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The Effects of Selective Serotonin Reuptake Inhibitors on Impulsivity in Young Adults with Major Depression in the Early Phase of Treatment

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ABSTRACT

Objective: Whether selective serotonin reuptake inhibitors (SSRI) increase suicide risk, especially in young adults, is still a controversial issue. This study aimed to examine the change in impulsivity characteristics and to evaluate the relationship between impulsivity and suicidality in young adults with major depression who were started on SSRIs.

Method: The study included 50 patients between the ages of 18-24 years with a diagnosis of major depression who were planned to start SSRIs. Participants were evaluated with the Beck Depression Scale, Beck Anxiety Scale, Young Mania Rating Scale, Columbia Suicide Severity Rating Scale, Barratt Impulsivity Scale, Daily Impulsivity Scale (DIS), and Go/No-Go Task (GNG) before and at the end of the first week of treatment.

Results: Seventy percent of the patients (n: 35) completed the assessments at baseline and at the end of the first week. At the end of one-week there was a statistically significant decrease in the DIS (t=2.283, p=0.029) and commission errors in GNG (t=3.19, p=0.003). In addition, 7 out of 11 patients who had suicidal ideation at the first evaluation did not continue to have suicidal ideation at the end of the first week and there was a significant decrease in the severity of suicidal ideation at the end of the follow-up (W:132.0, p<0.001).

Conclusion: One-week SSRI use in young adults resulted in a decrease in impulsivity in self-report scales assessing state impulsivity and in the GNG. It was observed that the severity of suicidal ideation decreased at the end of the one-week treatment period.

Keywords: Depression, Impulsivity, Selective Serotonin Reuptake Inhibitors, Suicide

INTRODUCTION

Major depression is a disorder that negatively affects psychosocial, physical, and emotional functioning, and is considered one of the leading causes of disability worldwide (Kessler and Bromet 2013). The onset age of major depression typically coincides with mid-to-late adolescence, and an early onset of the disorder is associated with severe clinical symptoms and a poor clinical course (Merikangas et al. 2010, Petito et al. 2020). According to findings from the New Zealand Mental Health Survey, the Netherlands Study of Adolescents' Individual Lives, the US National Comorbidity Survey, and the Children in the Community Study, the one-year prevalence of major depressive disorder among individuals aged 18-33 is estimated to be between 8.3% and 12.4% (Crawford et al. 2008, Gustavson et al. 2018, Moffitt et al. 2010, Ormel et al. 2015). The 18-25 age range encompasses the period referred to as emerging adulthood (Arnett 2000). During this period, individuals are engaged in exploring their identities while trying to fulfill various developmental tasks (Roisman et al. 2004). Experiencing depression during this critical period can disrupt this developmental process and hinder young people from achieving their academic and social goals. Mood disorders such as depression have been shown to significantly increase the risk of suicide among university students; and among young adults who attempt or commit suicide, depression is the most common diagnosis (Omar and Merrick 2013). Considering all these factors, it is clear that depression during the young adult period is an important issue that needs to be addressed with care.

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Selective serotonin reuptake inhibitors (SSRIs) are effective and generally well-tolerated agents, and are therefore used as the first-line treatment for major depression in adolescents and young adults (Masi et al. 2010). While many studies on the neurobiological effects of SSRIs are conducted in adults, similar studies in young people are limited (Murphy et al. 2021). Significant changes occur in the structure, function, and neurochemistry of cortico-striato-thalamo-cortical circuits during adolescence (Murphy et al. 2021). During this period, notable developments are seen in skills such as emotion regulation and impulse control. The potential effects of SSRI treatment on the developing brain of a young person are still not fully understood (Edinoff et al. 2021).

One of the most significant and controversial side effects associated with SSRI treatment is the potential increase in suicide risk among young adults due to SSRI use (Edinoff et al. 2021). According to a meta-analysis and review published by the US Food and Drug Administration in 2004, it was found that SSRI use in young people significantly increased the risk of suicidal thoughts and behavior compared to placebo (Hammad et al. 2006). These findings led to the emergence of black box warnings related to SSRI use in young adults aged 18-24 and resulted in a series of regulatory actions. Studies conducted in subsequent years have shown that the relationship between SSRIs and suicide risk is age-dependent and that SSRIs may be protective against suicide attempts after the age of 30 (Stone et al. 2009).

Whether antidepressants increase the risk of suicide, particularly in young adults, remains a controversial issue (Fornaro et al. 2019). Literature findings indicate that suicidal thoughts and behaviors associated with SSRIs are more frequently observed during the first week of antidepressant treatment (Amitai et al. 2015, Jick et al. 2004, Simon et al. 2006). However, the underlying mechanisms of this effect have not yet been fully clarified (Amitai et al. 2015). It has been reported that SSRIs can lead to a series of symptoms (impulsivity, restlessness, and/or insomnia) known as activation syndrome during the initial period of use in young people (Luft et al. 2018). Although researchers believe there may be a relationship between activation syndrome caused by SSRI treatment and suicide, the evidence in this regard is insufficient (Wong et al. 2004). Impulsivity, one of the symptoms of activation syndrome, has been reported to be possibly associated with suicide (Lopez-Castroman et al. 2020). However, differences in the assessment of impulsivity in studies regarding activation syndrome make it difficult to reach a consistent conclusion. In many studies, it has been observed that the clinician's evaluation has been taken as basis, and standardized measurement methods have not been used (Gokcen et al. 2019, Harada et al. 2014). It has been observed that some studies have used self-report scales that assess the trait aspect of impulsivity, which may provide limited information for a follow-up study (Lopez-Castroman et al. 2020). However, it would be more appropriate to use methods that can assess the state aspects of impulsivity to evaluate its changes in a follow-up study.

Impulsivity is the tendency to make decisions without acquiring sufficient information, considering the long-term consequences of an action, or adequately premeditating (Dalley et al. 2011). Impulsivity has long been known as a risk factor for suicide attempts (Gvion et al. 2015). Additionally, impulsivity in depression has been reported to be associated with suicidal thoughts (Ogut et al. 2023). Currently, two main methods are used to assess impulsivity: self-report scales and behavioral tasks (Ogut et al. 2023). In self-report scales, individuals are asked to report the extent to which statements related to impulsivity (e.g., "I act on the spur of the moment," "I do things without thinking") apply to themselves. In behavioral tasks, data is obtained about a person's performance related to impulsive behavior in a defined situation through repeated trials. For example, in tasks such as the Go/No-Go Task, which assesses response inhibition, individuals are asked to respond to targeted signals ("go") and not respond to other signals ("no-go") in a computer setting. By calculating the responses to the no-go targets, information is obtained about the individual's tendency toward impulsive actions. Particularly in disorders like depression, where subjective self-evaluation may be affected, relying solely on self-report methods can be limiting, therefore, it is believed that assessing individuals' impulsive performance through behavioral tasks may be important.

The aim of this study is to examine the changes in impulsivity traits at the end of the first week of SSRI treatment in young adults diagnosed with major depression, using both self-report scales and behavioral tasks simultaneously, and to evaluate the relationship between impulsivity and suicidal tendency.

The hypotheses of this study are the following:

- In young adults diagnosed with major depression, an increase in the dimensions of impulsivity assessed by self-report scales will be observed at the end of the first week of SSRI treatment.
- In young adults diagnosed with major depression, an increase in the dimensions of impulsivity assessed by behavioral tasks will be detected at the end of the first week of SSRI treatment.
- Increased impulsivity at the end of the first week of SSRI treatment is associated with suicidal thoughts and behaviors.

METHODS

In this study, which evaluated young adult patients with major depression who were scheduled to start antidepressant treatment, patients who applied to the Psychiatry Outpatient Clinic of Uşak Training and Research Hospital between February and September 2023 were assessed. Patients aged 18-24, who met the DSM-5 diagnostic criteria for major depression, had no prior diagnosis of a mental disorder, had no current or past history of psychotropic use, and were planned to start SSRI monotherapy by their attending physician, were invited to participate in the study. The research was designed as a natural follow-up study. The patients' treatment and follow-up plans were recorded, but there was no intervention in the physicians' decisions. Patients diagnosed with another comorbid mental disorder, those with a history of psychotropic use, and those with severe neurological and physical illnesses that could hinder the required assessments and interviews were not included in the study, as determined by the Structured Clinical Interview for DSM-5 Disorders - Clinician Version administered by the researcher. Patients included in the study were evaluated by clinical interviews and scales administered by the clinician, self-report scales, and behavioral tasks before the start of treatment and at the end of the first week of treatment. The purpose and design of the study were reviewed by the Uşak University Non-Invasive Clinical Research Ethics Committee, and committee approval was obtained (Ethics Committee No: 63-63-17).

Scales and Behavioral Tasks Used in Clinical Evaluation

Information Form: Sociodemographic and clinical information of the patients were systematically recorded with the information form prepared by the researchers.

Structured Clinical Interview for DSM-5 Disorders - Clinician Version: It is a structured clinical interview chart that investigates the presence of current and lifetime mental disorders according to DSM-5 (American Psychiatric Association 2013). The Turkish translation and reliability study has been conducted (Elbir et al. 2019).

Beck Depression Inventory: The Beck Depression Inventory is a self-report scale that evaluates depression symptoms experienced in the past week (Beck et al. 1961). It was used to measure the severity of depression symptoms in patients participating in the study. The total score obtained from the 21-item scale ranges from 0 to 63. Higher scores on the scale indicate more severe depression symptoms. The Turkish validity and reliability study identified factor structures related to "feelings of guilt," "vegetative symptoms," "hopelessness," "negative feelings towards oneself," and "somatic concerns" (Hisli 1988). The Cronbach's alpha value of the scale in the Turkish validity and reliability study was found to be 0.80 (Hisli 1988).

Beck Anxiety Inventory: The Beck Anxiety Inventory is a self-report scale that evaluates anxiety symptoms experienced in the past week (Beck et al. 1988). It was used to measure the severity of anxiety symptoms in patients participating in the study. The total score obtained from the 21-item scale ranges from 0 to 63. Higher scores on the scale indicate more severe anxiety symptoms. The Cronbach's alpha value of the scale in the Turkish validity and reliability study was found to be 0.93 (Ulusoy et al. 1998).

Young Mania Rating Scale: The Young Mania Rating Scale is used to determine the severity of a person's current manic state (Young et al. 1978). The 11-item scale has 4 items scored between 0-8 points and 7 items scored between 0-4 points. The total score that can be obtained from the scale ranges from 0 to 60. Higher scores on the scale indicate more severe manic symptoms. The Cronbach's alpha value of the scale in the Turkish validity and reliability study was found to be 0.79 (Karadag et al. 2002).

Columbia Suicide Severity Rating Scale: It was used to assess suicidal thoughts and behaviors in patients participating in the study (Posner et al. 2011). The section evaluating suicidal thoughts consists of 5 questions, each scored between 0 and 1 point. A score of 1 indicates the presence of death thoughts, while scores of 2 and above indicate suicidal thoughts. Higher scores in this section are associated with more severe suicidal thoughts. Information about the types of suicidal thoughts, the intensity of thoughts, and the forms of suicidal behavior was recorded. The sequential alpha values of the scale in the Turkish validity and reliability study were found to be 0.89 and 0.91 for recent and lifetime periods, respectively (Kilincaslan et al. 2019).

Barratt Impulsiveness Scale: It is a self-report scale designed to assess the trait aspect of impulsivity (Patton et al. 1995). It consists of three subscales: "Attentional Impulsivity," "Motor Impulsivity," and "Non-Planning". The scale includes a total of 30 items, each scored on a Likert scale ranging from 1 to 4, and the total score that can be obtained ranges from 30 to 120. Higher scores on the scale indicate higher levels of impulsivity. The Cronbach's alpha value for the scale in the Turkish validity and reliability study was found to be 0.81 for patients (Güleç et al. 2008).

Daily Impulsivity Scale: In the study by Ansell et al. (2015), it was aimed to evaluate the state impulsivity by adding "Today" to the beginning of items in the short form of the Barratt Impulsivity Scale and changing the sentences from present tense to past tense (Example: "Today I said something without thinking" instead of "I say things without thinking") (Ansell et al. 2015, Benk Durmus et al. 2022). The scale consists of 8 items, each scored on a Likert scale ranging from 0 to 3 in

terms of frequency. The total score that can be obtained from the scale is calculated between 0 and 24. In the study where the DIS was developed, McDonald's Omega (ω) internal consistency coefficients for "*between-subjects*" and "*within-subjects*" impulsivity measurements were determined as 0.961 and 0.776, respectively (Ansell et al. 2015). The Cronbach's alpha value for the Daily Impulsivity Scale in this study was found to be 0.814.

Go/No-Go Task: The Go/No-Go Task is a behavioral test used to evaluate attention and motor impulsivity, administered in a computer environment (Bezdjian et al. 2009). In the test, participants are expected to respond to targets appearing on the computer screen (go targets) or refrain from responding (no-go targets). The behavioral performance obtained at the end of the test is evaluated using two scores: omission errors for go targets and commission errors for no-go targets. Omission errors for go targets are used to assess inattentiveness, while commission errors for no-go targets are used to assess motor impulsivity (Bezdjian et al. 2009). The Go/No-Go Task used in the study was downloaded from the PEBL (The Psychology Experiment Building Language) platform at http://pebl.sourceforge.net/download.html. The Go/No-Go Task was conducted in a quiet room measuring 3m×3m, using the same computer (1.7 GHz, Intel Core i5 processor, 4 GB RAM, Intel HD graphics 4000 graphics adapter, and 14-inch color monitor, Windows 8). The Go/No-Go Task was initiated by the same researcher, and a short practice session was conducted before the test began. After ensuring that the participants understood the test, they were left alone in the room.

Statistical Analysis

Statistical analyses were performed using the Jamovi software (version: 2.3.28). Correlations related to changes in scores detected in self-report scales and behavioral tasks (obtained by subtracting the initial value from the final value) were calculated. Numerical variables were summarized by mean (standard deviation) or median (interquartile range) values. Whether numerical variables showed a normal distribution was evaluated using analytical and visual methods. Differences between two independent groups for numerical variables were assessed using the independent samples t-test (for normally distributed numerical variables) or the Mann Whitney U test (for non-normally distributed numerical variables). Differences between two dependent groups for numerical variables were assessed using the Paired Samples t-Test (for normally distributed numerical variables) or the Wilcoxon test (for non-normally distributed numerical variables). The Spearman test was used to investigate whether there is a relationship between non-normally distributed numerical variables, and the Pearson test was used for normally distributed variables. In this study, the level of statistical significance was set at 5% ($p<0.050$).

It was determined that a total of 36 individuals were required to obtain a medium effect size (d= 0.5) with 90% power and a 5% type-1 error. Considering those who might not continue with follow-up evaluations, at least 50 participants were planned to be included.

RESULTS

Sociodemographic and Clinical Characteristics of Patients

A total of 50 major depression patients who applied to the Psychiatry Outpatient Clinic of Uşak Training and Research Hospital met the inclusion criteria and agreed to participate in the study. 15 patients did not attend the evaluation interview scheduled for the end of the first week. Thus, a total of 35 people completed the evaluations conducted at the beginning and at the end of the first week. No statistically significant difference was found between the groups that completed and did not complete the study in terms of sociodemographic and clinical characteristics and self-report scale scores. It was determined that participants who completed the study made more commission errors in the Go/No-Go task compared to those who did not complete the study. The sociodemographic and clinical characteristics of the patients included in the study are summarized in Table 1, and the scores from the behavioral tasks and self-report scales are summarized in Table 2.

It was found that all patients who completed the study continued to use the recommended treatment. The treatments that patients used for a week were fluoxetine (n: 19, 54%), escitalopram (n: 9, 26%), sertraline (n: 5, 14%), and paroxetine (n: 2, 6%). Since this study was a natural follow-up study, there was no interference with the physicians' recommendations. Due to the variability in the participants' antidepressant dose increase processes, the total weekly antidepressant doses were calculated. The total weekly antidepressant doses used were 139 (±4.6) milligrams of fluoxetine, 62.8 (±4.4) mg of escitalopram, 105 mg of paroxetine (±49.5), and 280 (±64.7) mg of sertraline. At the end of one week of treatment, there was a statistically significant decrease in patients' Beck Depression Inventory, Beck Anxiety Inventory, and Young Mania Rating Scale scores (Table 3). There was a decrease in the total item scores for irritability ($W=300.0$, $p<0.001$) and sleep ($W=127.0$, $p=0.002$) on the Young Mania Rating Scale, while there was an increase in the total item scores for elevated mood ($W=5.0$, $p=0.023$) and increased motor activity and energy ($W=4.5$, $p=0.041$). No significant changes were observed in the total scores for disruptive-aggressive behavior ($W=1.0$, $p=1.0$),

Table 1. Sociodemographic and Clinical Features of the Participants

	Total (n: 50)	Participants Who Completed Follow-up (n: 35)	Participants Who Did not Complete Follow-up (n: 15)	Statistics	p value
Sociodemographic features, n (%)					
Age (years)					
Mean (SD)	20.9 (1.95)	20.9 (2.12)	21.0 (1.56)	0.235[c]	0.815
Median (IQR)	21.0 (3.00)	21.0 (3.50)	21.0 (2.00)	247[b]	0.748
Sex, n (%)				0.265[a]	0.607
Female	45 (90%)	31 (89%)	14 (93%)		
Male	5 (10%)	4 (11%)	1 (7%)		
Marital Status, n (%)				0.0361[a]	0.849
Single	44 (88%)	31 (89%)	13 (87%)		
Married	6 (12%)	4 (11%)	2 (13%)		
Occupation, n (%)				0.985[a]	0.611
Student	30 (60%)	20 (57%)	10 (67%)		
Employed	7 (14%)	6 (17%)	1 (7%)		
Unemployed	13 (26%)	9 (26%)	4 (27%)		
Educational level, n (%)				0.192[a]	0.662
High school	29 (58%)	21 (60%)	8 (53%)		
University	21 (42%)	14 (40%)	7 (47%)		
Years of education					
Mean (SD)	13.9 (1.69)	13.8 (1.71)	13.9 (1.71)	0.199[c]	0.843
Median (IQR)	14.0 (3.00)	14.0 (3.00)	14.0 (2.00)	253[b]	0.845
Clinical Characteristics, n (%)					
Physical disease	10 (20%)	8 (23%)	2 (13%)	0.595[a]	0.440
Family history of major depression	18 (36%)	15 (43%)	3 (20%)	2.38[a]	0.123
Family history of other mental disorders	15 (30%)	10 (29%)	5 (33%)	0.113[a]	0.736
Family history of suicide attempts	5 (10%)	4 (11%)	1 (7%)	0.265[a]	0.607
Depression-related features					
Age at first depressive episode					
Mean (SD)	18.4 (3.25)	18.26 (3.53)	18.60 (2.59)	0.339[c]	0.736
Median (IQR)	18.5 (3.75)	18 (3.50)	19 (4.00)	254[b]	0.856
Number of depressive episodes					
Mean (SD)	1.82 (1.00)	1.86 (1.06)	1.73 (0.88)	-0.396[c]	0.694
Median (IQR)	2.00 (1.00)	2 (1.00)	2 (1.00)	254[b]	0.845
Recent depression duration (month)					
Mean (SD)	6.37 (6.97)	6.51 (7.42)	6.03 (6.03)	-0.221[c]	0.826
Median (IQR)	4.00 (4.50)	3 (8.88)	4 (3.25)	233[b]	0.639
Self injury, within last week, n (%)	1 (2%)	1 (2.9%)	0 (0%)	0.437[a]	0.508
Self injury, lifetime, n (%)	10 (20%)	9 (25.7%)	1 (6.7%)	2.38[a]	0.123
Suicidal ideation, within last week, n (%)	13 (26%)	11 (31.4%)	2 (13.3%)	1.79[a]	0.181
Suicidal ideation, lifetime, n (%)	25 (50%)	20 (57.1%)	5 (33.3%)	2.38[a]	0.123
Suicide attempt (actual attempt) within last week, n (%)	1 (2%)	1 (3.0%)	0 (0%)	0.464[a]	0.496
Suicide attempt (actual attempt) lifetime, n (%)	13 (26.5%)	11 (32.4%)	2 (13.3%)	1.93[a]	0.165

n: Number, SD: Standard Deviation, IQR: Interquartile Range
a: Chi-square test for the comparison between study groups.
b: Mann-Whitney U test for the comparison between study groups.
c: Student's t test for the comparison between study groups.

Table 2. Self-report Scales and Behavioral Tasks Scores of the Participants

	Total (n: 50)	Participants Who Completed Follow-up (n: 35)	Participants Who Did not Complete Follow-up (n: 15)	Statistics	p value
	Mean (SD) Median (IQR)	Mean (SD) Median (IQR)	Mean (SD) Median (IQR)		
BDI	31.0 (11.4)	31.2 (11.8)	30.7 (11.0)	-0.1495[a]	0.882
	28.0 (20.3)	29 (20.0)	26 (14.5)	249[b]	0.783
BAI	26.8 (12.8)	26.8 (13.3)	26.7 (12.0)	-0.0334[a]	0.973
	29.0 (19.8)	29 (20.5)	31 (15.0)	259[b]	0.949
YMRS	3.92 (2.53)	4.06 (2.39)	3.60 (2.90)	-0.5815[a]	0.564
	4.0 (4.0)	4 (4.0)	4 (5.5)	239[b]	0.614
BIS					
Non-Planning	28.4 (5.87)	28.3 (5.80)	28.8 (6.22)	0.2967[a]	0.768
	29.0 (8.75)	29 (9.0)	29 (7.5)	256[b]	0.899
Motor	20.9 (5.49)	20.5 (5.82)	21.7 (4.70)	0.7163[a]	0.477
	20.5 (9.0)	19 (10.5)	22 (4.5)	230[b]	0.497
Attentional	19.7 (3.65)	19.7 (3.41)	19.8 (4.30)	0.1003[a]	0.920
	19.0 (5.0)	19 (5.0)	20 (6.5)	258[b]	0.924
Total	69.0 (13.0)	68.5 (13.2)	70.3 (12.9)	0.4639[a]	0.645
	67.5 (24.5)	67 (25.0)	70 (19.0)	232[b]	0.525
DIS	11.7 (4.92)	11.3 (5.33)	12.8 (3.73)	1.0174[a]	0.314
	11.0 (6.0)	10 (8.0)	13 (3.5)	209[b]	0.256
Go/No-Go Task					
OE	6.36 (12.5)	6.69 (14.4)	5.60 (6.53)	-0.2779[a]	0.782
	3.0 (4.0)	3 (4.0)	3 (6.0)	245[b]	0.709
CE	22.4 (11.3)	24.5 (10.5)	17.6 (12.1)	-2.0385[a]	**0.047**
	20.5 (16.8)	23 (12.0)	14 (7.5)	156[b]	**0.025**

n: Number, SD: Standard Deviation, IQR: Interquartile Range, BDI: Beck Depression Inventory, BAI: Beck Anxiety Inventory, YMRS: Young Mani Rating Scale, BIS: Barratt Impulsiveness Scale, DIS: Daily Impulsivity Scale, OE: Omission Error, CE: Commission Error
a: Student's t test for the comparison between study groups.
b: Mann-Whitney U test for the comparison between study groups.

thought content (W=1.0, p=1.0), sexual interest (W=1.0, p=1.0), language-thought disorder (W=0.0, p=1.0), speech rate and amount (W=0.0, p=0.346), appearance (W=0.0, p=1.0), and insight (W=0.0, p=1.0).

In the evaluation at the end of the first week, only one patient was found to be in clinical remission. While there was a significant decrease in the factor scores associated with "feelings of guilt" (t: 2.596, p=0.014, effect size: 0.445) and "vegetative symptoms" (W: 266, p=0.005, effect size: 0.634) on the Beck Depression Inventory across the entire group, there were no significant changes observed in the dimensions of "hopelessness" (t: 0.492, p=0.626), "negative feelings towards oneself" (t: 0.119, p=0.906, effect size: 0.020), and "somatic concerns" (W: 200, p=0.271).

Assessments Related to Impulsivity

In this study, different self-report scales were used to evaluate the state and trait aspects of impulsivity. Additionally, the patients' performance related to motor impulsivity was assessed using a behavioral task (Go/No-Go Task). The assessments related to impulsivity for the patients included in the study are summarized in Table 4.

No significant difference was found in the total and subscale scores of the Barratt Impulsiveness Scale in the evaluations

Table 3. Changes in the Clinical Assessment Scale Scores of the Participants During the Follow-up Period

	Participants (n: 35)		Statistics	p value	Effect Size
	Baseline Median(IQR) Mean (SD)	**Follow-up Median(IQR) Mean (SD)**			
BDI					
Total	29 (20.0)	26 (15.5)	531[b]	**<0.001**	0.783
	31.2 (11.8)	25.0 (11.5)	5.07[a]	**<0.001**	0.857
BAI					
Total	29 (20.5)	19 (15.5)	519[b]	**<0.001**	0.848
	26.8 (13.3)	20.3 (11.7)	4.95[a]	**<0.001**	0.836
YMRS					
Total	4 (4.00)	1 (4.00)	323[b]	**0.001**	0.7090
	4.057 (2.39)	2.114 (2.48)	3.7950[a]	**<0.001**	0.6415

n: Number, SD: Standard Deviation, IQR: Interquartile Range, BDI: Beck Depression Inventory, BAI: Beck Anxiety Inventory, YMRS: Young Mania Rating Scale
a: Paired Sample t-test for the comparison between study groups.
b: Wilcoxon test for the comparison between study groups.

Table 4. Changes in Participants' Impulsivity-related Features During the Follow-up Period

	Participants (n: 35)		Statistics	p value	Effect Size
	Baseline Median(IQR) Mean (SD)	**Follow-up Median(IQR) Mean (SD)**			
BIS					
Non-Planning	28.5 (9.00)	28 (8.25)	183[b]	0.894	
	28.206 (5.88)	28.147 (5.44)	0.0993[a]	0.922	
Motor	18.5 (10.50)	20.5 (8.00)	187[b]	0.786	
	20.500 (5.90)	20.353 (5.27)	0.4220[a]	0.676	
Attentional	19 (5.00)	19 (4.00)	267[b]	0.061	
	19.559 (3.38)	18.794 (3.36)	1.8877[a]	0.068	
Total	66.5 (25.00)	66.0 (19.80)	304[b]	0.459	
	68.265 (13.34)	67.294 (11.95)	0.8559[a]	0.398	
DIS					
Total	10 (8.00)	9 (7.00)	355[b]	**0.036**	0.4315
	11.257 (5.33)	9.657 (4.26)	2.2832[a]	**0.029**	0.3859
Go/No-Go Task					
OE	3 (4.00)	1 (4.00)	212[b]	0.078	
	6.69 (14.45)	2.91 (4.51)	1.52[a]	0.137	
CE	23 (12.0)	18 (13.5)	471[b]	**0.003**	0.582
	24.51 (10.50)	20.03 (11.11)	3.19[a]	**0.003**	0.539

n: Number, SD: Standard Deviation, IQR: Interquartile Range, BIS: Barratt Impulsiveness Scale, DIS: Daily Impulsivity Scale, OE: Omission Error, CE: Commission Error
a: Paired Sample t-test for the comparison between study groups.
b: Wilcoxon test for the comparison between study groups.

conducted before the antidepressant treatment and at the end of the first week of antidepressant treatment. It was shown that impulsivity decreased after one week of antidepressant treatment in the Go/No-Go Task and in the Daily Impulsivity Scale, which evaluate the state impulsivity characteristics (Figure 1).

A multiple regression analysis was applied to predict the change in impulsivity detected by behavioral tasks after one week of antidepressant treatment. In the model, gender, age, presence of suicidal thoughts, change in severity of depressive symptoms, change in severity of manic symptoms, and change in severity of anxiety symptoms were the independent

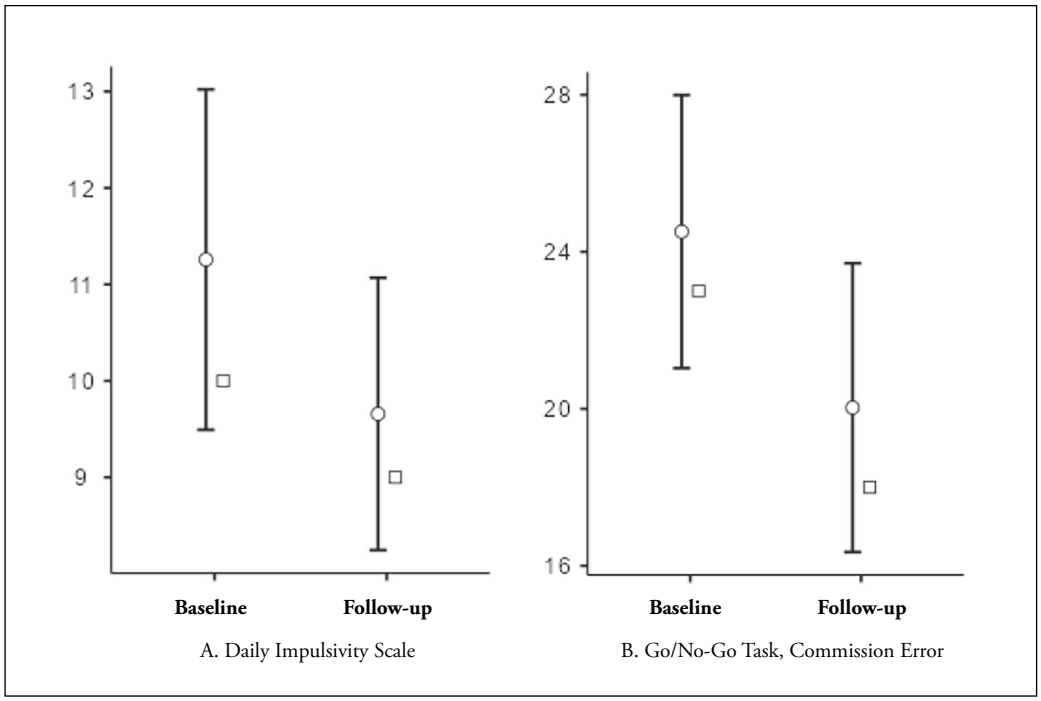

Figure 1. Box plot showing participants' impulsivity ratings at the first evaluation and at the end of the first week. **A.** Daily Impulsivity Scale scores. **B.** Commission errors in the Go/No-Go Task
The bar on the graph represents the 95% confidence interval for the mean values, the circle represents the mean value and the square represents the median value.

Table 5. Multiple Regression Analysis for Predicting the Change in Commission Error Scores

Variables	Beta Coefficient	SD	t	p value
R	7.9174	18.774	0.422	0.677
Age	-0.4893	0.828	-0.591	0.559
Sex	-2.8863	5.133	-0.562	0.579
Suicidal thoughts	-2.9103	3.475	-0.838	0.410
Changes in the YMRS total score	-0.5551	0.561	-0.989	0.331
Changes in the BDI total score	0.2857	0.247	1.156	0.258
Changes in the BAI total score	-0.0586	0.224	-0.261	0.796
R^2=0.130, F=0.675, p=0.671				

SD: Standard deviation, BDI: Beck Depression Inventory, BAI: Beck Anxiety Inventory, YMRS: Young Mania Rating Scale

variables, while the change in commission error scores on the Go/No-Go Task was the dependent variable. The regression model created was not found to be significant (p=0.671). The relationships between gender, age, presence of suicidal thoughts, and changes in the severity of depressive and anxiety symptoms with the change in commission error scores were not statistically significant (Table 5).

During the follow-up period, no significant correlation was found between changes in the Daily Impulsivity Scale and changes in commission error scores on the Go/No-Go Task (r=0.211, p=0.223).

A positive correlation was observed between changes in omission errors detected on the Go/No-Go Task and changes in the "vegetative symptoms" factor scores of the Beck Depression Inventory after the one-week follow-up period (r=0.497, p=0.003).

Evaluations Regarding Suicidal Thoughts and Attempts

While it was determined that 11 out of the 35 people who completed the study had suicidal thoughts in the first evaluation (in the past week), it was observed that 4 people still had suicidal thoughts in the evaluation carried out at the end of the week. A significant reduction in the severity of suicidal thoughts, as assessed by the Columbia Suicide Severity Rating Scale, was observed at the end of the first week of treatment (W=132.0, p<0.001, effect size=0.941).

When suicidal behaviors were assessed in the initial evaluation of the 35 participants who completed the study, one person had made an "actual attempt," one person had engaged in "self-injurious behavior without suicidal intent," and one person had a "aborted attempt," while no "interrupted attempts" or "preparatory actions and behaviors" were

detected. In the evaluation conducted one week later, one person was found to have engaged in "self-injurious behavior without suicidal intent," and no "actual attempts," "aborted attempts," "interrupted attempts," or "preparatory actions and behaviors" were observed. The number of individuals with suicidal behavior in the past week was insufficient for significant statistical comparisons.

DISCUSSION

The main purpose of this study is to investigate the change in impulsivity in young adult major depression patients at the end of the first week of SSRI use. The secondary purpose is to determine the relationship between changes in impulsivity and suicide. It has been demonstrated in this study with both self-report scales and behavioral tasks that there is a decrease in impulsivity after the first week of SSRI use. To the best of our knowledge, this is the first study to simultaneously examine changes in impulsivity characteristics in the early period of SSRI treatment using both self-report scales and behavioral tasks.

In this study, a decrease in the severity of depression and anxiety symptoms was observed at the end of the first week of SSRI treatment in young adults with depression. While it is commonly believed that SSRI treatment has a delayed onset of effect in the treatment of depression, a number of large-scale studies and meta-analyses have shown that clinical symptoms can improve as early as the first week of SSRI treatment, consistent with the findings of this study (Kasper et al. 2006, Papakostas et al. 2006, Posternak and Zimmerman 2005, Szegedi et al. 2003, Taylor et al. 2006). In this study, a decrease was also observed in YMRS scores at the end of the first week of SSRI. This reduction was determined to be primarily related to the improvement in symptoms of sleep and irritability, which may be associated with the depressive episode. Irritability is one of the most commonly reported symptoms in depressed children and adolescents and has been shown to be associated with impulse control problems, violent tendencies, and suicide risk (Fava et al. 2010, Jha et al. 2020a, Orri et al. 2018, Perlis et al. 2005). Consistent with the findings of this study, it has been shown that irritability has decreased starting from the first week of SSRI treatment in a study with a large sample (Jha et al. 2020b). Moreover, it was reported that single-dose fluoxetine use can suppress limbic system responses related to irritability in adolescents with depression (Capitao et al. 2019).

It has been reported that a series of symptoms, which also include impulsivity, called activation syndrome may arise during the initial period of SSRI use in young individuals (Luft et al. 2018). It was stated that the severity of activation syndrome caused by antidepressant treatment and severity of suicidal ideation can be related, and that high impulsivity can be a crucial factor in increased suicide risk (Lopez-Castroman et al. 2020). However, mentioned in this study where impulsivity was assessed in the second, fourth and sixth week of the antidepressant treatment with Plutchik's Impulsivity Scale, the fact that impulsivity was not assessed prior to the antidepressant treatment makes it difficult to form a causal relationship between antidepressant treatment and impulsivity (Lopez-Castroman et al. 2020). It has been reported that activation syndrome can be seen in the range of 7% to 42% with antidepressant use, and impulsivity was detected in the range of 2% to 10% among those with activation syndrome (Gokcen et al. 2019, Harada et al. 2014). However, in studies conducted in this field, it has been observed that impulsivity is evaluated based solely on clinicians' assessments (Gokcen et al. 2019, Harada et al. 2014). This makes it difficult to reach a consistent result regarding the relationship between antidepressant treatment and impulsivity. Contrary to previous study findings indicating that SSRIs might increase impulsivity, this study showed that impulsivity decreased in the early period of SSRI treatment. However, no sociodemographic or clinical changes that could predict the change in impulsivity were detected. The use of self-report scales adapted to assess the state characteristics of impulsivity and the evaluation of performance outcomes related to impulsive behavior in this study may have contributed to this difference. Additionally, the sample in this study, consisting only of individuals aged 18-24 without comorbid mental illnesses or past treatment history, may have caused this sample to respond differently to SSRIs compared to previous studies. Further studies in different samples are needed to predict changes in impulsivity during the early period of SSRI treatment.

It was observed that the severity of suicidal thoughts decreased after a one-week treatment period in patients who completed the study. The observed decrease in impulsivity and moderate improvement in depression symptoms (especially those related to feelings of guilt and vegetative symptoms) within one week of SSRI treatment in this patient group may be related to the reduction in the severity of suicidal thoughts. In a sample of 538,577 individuals using Swedish records, it was reported that the risk of suicide was lower in the first 30 days after starting SSRIs compared to the 30 days before starting SSRIs (Lagerberg et al. 2022). Similarly, another study reported a decrease in the risk of suicidal tendencies from the first week after starting SSRIs, and the reduction in suicide risk was statistically significant when comparing the periods one and a half months before and after treatment (Sorensen et al. 2022). These findings indicate that SSRI use may reduce suicide risk in the early stages of treatment. However, case reports of self-harm and suicide attempts developing in the early periods of SSRI treatment suggest that SSRIs may increase impulsivity

and the risk of suicide related to impulsivity in certain subgroups (King et al. 1991, Teicher et al. 1990, Wirshing et al. 1992). Therefore, large-sample studies that evaluate different dimensions of impulsivity are needed to identify possible subgroups sensitive to SSRI treatment.

LIMITATIONS

Although the sample size of this study is larger than many similar studies using behavioral tasks, it may have limited the statistical power of some comparisons related to rare symptoms such as suicidal behavior within the sample. Conducting further studies with samples that have suicidal thoughts and behaviors will address an important shortcoming.

When examining the sociodemographic characteristics of the sample participating in the study, it was observed that the majority of the sample was female. Studies evaluating impulsivity by gender have shown that men exhibit impulsive behaviors more frequently than women (Cross et al. 2011). However, studies evaluating the Barratt Impulsiveness Scale by gender have found conflicting results (Vasconcelos et al. 2012). Future studies with sample sizes large enough to investigate the effects of gender will be able to determine if there are any differences in this regard.

Although the inclusion of individuals without additional mental disorders and a history of medication use in the study sample provides an advantage in terms of controlling for confounding variables when examining the effects of medication, it may limit the generalizability of the results as it does not reflect the population encountered in practice. In future studies, selecting samples that reflect the general population and controlling for confounding factors could lead to more generalizable results.

The lack of evaluation and exclusion of personality traits that might affect impulsivity and suicidal behavior can be considered another limitation of this study. Nevertheless, the design of the study as a follow-up study reduces the potential confounding effects of personality disorders and interpersonal variability on comparisons related to impulsivity. One limitation of this study is that some participants who agreed to participate did not continue with the follow-up interviews. Additionally, the fact that participants who completed the study made more commission errors in the Go/No-Go Task compared to those who did not complete the study means that the data from a group with lower motor impulsivity could not be evaluated. Nonetheless, the lack of differences in sociodemographic and clinical characteristics between the groups who continued and those who did not continue contributes to the generalizability of the data obtained from the patients who completed the study.

Changes detected in self-report scales and behavioral tasks in the study were calculated by subtracting the initial value from the final value. However, the fact that this calculation method does not account for differences in initial values is a limitation. Applying statistical methods that consider interpersonal differences and calculate proportional changes can overcome this limitation in future studies.

The lack of Turkish validity and reliability study of Daily Impulsivity Scale used in this study is a limitation. Nevertheless, the use of the scale was deemed appropriate due to the high internal consistency reliability coefficients found in this study and the modification of items from validated scales by changing the assessment time interval.

In this study, the Go/No-Go Task was selected as the behavioral task because it has been shown to measure the impulsivity dimension associated with a tendency for suicide attempts in depression (Ogut et al. 2023). Using behavioral tasks covering other neurocognitive areas of impulsivity in future studies will fill the gaps of information in this field.

CONCLUSION

In this study conducted with young adults with major depression, it was demonstrated that impulsivity decreased in the early stages of treatment with SSRI use, both through self-report scales and behavioral tasks. Moreover, a decrease was observed in suicidal thought severity of patients at the end of the one-week treatment period. The findings of this study is crucial in terms of showing SSRI use in young adults can be safe in the early stages, as opposed to black box warnings and a series of regulatory implementation recommendations regarding SSRI use in young adults (Hammad et al. 2006). There is a need for large-sample studies that use behavioral tasks covering other dimensions of impulsivity to replicate these findings in order to more comprehensively understand the relationship between SSRI use and impulsive tendencies in young adults and to develop more effective treatment approaches.

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