

IS THERE A RELATIONSHIP BETWEEN CAFFEINE INTAKE AND SMOKING AND POSITIVE AND NEGATIVE SYMPTOM SEVERITY IN SCHIZOPHRENIA?

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SUMMARY

Background: It has been reported that caffeine intake and smoking are more frequent in patients with schizophrenia than the general population. However, the cause of high caffeine and smoking and its correlation with positive and negative symptoms is unclear. Therefore, the aim of the present study is to evaluate the correlation between daily caffeine intake and smoking and the severity of positive and negative symptoms in patients with schizophrenia.

Subjects and methods: This study included 177 participants, 89 of whom were healthy controls and 88 patients with schizophrenia. Scale for the Assessment of Positive Symptoms (SAPS) and Scale for the Assessment of Negative Symptoms (SANS) scales were applied to the patients with schizophrenia to measure the severity of positive and negative symptoms of the disease.

Results: The amounts of caffeine and tobacco consumption were significantly higher in the patients group than healthy controls ($p=0.001$ and $p<0.001$, respectively). There was no significant correlations between daily caffeine consumption and SAPS or SANS scores in patients with schizophrenia. There was a significant positive relationship between SAPS-delusions score and tobacco consumption.

Conclusions: Our study is the first study in the literature that examines the relationship between caffeine and cigarette intake and SANS and SAPS scales in patients with schizophrenia. Although caffeine intake is higher in patients with schizophrenia than healthy controls, this study is valuable as it shows that it is not associated with symptom severity. In addition, although it is known that smoking is high in patients with schizophrenia, this study showed a positive relationship between SAPS-delusion scores and tobacco consumption.

Key words: schizophrenia – caffeine – smoking - scale for the assessment of positive symptoms (SAPS) - scale for the assessment of negative symptoms (SANS)

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INTRODUCTION

The causes and consequences of excessive smoking in schizophrenia attract the attention of the scientific world (Winterer 2010). It is estimated that daily caffeine intake is almost 165 mg in the general population (Mitchell et al. 2014). Caffeine intake is significantly higher in patients with schizophrenia than those without schizophrenia (Strassnig et al. 2006), estimated at approximately 500 mg per day. Also, one-third of the patients with schizophrenia have been reported to intake more than 550 mg per day (Mayo et al. 1993). Among psychiatric patients, it has been observed that caffeine consumption increased primarily in schizophrenia, then in depression and anxiety disorders (Kim & O'Hanlon 2011). There are many reasons that may be explained why caffeine intake is higher in schizophrenic patients. For example; it may reduce negative symptoms and extrapyramidal side effects of neuroleptic drugs, or caffeine use may be increased as caffeine elimination increases as a result of increased smoking in patients with schizophrenia (Hughes et al. 1998). On the one hand, acute consumption of caffeine in toxic doses significantly alters psychopathology and may even exacerbate existing psychotic symptoms (Strassnig et al. 2006).

The reasons for increased intake of caffeine in the patients with schizophrenia have not been investigated. However, it has been reported that caffeine intake positively affected neurocognition in male patients diagnosed with schizophrenia (Núñez et al. 2015). Additionally, Topyurek et al. (2019) stated that literature assessing the effects of caffeine doses on sedation as well as cognitive and negative symptoms has been insufficient. Whether caffeine intake increases psychotic symptoms or treats negative symptoms in schizophrenia is unclear. The relationship of increased caffeine intake with symptoms in schizophrenia patients is not yet known. Investigating the relationship between the severity of positive and negative symptoms and caffeine intake in patients with schizophrenia may shed light on this issue. For this purpose, we examined the relationship between positive and negative symptom severity and caffeine intake as well as the amount of smoking and caffeine intake in patients diagnosed with schizophrenia.

SUBJECTS AND METHODS

Subjects

In this research, the sample size was calculated as 130 with the G power program (effect size = 0.43, alpha value = 0.05, power = 0.80, and group number = 2).

Our study included 177 individuals, 88 of whom were patients with schizophrenia admitted to a large hospitalization unit of Adiyaman University Training and Research Hospital and 89 were healthy controls. Inclusion criteria for patients were having diagnosis of schizophrenia according to DSM-V criteria, age between 18 and 65 years old and cognitive capacity to give correct answer to the questions. Non-inclusion criteria of the study were alcohol or substance use disorders according to DSM-V during the previous 12 months, any psychiatric disorder other than schizophrenia, alcohol-substance abuse, a history of organic mental disease, dementia, severe physical illness or intellectual disability. The control group consisted of those who were examined in our clinic to get a healthy report for reasons such as job application. The control group included healthy individuals with a similar age and gender distribution with the patient group. Non-inclusion criteria for controls were having a mental illness, alcohol or substance use disorders according to DSM-V during the previous 12 months, a history of organic mental disease, alcohol-substance abuse, dementia, intellectual disability or severe physical illness.

The flowchart for election of the patients was shown in Figure 1.

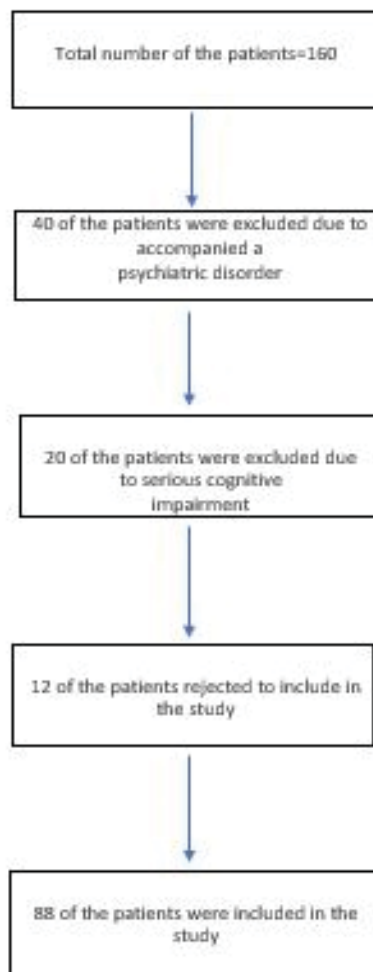


Figure 1. Election of the patients

Procedure

This study was approved by the Ethics Committee of Adiyaman University (no. 2020/3-26 dated April 21, 2020). All participants provided informed consent before taking part in the study. The diagnosis of schizophrenia was made through a structured clinical interview by the only specialist experienced in the field. The scales were filled in by the only researcher in the research group with psychiatric-psychometric experience. In addition to sociodemographic data, the daily amount of caffeine, the amount of cigarettes smoked and the antipsychotic drugs used by the patient were recorded in the sociodemographic data form. For the control group, in the sociodemographic data form, daily caffeine intake and daily smoking amount were recorded, as well as sociodemographic characteristics. The patient and control group were asked how much they took from caffeine-containing beverages. We made a distinction between coffee, tea or other caffeinated beverages, which have different caffeine quantities. We asked participants about type, brand, size of caffeinated beverages and other products. These beverages and products are known to include caffeine with online searches allowing for accurate caffeine content as milligrams (for example coffee, tea, green tea, energy drinks, drugs, chocolate). The caffeine contents of the drinks that the participants took daily were collected and the amount of caffeine they took daily was recorded as milligrams. Since these patients were hospitalized in the ward, we could observe objectively measure levels of caffeine intake and smoking. Scale for the Assessment of Positive Symptoms (SAPS) and Scale for the Assessment of Negative Symptoms (SANS) scales were applied to patients diagnosed with schizophrenia to measure the severity of positive and negative symptoms.

Clinical scales

Scale for the Assessment of Positive Symptoms

Positive symptomatology in schizophrenic patients was assessed using the Turkish version of the SAPS. It was developed by Andreasen (1990) to assess the level, distribution and severity of change in positive symptoms of schizophrenia. Erkoç et al. (1991a) conducted the validity and reliability of the Turkish version.

Scale for the Assessment of Negative Symptoms

Negative symptomatology in schizophrenic patients was assessed using the Turkish version of SANS. It was developed by Andreasen (1990) to assess the level, distribution and severity of change in negative symptoms of schizophrenia. Erkoç et al. (1991b) conducted the validity and reliability of the Turkish version.

Statistical Analysis

IBM SPSS Statistics for Windows, Version 22.0. (IBM Corp. Armonk, NY: USA. Released 2013) was used for all statistical analyses. Descriptive parameters

are expressed as mean ± standard deviation or number (percentage). The chi-square test was used to compare categorical data. Normality of distribution was tested with Levene's test and homogeneity tests. Normality distribution of continuous variables was analyzed in accordance with their skewness and curtosis values. Due to continuous variables fit the normal distribution parametric tests were used in analyzes of the datas. Continuous variables of the patients and healthy controls were compared by independent samples t test. The Pearson correlation analysis was performed to investigate the relationship between clinical and demographic parameters in patients with schizophrenia. A p value of <0.05 was considered statistically significant.

RESULTS

Sample Characteristics

This study included 88 patients with schizophrenia and 89 healthy controls. The sociodemographic features, caffeine and tobacco consumption (daily) of the patients and controls were compared in Table 1.

Daily caffeine and tobacco consumption amounts were significantly higher in the patients group than healthy controls (p=0.001 and p<0.001, respectively).

Comparison of caffeine and tobacco consumption of the female participants of the groups were shown at

Table 2. Accordingly, daily caffeine and tobacco consumption amounts were significantly higher in the female patients than female controls (p=0.003 and p=0.018, respectively).

Comparison of caffeine and tobacco consumption of the male participants of the groups were shown at Table 3. Accordingly, daily caffeine and tobacco consumption amounts were significantly higher in the male patients than male controls (p=0.039 and p=0.006). Additionally, daily tobacco consumption of the male patients was significantly higher than those females (p=0.001).

SANS and SAPS scores in patients with schizophrenia

There were positive correlations between daily tobacco consumption amount and SAPS-delusion subscale score and SAPS total score in patients with schizophrenia (r=0.28 and r=0.22, respectively). There was no significant correlations between daily caffeine consumption and SAPS or SANS scores in patients with schizophrenia (Table 4).

The sociodemographic features and SANS and SAPS scores of the male and female patients were compared at Table 5. SAPS-bizarre behaviors score of the female patients was significantly higher than those males (p=0.02).

Table 1. Comparison of sociodemographic features between the patients with schizophrenia and healthy controls

Variable	Patients (n=88) M±SD or N (%)	Healthy controls (n=89) M±SD or N (%)	χ ² or t value	p
Age	38±10.9	37.7±9	0.217 ^a	0.828
Gender (female)	24 (27.3)	35 (39.3)	2.893 ^b	0.089
Education (university)	9 (10.2)	62 (69.7)	75.891 ^b	<0.001
Marital status (married)	33 (37.5)	71 (79.8)	33.165 ^b	<0.001
Occupation (working)	18 (20.4)	79 (88.8)	107.776 ^b	<0.001
Residing (rural)	20 (23)	6 (3.9)	23.904 ^b	<0.001
Income level (income>expense)	1 (1.1)	21 (23.6)	30.042 ^b	<0.001
Tobacco consumption (Daily)	14±16	6.3±10.4	3.703 ^a	<0.001
Cafein consumption (Daily)	454.3±360.1	310.4±162.3	3.435 ^a	0.001

Abbreviations: ^a Independent samples t test; ^b Pearson Chi-Square test; M±SD - mean ± standard deviation; The significant results are presented in *italics*

Table 2. Comparison of tobacco and cafein consumptions between female patients with schizophrenia and female healthy controls

Variable	Female patients (n=24)	Female controls (n=35)	t	p
Tobacco consumption (Daily)	6.8±9.8	1.9±5.4	2.435	0.018
Cafein consumption (Daily)	457.5±307.6	270±145.6	3.132	0.003

The significant results are presented in *italics*

Table 3. Comparison of tobacco and cafein consumptions between male patients with schizophrenia and male healthy controls

Variable	Male patients (n=64)	Male controls (n=54)	t	p
Tobacco consumption (Daily)	17.2±17.3	9.2±11.8	2.814	0.006
Cafein consumption (Daily)	453.1±380.1	336.3±168.4	2.091	0.039

The significant results are presented in *italics*

Table 4. Correlations between sociodemographic features and SANS and SAPS scores in patients with schizophrenia

	Age	Disease duration	Number of hospitalization	Tobacco	Cafein
SANS-affective blunting	0.20	0.21	0.12	0.21	0.08
SANS-alogia	0.25*	0.30**	0.15	-0.02	-0.03
SANS-anhedonia	0.14	0.16	0.003	0.08	-0.07
SANS-attention	0.20	0.22*	0.20	-0.07	0.004
SANS-avolition	0.31**	0.32**	0.29**	0.13	0.10
SAPS-bizarre behaviors	0.18	0.25*	0.29**	-0.03	0.14
SAPS-delusions	-0.03	0.03	-0.03	0.28*	0.16
SAPS-hallucinations	-0.13	-0.05	-0.05	0.11	0.09
SAPS-positive formal thought disorder	0.04	0.11	0.22*	0.15	0.16
SANS-total	0.29**	0.33**	0.20	0.11	0.09
SAPS-total	0.002	0.09	0.13	0.22*	0.18

*p<0.05; **p<0.01

Table 5. Comparison of sociodemographic features and SANS and SAPS scores of the male and female patients

Variable	Female patients (n=24) M±SD	Male patients (n=64) M±SD	χ ² or t value	p
Age	38.6±13.2	37.8±10	0.285	0.778
Duration of disease (year)	14.3±11.1	13.5±8.7	0.343	0.734
Number of hospitalization	2.6±2.2	2.2±2.4	0.637	0.527
Education (university)	4 (16.7)	5 (7.8)	7.634	0.104
Marital status (married)	9 (37.5)	24 (37.5)	13.811	<i>0.001</i>
Occupation (working)	3 (12.5)	15 (23.5)	2.161	0.405
Residing (rural)	6 (26.1)	14 (21.9)	0.290	0.863
Income level (income>expense)	0 (0)	1 (1.6)	0.613	0.861
Tobacco consumption (Daily)	6.8±9.8	17.2±17.3	-3.380	<i>0.001</i>
Cafein consumption (Daily)	457.5±307.6	453±380	0.056	0.956
SANS-affective blunting	18.6±7	20.4±6.5	-1.088	0.283
SANS-alogia	9.5±5.8	9.3±4.1	0.206	0.838
SANS-anhedonia	9.6±4.3	11.2±4.5	-1.445	0.156
SANS-attention	5.3±3.3	4.4±3.3	1.091	0.282
SANS-avolition	9±5.4	8.2±7	0.550	0.584
SAPS-bizarre behaviors	8.1±6.2	4.7±4.4	2.441	0.020
SAPS-delusions	8.5±10.1	7.6±8.2	0.399	0.693
SAPS-hallucinations	6.3±7.3	5.7±6.6	0.347	0.731
SAPS-positive formal thought disorder	7.4±5.7	6.3±6.2	0.790	0.434
SANS-total	52.3±21.2	51.9±18	0.089	0.930
SAPS-total	30.4±22.3	25.8±17.2	0.913	0.368

M±SD - mean ± standard deviation; The significant results are presented in *italics*

DISCUSSION

This is the first study to examine the relationship between smoking and caffeine intake and SANS and SAPS scores in patients with schizophrenia. Consistent with the literature, both caffeine and cigarette consumption were higher in patients with schizophrenia than healthy controls. Moreover, when women and men were compared within themselves, female patients had significantly higher caffeine and cigarette consumption than female controls, and male patients had significantly more caffeine and cigarette consumption than male controls.

While male patients consumed more tobacco than females in the schizophrenia group, there was no difference in caffeine consumption. In a study conducted by Núñez et al. (2015) caffeine intake was found to be higher in male schizophrenic patients than in female schizophrenic patients. We think our results are valid, because our sample size is larger. In the same study, it was reported that caffeine intake has a positive effect on neurocognition in male schizophrenia patients (Núñez et al. 2015).

In our study, tobacco consumption was significantly higher in male patients than in female patients. This result was in agreement with the result of Núñez et al.

(2015). In their study, this neurocognitive well-being may also be due to cigarette consumption, since the male patient group had high consumption of both caffeine and cigarettes.

It is stated in the literature that there may be many reasons for increased caffeine consumption in schizophrenia. Smoking increases the metabolism of caffeine by inducing the CYP1A2 enzyme and diminish caffeine concentration (Carrillo & Benitez 1996). It has been previously reported that high-dose caffeine intake is associated with excessive smoking in patients diagnosed with schizophrenia (Gurpegui et al. 2004). On the other hand, it has been reported that the patients with schizophrenia had two times greater serum caffeine levels as compared to without any mental illness with similar smoking behavior (Gandhi et al. 2010). Arrojo-Romero et al. (2015) stated that tobacco smoking may explain in large part the apparent association between schizophrenia and caffeine use. In our study, although female patients had lower cigarette smoking than male patients, the amount of caffeine intake was higher, which does not support this hypothesis.

Rajkumar et al. (2013), stated that high dose caffeine intake (3 cups or more) reduces the effect of clozapine and therefore, patients diagnosed with schizophrenia may be taking more caffeine to reduce the sedative effect of clozapine. On the one hand, there are also concerns that caffeine intake will increase positive symptoms in schizophrenia patients. Two cases of schizophrenia exacerbated by caffeine intake were also reported in the literature (Mikkelsen 1978).

A recent animal study reported that caffeine may have beneficial effects in schizophrenia (Ramos et al. 2020). Although this raises the question of whether caffeine intake improves symptoms in schizophrenic patients, we could not find a relationship between symptom severity and caffeine consumption in schizophrenia.

In a previous study, it was stated that participants with high caffeine intake had fewer negative symptoms and more positive symptoms (Topyurek et al. 2020) We did not found significant correlations between daily caffeine consumption and SAPS or SANS scores in patients with schizophrenia. Although our results are inconsistent with this study, we would like to point out that their sample size was small.

We found a significant positive correlations between daily tobacco consumption amount and SAPS-delusion subscale score and SAPS total score in patients with schizophrenia. In those with positive symptoms, the need for cigarettes or excessive consumption of cigarettes may increase positive symptoms in patients with schizophrenia. The studies investigating smoking and symptom severity in schizophrenia have been conducted but those studies have reported controversial results (Šagud et al. 2018). Krishnadas et al. (2012) reported that patients with

severe nicotine dependence had greater positive symptoms. The results of our study also support their conclusion.

Recently, attention has been drawn to the relationship between smoking and symptoms in schizophrenia (Ding & Hu 2021). Nicotine has been known to modulate the release of nearly all neurotransmitters, including serotonin, dopamine, noradrenaline, glutamate, γ -aminobutyric acid and opioid (Subramaniyan & Dani 2015). This modulation may also explain the high SAPS-delusion and SAPS-total scores in our study.

A recent meta-analysis showed that chronic smoking in patients with schizophrenia was associated with a significant impairment in several cognitive functions such as attention (Coustals et al. 2020). Despite the positive correlations between SAPS-delusion subscale score and SAPS total score and tobacco consumption, there was no significant correlation between SANS-attention score and SANS-total score and smoking. When our findings are evaluated together with the literature, it can be thought that smoking may have a negative effect on symptom severity.

Our study has some limitations. This is an observational naturalistic study and the factors studied were not manipulated. We did not take into account the potential effects of medication in patients.

However, this study, which shows that caffeine intake is not associated with the severity of symptoms in schizophrenia, and that cigarette intake is positively related to the SAPS-delusion subscale score and SAPS total score, is valuable as it is the first in the literature.

CONCLUSION

In this study, we aimed to investigate the relationship between positive and negative symptom severity and caffeine intake in patients diagnosed with schizophrenia.

In conclusion, we found that caffeine and cigarette consumption were higher in patients with schizophrenia compared to healthy controls. We did not found significant correlations between daily caffeine consumption and SAPS or SANS scores in patients with schizophrenia. We found a significant positive correlations between daily tobacco consumption amount and SAPS-delusion subscale score and SAPS total score in patients with schizophrenia.

This study is the first in the literature that examines the relationship between caffeine and cigarette intake and SANS and SAPS scales in patients with schizophrenia. Although it has been previously reported in the literature that caffeine intake is high in patients with schizophrenia, this study is valuable because it shows that it is not associated with symptom severity.

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Conflict of interest: None to declare.

Contribution of individual authors:

Behice Han Almis: study design, data collection, first draft, approval of the final version, statistical analysis.
Atilla Tekin: data collection, first draft, statistical analysis.
Gunnur Hakyemez Geylani, Elif Baltaci & Asli Egeli: data collection, first draft.

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