

Original article / Araştırma**Theory of mind, aggression and impulsivity in patients with synthetic cannabinoid use disorders: a case-control study****Merih ALTINTAŞ,¹ Leman İNANÇ,² Ayşe Nazlı HUNCA,³ Cihan EKTİRİCİOĞLU,⁴ Nihan YILMAZ,³ Zehra Olcay TUNA,³ Rıdvan ÜNEY⁵****ABSTRACT**

Objective: To compare patients with synthetic cannabinoid use disorder with healthy controls in terms of impulsivity, aggression, and theory-of-mind skills, and to identify the correlation between the level of mentalizing skills and aggression and impulsivity. **Methods:** The study included 80 outpatients who applied to the Erenköy Mental Health Training and Research Hospital, Sancaktepe Addiction Treatment Outpatient Counselling Training and Rehabilitation Centre (BADEM), and were diagnosed with the synthetic cannabinoid use disorder according to the DSM-5 diagnosis criteria, and 50 healthy volunteers without substance use disorders. The study tools were the Reading the Mind in the Eyes Test, Addiction Profile Index, Beck Depression Inventory, Beck Anxiety Inventory, Barratt Impulsiveness Scale, and Buss-Perry Aggression Questionnaire. **Results:** The scores obtained from Beck Depression Inventory and Beck Anxiety Inventory by the patients' group were significantly higher than the control group. Although the total scores from Buss-Perry physical and verbal aggression subscales were significantly higher in the patient group, the anger and hostility subscale scores did not differ between the groups. The motor Barratt score was significantly higher in the patients' group than the control group. No significant difference was found between the groups in terms of Barratt attention, non-planning Barratt, and total Barratt scores. There was also no significant difference between the groups in terms of the Reading the Mind in the Eyes scores. A positive correlation was observed between Buss-Perry and Barratt scores. There was no significant correlation between the scores from both scales and the Reading the Mind in the Eyes scores. **Conclusion:** The patients with SC use disorder are frequently inclined to suffer from anxiety and depression, and may have an increased aggression. It was concluded that the aggression and impulsivity observed in those people might be associated with each other, whereas they have no correlation with the theory-of-mind skills. (*Anatolian Journal of Psychiatry* 2019; 20(1):5-12)

Keywords: theory of mind, mentalizing, synthetic cannabinoids, aggression, impulsivity

Sentetik kannabinoid kullanım bozukluğu hastalarında zihin kuramı, agresyon ve dürtüsellik: Olgu-kontrol çalışması**ÖZ**

Amaç: Bu çalışmada sentetik kannabinoid (SK) kullanım bozukluğu olan hastalar ile sağlıklı kontrolleri dürtüsellik, agresyon ve zihin kuramı becerileri açısından karşılaştırmak ve bu hastalarda zihinselleştirme beceri düzeyi ile agresyon ve dürtüsellik arasındaki ilişkinin saptanması amaçlanmıştır. **Yöntem:** Çalışmaya Erenköy Ruh ve Sinir Hastalıkları Eğitim ve Araştırma Hastanesi Sancaktepe Bağımlılık Ayakta Tedavi Danışma Eğitim ve Rehabilitasyon

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Merkezi'ne (BADEM) ayaktan başvuran, DSM-5 tanı ölçütlerine göre SK kullanım bozukluğu tanısı konulan 80 hasta ve madde kullanımı olmayan 50 sağlıklı gönüllü alındı. Örnekleme Veri Toplama Formu, Gözlerden Zihin Okuma Testi, Bağımlılık Profil İndeksi, Beck Depresyon Ölçeği, Beck Anksiyete Ölçeği, Barrat Dürtüsellik Ölçeği, Buss-Perry Saldırganlık Ölçeği uygulandı. **Bulgular:** Beck Depresyon Ölçeği ve Beck Anksiyete Ölçeği puanı hasta grubunda kontrol grubuna göre anlamlı olarak daha yüksek bulundu. Buss-Perry fiziksel ve sözel saldırganlık alt ölçekleri ve toplam puanı hasta grubunda anlamlı olarak daha yüksek saptanırken, öfke ve düşmanlık alt ölçek puanları gruplar arasında farklılık göstermedi. Motor Barrat puanı SK kullanan grupta kontrol grubuna göre anlamlı derecede daha yüksek bulundu. Barrat dikkat, tasarlanmamış Barrat ve toplam Barrat puanları bakımından gruplar arasında anlamlı fark saptanmadı. SK kullanan grup ve kontrol grubu gözlerden zihin okuma puanları açısından da anlamlı derecede farklı bulunmadı. Buss-Perry ile Barrat puanları arasında pozitif korelasyon saptandı. Her iki ölçek puanları ile zihin okuma arasında istatistiksel olarak anlamlı bir ilişki bulunamadı. **Sonuç:** Bu çalışmada elde edilen sonuçlar, SK kullanım bozukluğu olan hastalarda anksiyete ve depresyonun sık eşlik ettiğini ve bu kişilerin saldırganlıklarının artmış olabileceğini düşündürmektedir. Bu kişilerde gözlenen saldırganlık ve dürtüsellik birbirleriyle ilişkili olabileceği, ama zihin kuramı becerileri ile ilişkilerinin olmadığı sonucuna varılmıştır. (*Anadolu Psikiyatri Derg* 2019; 20(1):5-12)

Anahtar sözcükler: Zihin kuramı, mentalizasyon, sentetik kannabinoidler, agresyon, dürtüsellik

INTRODUCTION

Synthetic cannabinoids (SCs) are psychoactive substances with a strong agonistic effect on the endogenous cannabinoid receptors. As like all over the world, the use of the SCs has been rapidly increasing in Turkey, and the negative consequences caused by their use has become focus of interest. It is remarkable that those with SC use disorder might exhibit behavioral problems and experience problems in personal, familial and social areas also when they are not under the influence of a substance or when they do not suffer from abstinence. Clinicians observe the communicational and behavioral problems, which might appear outside these periods. It is deemed necessary in treating these people to know the fundamental concepts underlying the behaviors, which might turn into violence in those people who might sometimes be aggressive. Anxiety, depression, and cognitive impairment have been more commonly observed in people using SCs compared to those who use natural cannabinoids or do not abuse any substances.^{1,2} How the cognition-related mentalization is affected by these substances, which are reported to have negative effects on cognitive function, and whether they have a correlation may be an issue of concern. Theory of mind is defined as the ability to understand others' feelings and to make predictions about their thoughts, beliefs, wishes, and objectives.^{3,4} This concept is used in the same sense with mentalizing.⁵⁻¹⁰ There are limited studies, which investigate how the theory-of-mind skills are influenced during substance addiction.^{11,12} Allen brought forward that there was a two-way correlation between substance addiction and mentalizing-as intoxication impairs mentalizing, any deficits in the mentalizing skill causes an in-

crease in the tendency to substance use in stress situations.¹³ It was also pointed out that the affective dysregulation and aggression observed in patients with substance use disorder had similar genetic factors.¹⁴ The impulsive behaviors have also been reported to be higher in those with substance use disorder.¹⁵ Some suggest that the close correlation of the right side of prefrontal cortex with the mirror neuron system and empathy leads to an adverse effect on the mentalizing skill in case of any problems in this region, and that this is also associated with an increase in violent behaviors.¹⁶ However, no researches examining the theory-of-mind skills of SC users were found in the literature search.

This study aims to compare patients with SC use disorder with healthy controls in terms of impulsivity, aggression, and theory-of-mind skills, and to identify the correlation between the level of mentalizing skill and aggression and impulsivity in these patients.

METHODS

Study population

The study sample consisted of out-patients who applied to the Erenköy Mental Health Training and Research Hospital, Sancaktepe Addiction Treatment Outpatient Counselling Training and Rehabilitation Centre (BADEM), and healthy volunteers without substance use disorders. Among the patients who applied to BADEM and diagnosed with the SC use disorder according to the DSM-5 diagnosis criteria, 80 patients were consecutively included in the study. The healthy control group consisted of 50 people who were selected from among the relatives of center's staff members who were similar to those in SC group in terms of age and educational back-

ground, and who have never abused any substances. All the participants have agreed to participate in the study and signed the consent form. Patients who remained out of the age range 16 to 60, were illiterate, had experienced a sequel-leaving disease or a head trauma in the childhood, were diagnosed with a neurological disorder or mental retardation or a psychotic disorder, were abusing other substances in addition to SC for the last one year, and were under the influence/experiencing abstinence of substance or in the period of intoxication were excluded from the study.

Data collection tools

The following forms were completed for each participant: a demographic information form, Addiction Profile Index (API), Reading the Mind in the Eyes Test, Barratt Impulsiveness Scale (BIS-11), Buss-Perry Aggression Questionnaire, Beck Depression Inventory, and Beck Anxiety Inventory. Urine samples were collected from the patients on the day of interview, and no SCs were found in standard urine analyses.

Demographic Information Form: This is a detailed interview form prepared by the researchers. It contains questions on age, gender, marital status, education, place of residence, level of economic income, age of starting substance abuse, age of starting SC use, duration and amount of use, etc.

Addiction Profile Index (API): Developed by Ogel et al.¹⁷ to measure the factors associated with addiction, it consists of 37 questions scored from 0 to 4 through a Likert-type scale, and 5 subscales, which are the substance abuse characteristics (the substances abused, frequency of abuse), addiction diagnosis criteria, effects of substances abuse on abuser's life, strong desire to abuse the substance, and the abuser's motivation to give up using the substance.

Reading the Mind in the Eyes Test: It evaluates the ability to recognize mind theory and emotions involving understanding a mental status from the eyes.¹⁸ It consists of 36 photographs which contain only the eyes of actors and actresses. The participants are asked to select the emotion, which best shows the mental status of the person appearing on the photograph. It is accepted as an indication of the theory-of-mind skill rather than emotion recognition. Four items of the test in Turkish were excluded for having a low internal consistency, so the Turkish form consisted of 32 items.¹⁹ The

higher the total score, the better are the social cognition and theory-of-mind skills.

Barratt Impulsiveness Scale (BIS-11): This is a self-assessment scale, which consists of 30 items assessing impulsivity. Three sub-factors were obtained through factor analysis: attention-associated impulsivity, motor impulsivity, and non-planning impulsivity. Higher scores are an indication of higher impulsivity.²⁰ Its Turkish validity and reliability have been shown by Gulec et al.²¹

Buss-Perry Aggression Questionnaire (BPAQ): Developed by Buss and Perry to measure the level of aggression and anger, this questionnaire consists of 29 items.²² Each of the items is scored from 0 (extremely uncharacteristic) to 4 (extremely characteristic) through a Likert-type scale. The scale has four subscales: physical aggression, hostility, anger, and verbal aggression. Demirtas Madran²³ conducted its Turkish validity and reliability study

Beck Depression Inventory (BDI): It measures the severity of depression.²⁴ It consists of twenty-one items, and these items were ranked from slight to severe between 0 and 3. The result is obtained by the sum of the scores, 0-9 indicating minimal, 10-16 slight, 17-29 medium, and 30-63 severe depression. Its Turkish validity and reliability has been shown.²⁵

Beck Anxiety Inventory (BAI): It is a Likert-type self-assessment scale for the severity of anxiety symptoms, which consists of 21 items scored from 0 to 3.²⁶ The higher the total score, the more severe is the anxiety experienced by the respondent. Total score of 8-15 indicates slight anxiety, 16-25 medium anxiety, and 26-63 severe anxiety. The validity and reliability of the Turkish scale was conducted by Ulusoy et al.²⁷

Statistical analysis

The statistical analyses were performed using SPSS version 22. The conformity of variables to normal distribution was analyzed by using visual (e.g., histogram and probability diagrams) and analytical (e.g., Kolmogorov Smirnov and Shapiro-Wilk tests) methods. For comparison of continuous variables of two groups, Mann Whitney-U test and Student's t-test were used for non-normally or normally distributed data, respectively. The categorical variables of two groups were compared by chi-square test. The correlation of variables was evaluated by using Spearman's correlation analysis. The statistical significance level was set to $p < 0.05$.

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RESULTS

The mean age of the patients with SC use disorder was 27.0 ± 6.3 years, and that of the control group was 30.2 ± 9.1 years. No statistically significant difference was found between the groups in terms of age, having children, and duration of education (Table 1).

However, in comparison to the control group, the patients' group had lower rate of the married participants (28.2% and 52.0%, respectively, $p=0.007$), lower rate of employment (72.2% and 88.0%, respectively, $p=0.036$), and higher rate of application to psychiatry clinic due to non-substance reasons (33.8% and 14.0%, respectively, $p=0.013$) (Table 1).

Table 1. Comparison of the group with SC use disorder and the control group in terms of sociodemographic characteristics

	Patient (n=80)		Control (n=50)		p
	n	%	n	%	
Age (Mean \pm SD, years)	27.0 \pm 6.3		30.2 \pm 9.1		0.17 ^a
Median (min-max)	26.0 (18-50)		27.5 (18-52)		
Educational background					0.340 ^a
Primary school graduate	18	22.8	14	28.0	
Secondary school graduate	40	50.6	14	28.0	
High school graduate	15	19.0	16	32.0	
University graduate	6	7.6	6	12.0	
Marital status					0.007 ^b
Married	22	28.2	26	52.0	
Single	56	71.8	24	48.0	
Employment status					0.036 ^b
Employed	52	72.2	44	88.0	
Unemployed	20	27.8	6	12.0	
Having children					0.082 ^b
No	54	68.4	26	53.1	
Yes	25	31.6	23	46.9	
Non-substance-associated psychiatric application					0.013 ^b
No	53	66.3	43	86.0	
Yes	27	33.8	7	14.0	

^a: Mann Whitney U test; ^b: Chi-square test

Among the group with SC use disorder; the age of starting substance abuse was 17 ± 4 years, the age of starting SC use was 22.1 ± 6.5 years, the

duration of substance abuse was 121.4 ± 65.1 months, and the duration of SC abuse was 59.0 ± 34.0 months (Table 2).

Table 2. Starting age and duration of substance, and SC abuse of the patients with SC use disorder

	Mean \pm SD	Median (min-max)
Age of starting substance abuse (years)	17.0 \pm 4.0	16 (10-30)
Duration of substance abuse (months)	121.4 \pm 65.1	114 (12-312)
Age of starting SC abuse (years)	22.1 \pm 6.5	20 (1-50)
Duration of SC abuse (months)	59.0 \pm 34.0	60 (12-168)

In the group with SC use disorder, 12 (16.9%) participants had an imprisonment history, four of which due to crimes associated with substance use (5.6%).

Self-mutilative behavior was recorded in 45.7% (n=32) of the group with SC use disorder. The scores from Beck Depression Inventory and Beck Anxiety Inventory were significantly higher

in the patients' group compared to the control group ($p < 0.001$ for both) (Table 3).

In the BPAQ, which assesses aggression, the subscales of physical aggression ($p = 0.017$) and verbal aggression ($p = 0.002$) and the Buss-Perry total score ($p = 0.004$) were significantly

higher in the patients group; however, no significant difference was found between the groups in terms of the scores from the subscales of anger and hostility ($p = 0.152$ and $p = 0.203$, respectively) (Table 3).

Table 3. Comparison of the group with SC use disorder and the control group in terms of Beck Depression Scale, Beck Anxiety Scale, and Aggression Scale scores

	Patients (n=80)		Control (n=50)		p
	Mean±SD	Median (min-max)	Mean±SD	Median (min-max)	
Beck Depression Inventory	22.3±12.2	21.5 (0-46)	8.9±9.5	6.0 (0-36)	<0.001 ^a
Beck Anxiety Inventory	16.9±12.0	14.0 (0-55)	10.0±10.7	6.0 (0-40)	<0.001 ^a
Buss-Perry Scale					
Physical aggression	16.3±7.9	16.0 (0-36)	12.9±7.1	12.0 (0-29)	0.017 ^b
Verbal aggression	8.9±4.5	8.0 (0-20)	6.2±4.2	5.0 (0-16)	0.002 ^a
Anger	20.2±5.0	21.0 (0-28)	18.98±5.1	19.5 (3-23)	0.152 ^a
Hostility	33.1±5.0	32.0 (1-32)	34.0±4.5	33.0 (2-29)	0.203 ^a
Total	55.9±21.8	58.0 (5-116)	44.3±20.5	41.0 (7-88)	0.004 ^b

^a: Mann Whitney U test; ^b: Independent-Samples t-test

In the Barratt Scale, which assesses impulsivity, the motor Barratt score was significantly higher in the group with SC use disorder than the control group ($p < 0.001$), as no significant difference was found between the groups in terms of the scores from the Barratt attention ($p = 0.203$) and the non-planning Barratt ($p = 0.337$), and the

total Barratt scores ($p = 0.50$) (Table 4). No statistically significant difference was found between the group with SC use disorder and the control group in terms of the scores from the Reading the Mind in the Eyes test ($p = 0.152$) (Table 4).

Table 4. Comparison of the group with SC use disorder and the control group in terms of the scores from impulsivity and Reading the Mind in the Eyes test

	Patients (n=80)		Control (n=50)		p
	Mean±SD	Median (min-max)	Mean±SD	Median (min-max)	
Attention Barratt score	33.1±4.97	32.0 (24-50)	34.0±4.5	33.0 (24-44)	0.203 ^a
Motor Barratt score	14.5±3.5	14.0 (9-26)	12.0±2.8	12.0 (8-21)	<0.001 ^a
Non-planning Barratt score	19.8±3.6	20.0 (13-36)	20.3±3.3	20.0 (15-26)	0.337 ^a
Total Barratt score	67.5±9.8	67.0 (49-112)	66.3±8.0	67.0 (50-84)	0.500 ^b
Total score from the Reading the Mind in the Eyes test	20.2±5.0	21.0 (4-29)	18.98±5.14	19.5 (7-28)	0.152 ^a

^a: Mann Whitney U test; ^b: Independent-Samples t-test

When the correlation between the scores from aggression, impulsivity and Reading the Mind in the Eyes tests was evaluated in the group with SC use disorder, a positive correlation was found between Buss-Perry and Barratt scores whereas there was no statistically significant difference between the scores from the both scales and the

score from Reading the Mind in the Eyes test (Table 5).

DISCUSSION

In addition to their metabolic effects, SCs cause certain psychiatric problems like paranoia, hallu-

Table 5. Correlation between the scores obtained by the group with SC use disorder from aggression, impulsivity and Reading the Mind in the Eyes tests

	Buss-Perry total r^a	Barratt total r^a	Reading the Mind in the Eyes r^a
Buss-Perry			
Physical aggression	0.923**	0.348**	0.111
Verbal aggression	0.896**	0.415**	-0.018
Anger	0.816**	0.309**	0.103
Hostility	0.862**	0.396**	-0.003
Aggression	1.000	0.439**	0.078
Total	1.000	0.439**	-0.120
Barratt			
Attention-associated impulsivity	0.235*	0.856**	-0.092
Motor impulsivity	0.515**	0.701**	0.004
Non-planning	0.329**	0.706**	-0.120
Total impulsivity	0.439**	1.000	-0.120

*: $p < 0.05$; **: $p < 0.01$; ^a: Spearman's correlation analysis

cination, panic attack, anxiety and depression.^{2,28} It has also been reported that there is an increase in the number of suicides following the use of SCs.²⁸ In our study, supporting the literature, the depression scores of patients with SCs use disorder were significantly higher than healthy control group.

Anxiety is one of the important side effects of SCs treatment.²⁹ Intense anxiety and sudden depression are also observed during the withdrawal period following the chronic SC use.³⁰ SCs create up-regulation in the 5-HT_{2A} receptors over the CB₂ receptors, which leads to psychotic symptoms and anxiety.³¹ On the other hand, the cannabidiol substance, which exists in the natural cannabis and has an anxiolytic effect itself, is not present in the SCs.³² Likewise, similar to the previous reports, the anxiety scores of the patients with SC use disorder were significantly higher than those of the control group in the present study. Additionally, considering our study population was neither under the influence of a substance nor in the withdrawal period, we propose that the anxiety in these patients continue during other periods.

Aggression is a multi-dimensional behavior aiming to cause harm to the others.³³ This behavior may result from the interaction of the biological, emotional, social, and cognitive factors.³⁴ In our research, the total score of aggression in the SC users was significantly higher than that in the control group, and additionally the scores of the sub-scales of physical and verbal aggression were also significantly higher. These components of aggression may be important in

terms of communication and social relationships. The fact that these people sometimes have trouble in problem-solving and sometimes tend to exhibit aggressive behaviors may explain our findings. Therefore, aggression in these people should not be ignored.

Impulsivity is the act of being inclined to exhibit quick and unplanned reactions against internal or external stimuli without taking the negative consequences into consideration, and is the failure in resisting against an impulse or a stimulus. It is also defined as the failure to prevent the desire to do harm to self or to others.³⁵ In the present study, while no difference was found between the two groups in terms of impulsivity, the motor Barratt score was significantly higher in the patients' group. There are some studies which confirm the correlation between impulsivity and the substance use disorder, and which report that the impulsivity levels are higher than that in the normal population.¹⁵ Impulsivity, which is believed to play a key role in the etio-pathogenesis of the affection disorders as a constituent or initiation of a behavior, may cause behavior changes in our population. It is very common that these people express impulsivity and emotions inappropriately and in an imbalanced manner.

People with substance use disorder are known to have a higher rate of personality disorders. Conflicting results were found on theory of mind in people with borderline personality disorders. Although theory of mind skill disorders were found in certain studies, no difference was found in other studies compared to the healthy con-

trols.^{36,37} Richell et al.³⁸ reported that the theory of mind skills were not affected in case of personality disorders.

It has been suggested that SCs impair the cognitive functions.² A three-week SC use has been reported to have speech-pausing and avoidant eye contact effects. However, the cognitive functions are reported to be severely impaired in chronic use for eight weeks.³⁰ The theory of mind is also associated with the executive functions and working memory. Our study was inspired by the question whether the SCs is associated with the theory of mind of cognitive dysfunctions and whether it underlies certain behavioral problems. According to our data, no significant difference was found between the group with SC use disorder and the control group in terms of the theory of mind skills. There are publications, which suggest that psychosis negatively affects the theory of mind. The meta-analytical data reveal that there are mentalizing impairments in psychotic patients independent of IQ level.³⁹ This study investigated the effect of SC use on mentalizing independently of psychosis, and it was observed that the theory of mind functions of SC users were not different from

those of the control group. We believe that the absence of psychosis may be one of the factors, which leads to this finding.

Limitations of research: Our study population consists of patients who apply to an addiction center, who generally are motivated for treatment. The study did not include patients who refrain from collaborating, do not apply for treatment, and are likely to frequently exhibit impulsive and aggressive behaviors. The fact that the control group consists of the relatives of the center's staff members is a limitation of the research. Since our research is cross-sectional, the parameters assessed here need to be investigated extensively in larger groups and with monitoring studies.

In conclusion, the use of SCs is increasing day by day, driving clinicians to face with its long-term effects. Beyond being just a health problem, the outcomes of these substances, which create a social problem in all aspects, should be well known. We believe that revealing the concepts investigated in our study would provide benefit for SC users in terms of determining efficient methods of pharmacotherapy and therapy.

Authors' contributions: M.A.: design of the study, literature review, data collection, statistical analysis, manuscript writing; L.İ.: design of the study, manuscript writing; A.N.H.: literature review, statistical analysis; C.E.: applying scales, literature review; N.Y.: data collection, literature review; Z.O.T.: data collection; R.Ü.: literature review.

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