individuals with recurrent depressive episodes is poorer than both healthy controls and first-episode MDD patients (Lampe et al. 2003, Karabekiroğlu et al. 2010, Aker et al. 2014, Talarowska et al. 2015, Albert et al. 2018, De Nooij 2020). The present study also demonstrated that MDD patients with recurrent episodes had poorer cognitive functions than first-episode MDD patients.

When executive functions are considered separately, working memory performance was poorer both in individuals diagnosed with MDD compared to the control group and in the MDD group with recurrent episodes compared to the first-episode MDD group (Stordal et al. 2004, Rose and Ebmeier 2006, Smith et al. 2006, Gohier et al. 2009, Parlar et al. 2016). Furthermore, abnormal functional connections have been reported in neuroanatomical regions related to working memory in recurrent MDD cases (Cao et al. 2021). Therefore, it is thought that working memory capacity deteriorates with the presence of MDD, and the deterioration in working memory becomes more persistent with increasing episodes. Consistent with the literature, MDD patients with recurrent episodes had lower working memory capacity than first-episode MDD patients in the present study. When the attention dimension of executive functions was evaluated, planning skill, one of the attention functions, was reported to deteriorate with the first episode.

In contrast, updating skills deteriorated with recurrent episodes (Knight and Boune 2018). Inhibition skill was poorer than in the control group and deteriorated with the first episode, while there was no change in inhibition with recurrent episodes. However, in a longitudinal study, the deterioration in inhibition was observed to be long-lasting and progressed on a permanent basis (Paelecke-Habermann et al. 2000, Must et al. 2006, Gohier et al. 2009, Karabekiroğlu et al. 2010, Ardal and Hammer 2011, Dai and Frenk 2011, Rizk et al. 2017, Canpolat et al. 2018). Likewise, the ability to change the set-up was impaired with the first episode, which persisted with recurrent episodes (Fossati et al. 2002, Westheide et al. 2007). Inhibition and set-up maintenance skills, among the attentional functions, were found to be more impaired in the recurrent MDD group in the present study.

MDD patients with recurrent episodes exhibited slower psychomotor speed and resistance to interference, made more perseverative errors, and failed to maintain the set-up. These results were consistent with the existing evidence in the literature.

When decision-making processes, a high-level cognitive process, are examined in MDD cases, decision-making behavior is impaired with depression. Some studies reported that decision-making skills were impaired in MDD compared to healthy controls (Han et al. 2011, Rinaldi et al. 2020). However, no study examines decision-making processes in MDD patients with recurrent episodes in the literature. The current study demonstrated that decision-making functions were impaired in patients with recurrent MDD. Therefore, MDD patients with recurrent episodes were observed to make more risky choices, and they could not demonstrate learning performance for the test and ended the test with more losses. These findings are considered significant for the literature, and it is recommended that this difference be reconsidered in further studies.

This study has some limitations. First of all, the study is cross-sectional, and the sample was limited by age and educational status due to the possibility of confounding variables affecting neuropsychological test performances. Future studies that replicate the existing variables in different age and education groups and examine the existing relationships within the framework of cause-effect relationships with longitudinal studies will contribute to existing literature. In addition, the number of participants was limited due to the COVID-19 pandemic conditions during the data collection process. Further studies with a larger sample size will be critical for the generalizability of the findings. The study could not include the control group for the same reason. Although the lack of a control group prevented the comparison of the study's findings with the healthy sample, many other studies in the literature explain the relationship between the healthy and MDD-diagnosed group. Thus, we primarily aimed to determine the differences between MDD patients with the first episode and recurrent episodes in the current study, and the findings obtained are complementary to the relevant studies.

Conclusion

In the current study, the factors that may be related to the number of episodes in individuals diagnosed with MDD were addressed, and the findings indicated that the severity of depression was not related to the number of episodes and treatment adherence. However, there was a significant relationship between the number of episodes and treatment adherence. Meanwhile, perceived stress level and treatment adherence decreased as the number of episodes increased, whereas reward dependence and novelty seeking among personality traits increased. When the dimensions of medication adherence were considered, the knowledge about medication correlated significantly with the number of episodes. In addition, losses in executive functions and decision-making behavior were observed as the number of episodes increased. This finding suggests that in addition to factors such as the severity of depression, medication adherence, stressor factors, and personality, several cognitive functions should also be carefully considered and monitored in MDD patients, and it is crucial to address these factors together in the treatment process. Developing and implementing cognitive intervention programs in addition to therapy and medical treatments is deemed essential for the treatment protocols of MDD. Treatment of impairments in cognitive functions is expected to reduce the likelihood of recurrence of MDD episodes.

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