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The severity of dissociative symptoms among patients with cannabis and synthetic cannabinoid use disorder: association with substance use characteristics and suicide

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ABSTRACT

OBJECTIVE: Cannabis (C) and synthetic cannabinoids (SCs) are commonly used substances. Pharmacodynamic and pharmacokinetic differences predict that SCs involve a greater risk of dependence than C. Dissociative symptoms and suicidality are also frequent in treatment-seeking substance users, however, there is not enough data about the dissociative effects of C and SCs. The present study aimed to examine SC users in terms of demographic features and severity of dissociative symptoms in comparison to C users. It was also aimed to explore the relationships between dissociation and suicide attempts.

METHODS: The study was performed at the Alcohol and Substance Research, Treatment, and Training Centre of Ankara Numune Training and Research Hospital, Turkey. 84 patients with C or SC use disorder included in the study and all the participants were administered a sociodemographic data form assessing also substance use features and suicide attempts and Dissociative Experiences Scale (DES). The patients were separated into three groups as only C users (CU), only SC users (SCU) and both C and SC users (C&SCU) and also categorized as DES score <30 as the low dissociation level and DES score of ≥30 as the high dissociation level. Correlations between variables were tested using Spearman correlation coefficients and the predictors of high dissociation level were evaluated using logistic regression analysis. A value of $p < 0.05$ was considered statistically significant.

RESULTS: DES mean score was 28.82 in all participants. Dissociation levels ($p = 0.058$) and high dissociation rates ($p = 0.443$) were similar among CU, SCU, and C&SCU groups. Age at onset of substance use was negatively correlated with the severity of dissociative symptoms ($r = -0.22$, $p = 0.042$). DES mean score of patients with a history of suicide attempt was 40.51, significantly higher than that of those without (23.47). Age at onset of substance use, lifetime years of substance use, type of substance used (C, SC, and C&SC usage) were not significant predictors, only the history of suicide attempt was the significant predictor of high dissociation level ($B = 1.886$, $S.E. = 0.542$, $Wald = 12.104$, $df = 1$, $p = 0.001$, $OR = 6.596$, $95\% CI = 2.279-19.089$).

CONCLUSIONS: The findings support that dissociation levels are high in C and SC users as in other substance users, however, dissociative effects of C and SCs do not differ from each other. Besides the dissociative effects of C and SC use, there is also a significant effect of the suicide attempt history on the severity of dissociative symptoms. Although the relationship between dissociation and type of substance used is not clear, there is an association between dissociation and the history of suicide attempt. C and SC users are also concerned with dissociative symptoms that should be considered by the clinician since it affects the treatment modality and treatment response.

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cannabis; dissociation;
suicide

Introduction

Substance use continues to be a major health problem and cannabis (C) is the most commonly used illicit substance in the world [1]. In the recent past, the designer drug industry has exploded and synthetic derivatives of C have become popular. Synthetic cannabinoids (SCs) were first reported in 2004, with initial increased use reported in 2008 in Europe and in 2010–2011 in the United States (U.S.) [2,3]. Compounds similar to tetrahydrocannabinol (THC), the major psychoactive constituent of C, has been

synthetically produced and sold under several commercial brands, with “Spice” the most common in Europe, “K2” in the U.S., “Kronic” in Australia and “Bonzai or Jamaica” in Turkey [4,5]. Annual prevalence was found to be 11.4%, making SC the second most widely used class of illicit substance after C among 12th graders in 2011 and after the federal ban in the U.S., the 2013 rate was 7.9%, respectively [6]. The likelihood of addiction produced by SCs is of concern for the scientific community, where there is also interest in the potential therapeutic value of

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cannabinoids. Pharmacodynamic and pharmacokinetic differences predict that SCs involve a greater risk of dependence than C [7]. SCs act at the cannabinoid type 1 (CB1) and cannabinoid type 2 (CB2) receptors in the central nervous system and peripheral organs as similar to THC. However, SCs exert full agonism at CB1 receptors and therefore produce a more intense effect than THC, which is only a partial agonist [8–10]. There is a growing number of reports detailing adverse effects of SCs. Case reports suggest that tolerance develops quickly and withdrawal has been observed following chronic use [11], furthermore Gunderson et al. claimed that SCs can mitigate symptoms associated with C abstinence syndrome and demonstrate the pharmacological specificity of C withdrawal [12].

The coexistence of substance use and dissociative symptoms is an issue which has been studied for many years. Studies have reported a high prevalence of dissociative symptoms in treatment-seeking substance users [13,14] but SCs have not yet been studied in relation to dissociation. In a previous case report, persistent depersonalization/derealization disorder was reported after even a single dose SC administration [15] suggesting that SCs have a significant dissociative effect. Evren et al. revealed that among Turkish inpatients with substance use disorder, 29.0% obtained a Dissociative Experiences Scale (DES) score of 30.0 or above [16]. Tamar-Gurol et al. reported that mean DES score was 29.0, and 46.2% of patients with substance use disorder had a DES score >30 and the dissociative group had a higher prevalence of suicide attempts [17]. In a study of inpatients with alcohol use disorder female gender, a younger age, history of suicide attempt were found to be more frequent in patients with dissociative disorder [18]. Patients with high dissociation levels experience shifts in personality states and hence exhibit impulsive behaviours such as abandoning treatment [18] and also likely to have attempted suicide [19]. In patients with alcohol and substance use disorders, mean DES score was found to be higher among those with a history of suicide attempt [16]. In fact, the risk for SC use disorder is higher than C use disorder pharmacodynamically, but it is not known how this difference affects dissociative symptoms and suicidal behaviours. The fact that SCs are more intense than C and the rapid tolerance development suggests that the dissociative effect may also be more pronounced.

The aim of this study was to investigate the unique profile of patients with SC use disorder admitted to an Alcohol and Drug Research, Treatment and Training Centre in terms of demographic features and severity of dissociative symptoms in comparison to C users. It was also aimed to explore the relationship between dissociation and history of suicide attempt among patients with C and SC use disorder.

Methods

Participants

The study included 84 patients with C or SC use disorders who were admitted to the Alcohol and Substance Research, Treatment, and Training Centre of the Ankara Numune Training and Research Hospital between June and November 2014. Inclusion criteria for the study were age ≥ 18 years, and continuous consumption (more often than once a week) of SCs and/or C for at least the last 12 months. The exclusion criteria were as follows: (a) comorbid Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-5) axis 1 psychiatric disorder (e.g. psychotic disorder, affective disorder, alcohol use disorder); (b) mental retardation and (c) organic mental disorder. Detailed information on the study was given to the patients, and informed consent forms were obtained. Approval for the study protocol was given by the Local Ethics Committee of Ankara Numune Training and Research Hospital at June 04, 2014, with a decision number E-14-208.

All patients were interviewed by three independent clinicians and the value of Fleiss' kappa was 0.82. The subjects were selected based on the DSM-5 [20]. Substance use disorder in participants was diagnosed according to the DSM-5 criteria, and they were divided into three groups as only C users (CU), only SC users (SCU) and both C and SC users (C&SCU).

Measures

The patient sociodemographic data and clinical features of C/SC use were evaluated using a semi-structured data form that the patients were asked about the age, education, marital status, monthly income, occupation, years of lifetime substance use, frequency of substance use and history of suicide attempt.

Dissociative symptoms were assessed with DES [21]. This is not a diagnostic tool but serves as a screening device for chronic dissociative disorders. This reliable and valid self-report questionnaire is the most widely used instrument for dissociative symptoms in clinical samples. In the introduction of questionnaire, participants are instructed to report only experiences when they were not under the influence of alcohol or drugs. Possible scores range from 0 to 100 and a cut-off score of 30 had been shown to be useful in screening dissociative disorders in Turkey [22]. Patients were categorized as DES score < 30 as the low-dissociation group and a DES score of ≥ 30 as the high-dissociation group.

Statistical analysis

All statistical analyses were performed using IBM SPSS version 22.0 software. Conformity of the data to a normal distribution was assessed with the Shapiro Wilk

test. Continuous variables were compared using the Mann–Whitney U test and the Kruskal Wallis test when the data were not normally distributed. The Mann Whitney U test was performed to test the significance of pairwise differences using Bonferroni correction to adjust for multiple comparisons. Categorical variables were compared using Pearson's Chi-square test and Fisher's Exact test. Correlations between variables were tested using Spearman correlation coefficients. Predictors of high dissociation were evaluated using logistic regression (enter method) analysis. A value of $p < 0.05$ was considered statistically significant.

Results

During the period of data collection, 98 patients were initially enrolled in the study and the data of 14 patients were excluded from the study as they were incorrect or incomplete. CU, SCU and C&SCU groups included patients with C, SC and both C and SC use disorders, respectively. In the CU group, 2 patients had used SCs in the last 12 months but not more often than once a month. There was only one SC user without a history of C use in the SCU group, and 96.4% of SCU group had a history of C use. Sociodemographic characteristics including age, gender, education, occupation, and marital status were similar among three groups (Table 1).

The mean age at onset of substance use was 20.2 ± 6.7 years in CU, 18.6 ± 6.2 years in SCU, and 15.9 ± 2.9 years in C&SCU. The C&SCU group was determined

to be significantly younger than the CU group when they first used a substance ($p = 0.012$). The mean lifetime years of substance use was 4.7 ± 2.9 years in CU, 5.9 ± 3.5 years in SCU, 6.4 ± 3.9 years in C&SCU and there was no significant difference between the groups ($p = 0.100$).

DES mean score was 28.82 ± 20.5 in all participants. DES mean scores of SCU (32.8 ± 21.7) and C&SCU (31.8 ± 19.4) were >30 , indicating a high dissociation level, and higher than those of CU (21.6 ± 19.3) but the difference was not statistically significant. Of the total 84 participants, 36 (42.9%) were high-dissociators and the distribution of high dissociators among the CU, SCU and C&SCU groups was similar. The history of suicide attempt was determined in 31% ($n = 26$) of all the participants, as in 25.9% ($n = 7$) of CU, in 28.6% ($n = 8$) of SCU, and in 37.9% ($n = 11$) of C&SCU. There was no statistical difference between the groups ($p = 0.590$) (Table 2). In the CU, DES mean score of those who had a history of suicide attempt was significantly higher than the DES mean score of those who had not a history of suicide attempt ($p < 0.001$) however, there was no significant difference in SCU ($p = 0.070$) and C&SCU ($p = 0.256$) (not shown).

DES mean score of those with a history of suicide attempt was 40.51 ± 18.88 , which was higher than that of those without a history of suicide attempt (23.47 ± 19.24) ($p = 0.001$) among all participants. The history of suicide attempt was determined in 14.6% ($n = 7$) of low dissociation group, 52.8% ($n = 19$) of high dissociation group and there was a significant difference between groups ($p < 0.001$).

When age, age at onset of substance use, lifetime years of substance use and history of suicide attempt were correlated with DES mean score, only the age at onset of substance use was correlated with DES mean score (Table 3). To assess the predictors of the low/high dissociation levels a multivariate logistic regression analysis was performed, using the presence of high dissociation as the dependent variable. The independent variables were age at onset of substance use, lifetime years of substance use, the history of suicide attempt and type of substance used (C, SC, and C&SC usage). Only the history of suicide attempt predicted high dissociation significantly and presence of a history of suicide attempt increased the risk of high dissociation by 6.6 times (Table 4).

Table 1. Sociodemographic features of participants.

	CU ($n = 27$)	SCU ($n = 28$)	C&SCU ($n = 29$)	p
Age (years) (median)	23 (18–46)	23 (18–42)	22 (18–37)	0.443**
Gender				
Male	25 (92.6)	26 (92.9)	28 (96.6)	0.780*
Female	2 (7.4)	2 (7.1)	1 (3.4)	
Birthplace				
Rural	12 (44.4)	3 (10.7)	10 (34.4)	0.080*
Urban	15 (55.6)	25 (89.3)	19 (65.6)	
Place of residence				
Rural	2 (7.4)	3 (10.7)	5 (17.2)	0.235*
Urban	25 (72.6)	25 (89.3)	24 (82.8)	
Education				
Primary school	14 (51.8)	20 (71.4)	20 (68.9)	0.253*
High school	11 (40.7)	4 (14.3)	8 (27.6)	
College/University	2 (7.4)	4 (14.3)	1 (3.4)	
Marital status				
Single/divorced	19 (70.4)	22 (78.6)	27 (93.1)	0.089*
Married	8 (29.6)	6 (21.4)	2 (6.9)	
Occupation				
Unemployed	4 (14.8)	4 (14.3)	10 (34.5)	
Employee	18 (66.6)	16 (57.2)	14 (48.2)	0.626*
Student	4 (14.8)	5 (17.9)	3 (10.3)	
Others	1 (3.7)	3 (10.7)	2 (6.9)	
Monthly income				
≤ 800 TL	6 (23.1)	5 (17.9)	8 (27.6)	0.230*
801–1500 TL	9 (34.6)	17 (60.7)	15 (51.7)	
1501–3000 TL	5 (19.2)	2 (7.1)	5 (17.2)	
>3000 TL	6 (23.1)	4 (14.3)	1 (3.4)	

CU: Cannabis users, SCU: Synthetic Cannabinoid users, C&SCU: Both Cannabis and Synthetic Cannabinoid Users, TL: Turkish Liras. Qualitative variables "number (percentage)", quantitative variables "median (min-max)".

*Chi-Square Test.

**Kruskal Wallis Test.

Discussion

In this study, DES mean score of the all participants were 28.8 and the dissociation levels and rates of high dissociators were similar across CU, SCU and C&SCU groups. Age at onset of substance use was correlated negatively with levels of dissociation. DES mean score of patients with a history of suicide attempt was significantly higher compared to those without a

Table 2. Comparison of dissociation levels and the history of suicide attempt among groups.

(n = 84)	CU (n = 27) n (%)	SCU (n = 28) n (%)	C&SCU (n = 29) n (%)	p
DES mean score (±SD)	21.6 ± 19.3	32.8 ± 21.7	31.8 ± 19.4	0.058**
DES mean score of patients with a history of suicide attempt (±SD)	42.4 ± 18.4	44.5 ± 19.9	37.0 ± 18.8	0.432**
Dissociation level				
<30 (low dissociation)	18 (66.7)	14 (50.0)	16 (55.2)	0.443*
≥30 (high dissociation)	9 (33.3)	14 (50.0)	13 (44.8)	
History of suicide attempt				
Suicide attempted	7 (25.9)	8 (28.6)	11 (37.9)	0.590*
Non-suicide attempted	20 (74.1)	20 (71.4)	18 (62.1)	

n: number of patients, %: percent.

*Chi-Square Test.

**Kruskal Wallis Test.

history of suicide attempt and the sole significant predictor of being a high dissociator was the history of suicide attempt.

The rate of high-dissociators was 42.9%, which was higher than reported in previous studies, suggesting that dissociation levels are high in patients with C and SC use disorder, but the difference between C and SCs is not so clear. Dunn et al. reported that DES mean score was 15.4 in a sample of veterans and 16% were high dissociators in an inpatient substance use unit [13]. In a study of 62 patients with alcohol use disorder and 76 patients with cocaine-heroin use disorder, both had reported high levels of dissociation and patients with alcohol use disorder reported higher levels than the patients with substance use disorder in every category of DES [14]. In another study in Turkey, DES mean score was 21.6 and 29% of the patients with alcohol/substance use disorder were high dissociators, however, there was no difference in high-dissociator rates between the two groups with alcohol and substance use disorder. [16]. The findings of the current study could have been the result of recent use of C or SCs, as another study reported that length of abstinence from all substances was associated with a decrease in DES mean score among treatment-seeking substance users [23] or another possibility is that C and SCs could have their own high dissociative effects.

C is the most commonly used substance and probably due to the similar appearance and psychoactive effects, C users are vulnerable to use SCs. It was relevant that 96.4% of SC users in this sample had a history of C use and in a previous study which collected data online from participants primarily recruited from internet drug forums, 84% of SC users reported C intake [24]. While C has dissociative effects such as

depersonalization and disturbances in perceptions of time, SCs have similar effects with memory and concentration disturbances, alteration of time perception and confusion [25]. Age at onset of substance use, recent and long-term effects of substances, in fact, the chronicity of substance use is thought to be related with dissociation. However, in the study of Tamar-Gurol et al., 59.3% of the patients with dissociative disorder reported that dissociative experiences had started before drug use [17]. Wenzel et al. found significant correlations between years of regular alcohol and cocaine use and levels of dissociation consequently, suggested that dissociation could be a chronic residual effect of long-term substance use [14]. Age at onset of substance use was correlated with high dissociation nevertheless the lifetime years of C/SC use was not and none of them was a significant predictor of being a high dissociator in the current study. So that further research with larger samples is needed to investigate the cause and consequence relationship between C/SC use and the dissociation levels.

In the present study the history of suicide attempt was determined in 31% of the participants, which was higher than the rate reported in a study of 250 adolescents with chemical dependency that the history of suicide attempt rate was 20% and the suicidal group was found to be more psychologically distressed than were the other non-chemically dependent and non-suicidal high school student groups [26]. The similarity between CU and SCU for the history of suicide attempt in respect of dissociation levels suggests that the type of the substance used is neither related to the severity of dissociative symptoms nor the history of suicide attempt. Nevertheless, the dissociation level was higher in the patients with a history of suicide attempt in accordance with the literature. Higher levels of dissociation were found to be a significant predictor of past suicide attempts among patients with substance use disorders in a previous study [27] and another suggested that dissociative symptomatology was the most significant predictor of past suicide attempt [19]. Additionally, in a recent meta-analysis, patients with dissociative disorder were found more likely to have a lifetime history of suicide attempt in

Table 3. Correlation between clinical features and DES mean score.

	DES mean score	
	r	p
Age	-0.19	0.077
Age at onset of substance use	-0.22	0.042
Lifetime years of substance use	0.15	0.181

r: Spearman correlation coefficient.

Table 4. Predictors of high dissociation using logistic regression (enter method) analysis.

	B	S.E.	Wald	df	p	OR	95% C.I.
Age at onset of substance use	-0.014	0.047	0.089	1	0.766	0.986	0.898–1.082
Lifetime years of substance use	0.017	0.071	0.060	1	0.806	1.018	0.885–1.170
History of suicide attempt	1.886	0.542	12.104	1	0.001	6.596	2.279–19.089
CU			1.504	2	0.471		
SCU	0.726	0.617	1.387	1	0.239	2.068	0.617–6.925
C&SCU	0.231	0.646	0.128	1	0.720	1.260	0.355–4.469
Constant	-0.880	0.288	9.314	1	0.002	0.415	

*number of patients(n)= 84 †S.E.:Standart Error, OR: Odds Ratio, 95% C.I.: 95% Confidence Interval.

‡Nagelkerke R square: 0.234 §Hosmer and Lemeshow test significance: 0.822.

comparison to patients without dissociative disorder (Odds Ratio = 6.07, 95% Confidence Interval = 3.73–9.87) and suggested that the presence of dissociative disorder diagnosis or higher DES scores was related to suicide attempts in psychiatric patients [28]. From another point of view, in the present study suicidal history was found to be the only predictor of high dissociation in a sample of substance use disorder suggesting that the engagement in suicidal behaviour may represent an attempt to cope with dissociative symptoms or an ultimate attempt to reach a dissociative state [28]. In fact, these findings indicate a greater psychopathology and offer areas of clinical intervention to address. The assessment of dissociative symptoms is often skipped, but simply to be asked about the history of suicide attempt may be an important clue for dissociative symptoms. Thus, dissociation and suicidal behaviours are frequent in patients with C and SC use disorders, as are in other substance use disorders, and play an important role in prevention and treatment of substance use.

Interpretation of this survey should be considered with caution due to methodological limitations. The sample size was small in this study and owing to the cross-sectional design, there could be no observation of how symptoms changed over time. In addition, the semi-structured data form included items but no structured interview was conducted to determine the details of suicide attempts limiting the assessment. As the measure of dissociation that was used, DES asks subjects about their typical degree of dissociation when not under the influence of substances or alcohol but it is uncertain how accurately patients were able to make that determination. DES scores depend on the ability of individuals to differentiate substance-related and independent symptoms. Furthermore, patients included in the study were actively using substances that may have contributed to the dissociative experiences scores. Future studies using diagnostic interviews are necessary to be able to more fully understand the contribution of comorbid psychopathology to dissociation in patients with C and SC use disorders.

Conclusion

This study can be considered to extend the information in literature on treatment-seeking patients with C and

SC use disorders, and the clinical and especially the dissociative effects of SCs in comparison with C. The history of suicide attempt is frequent among treatment-seeking patients with C and SC use disorders and a significant predictor of dissociative symptoms that may complicate the treatment and make it difficult to benefit from cognitive or psycho-educational therapies. The relationship between substance use, dissociation and suicide are still not clear, however, these findings have potentially important implications for both research and treatment as previous studies have presented conflicting outcomes. Future studies with larger sample sizes and prospective design are needed to guide clinical practice and should include structured interviews for dissociative disorders and suicidality with different substance types to clarify the inconsistent findings.

Conflict of interest

The authors have no conflicts of interest to declare.

Disclosure statement

No potential conflict of interest was reported by the author(s).

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