

Depressive Temperament in Relatives of Patients with Schizophrenia Is Associated with Suicidality in Patients with Schizophrenia

Esra Yazici¹, Zerrin Cimen², Ipen Ilknur Unlu Akyollu², Ahmet Bulent Yazici², Betul Aslan Turkmen², Atila Erol¹

¹Department of Psychiatry, Faculty of Medicine, Sakarya University, ²Department of Psychiatry, Sakarya University Training and Research Hospital, Sakarya, Turkey

Objective: Suicide is a major cause of death in patients with schizophrenia; thus, predicting and preventing suicide in patients with schizophrenia is examined in various studies. Affective temperaments which are accepted as precursors of mood disorders may be an important factor in predicting suicidality. This study investigated the relationship between affective temperaments of relatives of schizophrenia patients and suicidal thoughts and other clinical correlates of patients with schizophrenia.

Methods: Patients with schizophrenia and their first degree relatives are included to the study. All of the participants were evaluated with Structured Clinical Interview for DSM-IV axis I disorders and relatives with active psychiatric diagnosis were excluded. Positive and Negative Symptom Scale, Clinical Global Impression Scale, Turkish version of cognitive assessment interview were administered congruently to the patients. Relatives of the patients were evaluated with Temperament Evaluation of Memphis, Pisa, Paris and San Diego-Auto-questionnaire.

Results: Depressive temperament scores of relatives of schizophrenic patients who had suicidal thoughts were higher than the scores of the relatives of the patients who did not have suicidal thoughts. Depressive temperament also predicted number of suicide attempts in regression analysis. Number of suicide attempts was also related with number of hospitalization and functionality of the patient.

Conclusion: Suicidality in schizophrenia is related with relatives' affective temperaments and patients' own positive symptom scores. The relationship between suicidal thoughts and depressive temperament is high lightened in this study

KEY WORDS: Suicide; Schizophrenia; Family; Temperament; Depressive mood.

INTRODUCTION

Suicide is an important public health problem with nearly one million deaths across the world per year.¹⁾ Suicide is a major and one of the most significant causes of unexpected death in people with schizophrenia particularly during the early phase of the illness.^{2,3)} The risk of suicide in patients with schizophrenia is reported as 20 to 50 fold higher than general population.⁴⁾ Lifetime suicide risk rate of the patients with schizophrenia has been recently reported to be between 2% to 5% and moreover

50% of the patients who have schizophrenia attempt suicide during their lifetime.³⁻⁵⁾ Suicidal thoughts occur frequently in patients with schizophrenia, reported to be at rates as high as 42%. Suicide is a major cause of death in patients with schizophrenia; thus, predicting and preventing suicide in patients with schizophrenia is examined in various studies.^{6,7)}

Some recognized risk factors for suicidal patients with schizophrenia are similar to those in the general population. Being male, living alone, hopelessness, previous suicide attempts, comorbid depressive disorders, comorbid alcohol and drug misuse, younger age, higher education, agitation or motor restlessness, low self-esteem, active hallucinations and delusions comorbid chronic physical illness and a family history of suicide have been associated with increased suicide risk in patients with schizophrenia.⁸⁻¹⁰⁾

Depressive symptoms in schizophrenia are clinically

Received: May 16, 2017 / **Revised:** July 16, 2017

Accepted: August 11, 2017

Address for correspondence: Ahmet Bulent Yazici, MD
Department of Psychiatry, Sakarya University Training and Research Hospital, Sakarya 54290, Turkey
Tel: +90-5325994988, Fax: +90-264-2552105
E-mail: a.bulentyaz@gmail.com
ORCID: <https://orcid.org/0000-0001-5631-3100>

© This is an Open-Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (<http://creativecommons.org/licenses/by-nc/4.0>) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

very important because they are associated with high suicide risk.^{11,12} Family history of depressive disorder is a risk factor for depression in schizophrenia.¹³ Depressive symptoms are often seen in patients with schizophrenia and the prevalence of depressive symptoms in schizophrenia is reported to range from 25% to 81%.¹⁴

The affective temperament of an individual is one of the structural, biological, and genetic factors determining the risk of depression and mania¹⁵ and clinical characteristics proposed to be associated with suicidal risk include affective temperaments types. Several studies have shown that affective temperaments which are accepted as precursors of mood disorders may be an important factor in predicting suicidality.⁶ It is shown that the anxious temperament plays a strong role in predicting suicide attempts in the community. Also, depressive and irritable temperaments are shown to be associated with an increased risk for suicidality.¹⁶ Affective temperaments in relatives of schizophrenics and their correlates have not been studied yet. In this study, patients with schizophrenia and their first-degree relatives with affective temperament characteristics were evaluated.

METHODS

This study was conducted with 101 schizophrenic patients and their first-degree relatives. An ethic committee approval was obtained for this study from Sakarya University Ethics Committee (No. 71522473/050.01.04/07). All the patients and relatives gave a written consent for the study.

Sampling

The treatment and rehabilitation programmes of the patients were routinely conducted by Sakarya University Training and Research Hospital Community Counseling Centre (Sakarya TRSM). All patients have clinical records and personalized treatment programmes in Sakarya TRSM. Consecutive 150 patients known as schizophrenia according to their clinical records and their first-degree relatives were asked to join the study. One hundred thirty-one patients; who have a first degree relative, both of the patient and the relatives accepted to join to the study were evaluated with Structured Clinical Interview for DSM-IV axis I disorders (SCID-I), 126 of the 131 patients' diagnosis was replicated as schizophrenia and 5 of them

were excluded due to the diagnosis of other disorders (schizoaffective disorder, organic disorders, etc.). Also 21 of the relatives had an active psychiatric disorder (depression, bipolar disorder, etc.), so they were excluded from the study as well. Finally 101 patients and their relatives who have clinically enough cognitive level to understand and answer the questions of the study were included to the study.

Patients with schizophrenia were evaluated with a detailed form that asks clinical and social properties of patients such as duration of illness, number of hospitalization, suicidality (lifetime suicidal thoughts, lifetime number of suicide attempts), etc. and the Positive and Negative Symptom Scale (PANSS), Clinical Global Impression Scale (CGI) and General Assessment of Functioning Scale (GAF) for the assessment of the patient's functionality and severity of illness. Also, Turkish version of cognitive assessment interview (CAI-TR) were administered congruently to the patients. Relatives of the patients were evaluated with Temperament Evaluation of Memphis, Pisa, Paris and San Diego-Auto-questionnaire (TEMPS-A).

Material

Sociodemographic data form

SCID-I: SCID-I clinical version (SCID-CV)

The SCID-I is a semi-structured diagnostic interview containing the DSM-IV diagnoses, translated to Turkish and confirmed for validity/reliability by Çorapçıoğlu *et al.*¹⁷ The SCID-I begins with a socio-demographic data guide and covers seven diagnosis groups: mood disorders, psychotic disorders, alcohol and substance-related disorders, anxiety disorders, somatoform disorders, eating disorders, and adjustment disorders. It has high reliability for psychiatric disorders. It is used as a standard interview to affirm the diagnosis in clinical studies.

TEMPS-A

The TEMPS-A was used in this study to assess the score averages of the subtypes of the affective temperaments of the participants. It was originally designed by Akiskal *et al.*^{18,19} in 1997 and adopted into Turkish by Vahip *et al.*²⁰ It is a self-assessment scale, involving "true" or "false" indications that aim to take into account the entire life of the

individual. It consists of five sub-dimensions that establish depressive, cyclothymic, hyperthymic, irritable, and anxious temperament.

PANSS

It is a semi-structured interview scale developed by Kay *et al.*²¹⁾ The scale evaluates positive and negative symptoms and general psychopathology by 30 items which are rated with seven point-severity scale. Total score is between 30 and 210. Higher ratings reflect a greater severity of symptoms. Turkish reliability and validity of the scale was studied by at Kostakoglu *et al.*²²⁾

GAF

This scale helps monitor the clinical progress of an individual in its general framework by using a single measurement. With the GAF scale, which is structured in line with the DSM-IV, patients' psychological, social and occupational functioning is assessed. The scale involves a general rating of a person's functioning at that moment or in the past by a clinician who gives a point between 1 and 100.²³⁾

CGI

A scale used to assess the severity, improvement rate and medication side effects of psychiatric disorders. The illness severity subscale was used in this study. The scale for severity of illness refers to the clinician's global impression of the patient, and scored between 1 and 7. The scale scores rise as the severity of illness increases.²⁴⁾

CAI-TR

The Cognitive Assessment Interview (CAI) is an interview-based measure developed to assess cognitive functioning of schizophrenia patients. It was developed by the Ventura *et al.*²³⁾ and reliability and validity of the CAI-Turkish version (CAI-TR) was conducted by Bosgelmez *et al.*²⁵⁾ It is scored by a clinician according to patient and informant interview. CAI is a 10-item scale completed by the examiner during interviews with the patients and their relatives, where each question is given a score on a Likert scale ranging from 1 to 7. Patient's, relative's and the interviewer's assessment are scored separately.

Statistical Analysis

The data were analyzed by the SPSS ver. 17.0 (SPSS

Inc., Chicago, IL, USA) statistical program. Distributions of the data were evaluated with one sample Kolmogorov-Smirnov test and the data with normal distributions was compared with Student *t* test. The ones which do not have normal distribution are compared with Mann-Whitney *U* test. One-way ANOVA was used to compare linear variables of the groups and chi-square test was used to compare categorical variables between two or more independent groups. Pearson correlation analysis was used to determine the relationship between linear variables. Multivariate analysis of covariance (MANCOVA) and regression analysis were conducted to identify and adjustment of confounding factors. Also predictors of suicide attempts were evaluated with linear regression analysis. The $p < 0.05$ is established as determinant of significance.

RESULTS

Sociodemographic Data

The study included 101 patients and their 101 first-degree relatives from Sakarya TRSM. The mean age of the patients was 41.63 ± 9.18 (range, 24-65) years. Seventy of the patients were male (69.3%), and 43 of the first-degree relatives of the patients were male (42.6%). Relatives of the patients were consist of mothers or fathers ($n=43$, 42.6%) or siblings ($n=45$, 44.6%) or children ($n=13$, 12.9%) of patients. Sociodemographic data of patients and their first-degree relatives are presented at Table 1.

Clinical Data of the Patients

Age of onset was 23.43 ± 7.04 (range, 10-47) years and mean duration of the illness was 5.20 ± 7.09 (range, 1-30)

Table 1. Sociodemographic data

Characteristic	Patients (n=101)	Relatives (n=101)
Age (yr)	41.63±9.18 (24-65)	49.46±14.89 (18-70)
Gender (male:female)	70:31	43:58
Year of education (yr)	8.06±3.38	7.20±4.58
Marital status		
Married	21	67
Divorced/ widowed	23	19
Single	57	15
Occupational status		
Employed	14	32
Unemployed	87	69

Values are presented as mean±standard deviation (range) or number only.

Table 2. Clinical data of the patients

Variable	Data
Age of onset (yr)	23.43±7.04 (22, 10-47)
Duration of schizophrenia disorder (yr)	5.20±7.09 (1, 1-30)
Total duration of hospitalization (mo)	81.76±86.64 (51, 0-444)
Number of hospitalization	2.91±2.5 (2, 0-16)
Global CAI score	3.79±1.07 (4, 1-6)
Cognitive functionality PANSS score	56.00±10.03 (55, 25-90)
Positive	24.30±7.23 (24, 14-45)
Negative	24.76±7.25 (24, 11-43)
General	55.37±13.70 (55, 18-96)
Total	104.67±24.95 (106, 64-174)
CGI	4.01±0.88 (4, 2-6)
General assessment of functionality	56.0±10.03 (55, 25-80)

Values are presented as mean±standard deviation (median, range). CAI, cognitive assessment interview; PANSS, Positive and Negative Symptom Scale; CGI, Clinical Global Impression Scale.

years. Information regarding patients and their clinical status is presented in Table 2.

The relationship between the familial affective temperament and patients' clinical status

There was no relationship between affective temperaments of the relatives and the clinical severity of the symptoms and functionality of the patients according to correlation analysis. Mean scores of relatives of the patients' affective temperaments were as follows: depressive temperament 6.21±3.71 (0-16), cyclothymic temperament 6.16±4.76 (0-18), hyperthymic temperament 11.01±5.07 (0-26), irritable temperament 3.18±3.50 (0-14), anxious temperament 5.56±5.02 (0-20).

The relationship between suicidality and patients' clinical properties

Patients with a rate of 24.8% had a suicide attempt previously. Also 52.4% of the number of suicide attempts

Table 3. Sociodemographic clinical properties of patients with or without suicidality

Variable	Patients with suicidal attempt (n=25)	Patients with suicidal idea (n=53)	Patients with no suicidality (n=48)	p value
Gender (male:female)	18:07	37:16	33:15	
Marital status				
Single	18	32	25	
Married	5	10	11	
Divorced	2	11	12	
Age	40.08±9.53 (29-63)	40.30±9.14 (24-65)	43.10±9.08 (27-59)	0.126
Education (yr)	6.44±4.61 (0.00-14.0)	6.50±4.82 (0-17)	7.96±4.22 (0-16.5)	0.111
Monthly income (Turkish Liras)	422.8±496.9 (0-2,400)	477.0±508.7 (0-2,400)	706.8±664.0 (0-2,900)	0.053
Number of hospitalization	3.72±2.20 (0-8)	3.15±2.78 (0-16)	2.64±2.14 (0-8)	0.313
Temperament scores of relatives				
Depressive	7.24±4.15 (1.00-16.00)	6.98±3.94 (1-16)	5.32±3.25 (0-11)	0.026*
Cyclothymic	6.52±4.79 (0.00-16.00)	7.01±5.02 (0-18)	5.22±4.31 (0-17)	0.059
Hyperthymic	10.44±4.60 (2.00-18.00)	11.49±4.89 (2-6)	10.50±5.27 (0-20)	0.33
Irritable	3.48±3.51 (0.00-13.00)	3.58±3.61 (0-14)	2.75±3.35 (0-14)	0.233
Anxious	6.44±5.11 (0.00-18.00)	6.45±5.04 (0-20)	4.58±4.87 (0-18)	0.062
PANSS				
Positive	28.24±7.60 (15-45.00)	25.79±7.21 (14-45)	22.66±6.96 (14-40)	0.029*
Negative	26.80±6.23 (14.0-41.0)	24.94±6.99 (13-1)	24.56±7.61 (11-43)	0.794
General	62.64± 3.17 (38-96.00)	57.64±13.3 (33-96)	52.87±13.84 (18-95)	0.081
Total	117.6±23.85 (69-174.0)	108.3±24.94 (64-174)	100.6±24.59 (64-157)	0.121
CAI-TR				
Total score	4.04±1.01 (2.00-6.00)	3.73±1.12 (1-6)	3.85±1.03 (2-6)	0.585
Functionality	51.56±10.27 (25-70.0)	56.28±11.13 (35-90)	55.66±10.80 (25-75)	0.779
CGI	4.24±0.92 (2.00-6.00)	4.01±0.88 (2-6)	4.02±0.887 (2-6)	0.991
GAF	51.48±10.96 (25-70.0)	55.92±10.77 (25-82)	55.89±8.56 (27- 70)	0.988

Values are presented as number only or mean±standard deviation (range). PANSS, Positive and Negative Symptom Scale; CAI-TR, Turkish version of cognitive assessment interview; CGI, Clinical Global Impression Scale; GAF, General Assessment of Functioning Scale.

*Statistical significance.

was between 0 to 4 (0.51 ± 0.90), when all schizophrenic patients taken in the account, and when the ones who did not attempt suicide were excluded, then the median number of suicides was 1 (range, 1-4).

Suicidality was assessed in two topics: suicidal thoughts and suicidal attempts. Patients with suicidal thoughts had significantly higher positive PANSS scores than patients did not ever had suicidal thoughts (18.79 ± 7.21 vs. 15.66 ± 6.96 ; $p=0.043$). Patients with no suicidality (with no suicidal thoughts and attempts ever) were compared with patients with suicidality with one-way ANOVA analysis. Results are abstracted at Table 3.

Suicidality and affective temperaments

There was a positive correlation between the number of suicide attempts of patients and the number of hospitalizations and a negative correlation between general functioning ($r=0.216$ and -0.242 , respectively; $p<0.05$). There was a positive correlation between the suicide attempts of patients and depressive temperament scores of their relatives ($r=0.221$; $p<0.05$).

Depressive temperament scores were higher in the relatives of schizophrenic patients who had suicidal thoughts ($t=2.285$, $p<0.05$). Comparison of affective temperament scores of relatives of patients with schizophrenia who did have or who did not have suicidal thoughts is shown in Figure 1 and Table 3.

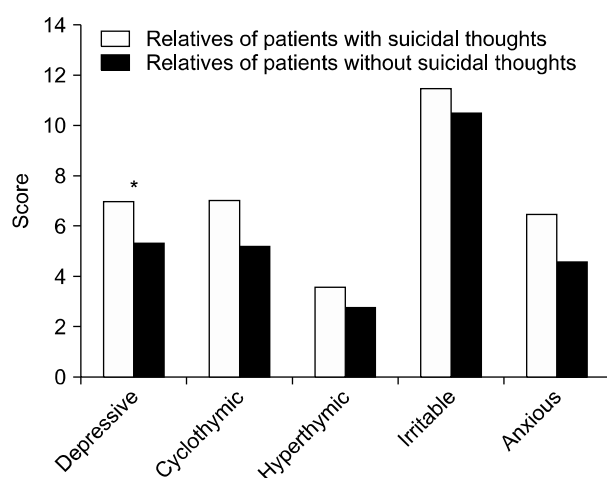


Fig. 1. Affective temperament scores of relatives of patients with schizophrenia who had or did not have suicidal thoughts.

* $p<0.05$.

Adjustment for confounding factors

Initially, MANCOVA analysis was conducted to evaluate the efficacy of covariates for relationship with suicidality. A model was set by the significant results obtained from this study for dependent variables suicidal attempts and suicidal thoughts and covariates (number of hospitalisation, GAF scores, depressive temperament scores, PANSS positive scores). Depressive temperament scores and PANSS positive scores were still significant for suicidal thoughts ($F=4.751$, $p=0.032$ and $F=5.149$, $p=0.026$, respectively; and $R^2=0.106$, adjusted $R^2=0.068$).

Also a linear regression model was established using the data obtained from this respective study and the factors that are indicated to be related to suicide in literature. Age, gender, marital status, monthly income, years of education, number of children, age at onset, number of hospitalizations, duration of hospitalizations and depressive temperament scores of the relative were included in the analysis as independent variables and the number of suicide attempts was a dependent variable in this model. In this model, the marital status of the patient (being single) and the depressive temperament scores of the patient's relative were found to be independent predictors (beta for depressive temperament= 0.225 , $t=2.098$, $p<0.05$; beta for marital status= -0.247 , $t=-2.085$, $p<0.05$).

DISCUSSION

This study presents an important data about the relationship between suicidality and relatives affective temperament of patients with schizophrenia. Relatives of schizophrenics who have had suicidal thoughts have statistically higher depressive temperament scores than the ones whose relatives did not have suicidal thoughts.

Suicidality is a major health problem and patients with schizophrenia has higher risk for suicidal thoughts.^{9,26} In this study more than a half of the patients had suicidal thoughts and approximately a quarter of all of the patients had a suicidal attempt. This is an important ratio and needs to be predicted and prevented if possible.

This study found depressive temperament scores of relatives as a predictor of suicidal thoughts in schizophrenia. Also number of suicide attempts was correlated with depressive temperament scores of his/her relatives in our results. Affective temperaments are shown to have genetic background and related with affective disorders indeed.²⁷

Also, affective temperaments are shown to be strong predictors for suicidality.¹⁶⁾ Suicidality may be an expression of affective component on schizophrenia. In the study, patients did not have any affective disorder but cross-disorders' functional associations or common genetic implications are previously shown between mood disorders and schizophrenia.²⁸⁾

It is also shown that suicidality is more frequent and severe in patients with mood disorders. So the question is; whether there is a different biological mechanism that dominates suicidal behavior in patients with schizophrenia and mood disorders or not. And the further question is; may the mechanism/pathway be a common way for schizophrenia and mood disorders of which the key is hidden in depressive temperament. Of course these are just speculative questions and needs to be investigated by genetic and neuroimaging studies.

According to the results of this study, the cross-sectional evaluation of the patients' symptom severity, clinical severity of schizophrenia and functionality of the patients were not related with affective temperament of the relatives. Also cognitive functionality of the patients was not related with suicidality according to results of this study. Previous studies have reported no association between suicidal behavior and positive or negative symptoms.²⁹⁾ Previously, it was reported that there was no association between the delusions and other psychotic symptoms and the history of suicide attempts in patients with schizophrenia.^{30,31)} In contrast, it has been reported that command hallucinations could be a risk factor for suicide attempts.³²⁾ In this study our sample size was not large, which may have led to a type II error. Therefore, further research with larger sample sizes is warranted to elucidate the relationship between suicide attempts and the symptoms of schizophrenia. In the other hand, a relationship was found between affective temperaments and suicidality. Affective temperament is a lifelong matter and number of suicides is a longitudinal data about the prognosis of the illness rather than cross-sectional symptom analysis. Schizophrenia is a progressive disease that continues as episodes and remissions. So the severity of the symptoms may differ according to the timing of the study. In addition, regular use of medication, social support or other environmental factors during the study, and also other various factors may be related with the severity of the illness.³³⁾ This study claims that, suicidality is related with the type of the symptoms (positive symptom scores) rather than the se-

verity of the illness. This data provides an phenomenological data for identifying risk groups for suicidality in schizophrenia.

This study examined suicidal thoughts and number of suicides retrospectively. This is a limitation for the objectivity of data which is now limited with the patients' and relatives' comments. Also suicidal attempts and suicidal ideation had different correlates in sub-parameters claims that there may be separate clinic process related with suicidal thoughts and attempts. This study investigated suicidality as one of clinical properties of schizophrenia and did not conduct any detailed analysis for attempts and kind of suicidal thoughts so discrimination of these phenomena may be subject to a further study. In this study the affective temperaments of the patients were not evaluated due to the severity and chronicity of the illness of the study sample and its probable cognitive results' projections to patient affective temperament scores. This is a limitation of the study and further studies needs to find out if there is a correlation between the patients' affective temperaments and relatives' affective temperaments. But this is the first study which investigates the relatives' affective temperaments and symptom severity-prognosis of schizophrenia. And depressive temperaments of relatives' as a predictor of schizophrenia is an important data added to literature.

Further studies may find a genetic or a biological explanation for the suicidality of patients with schizophrenia and its relationship with affective temperaments. Major characteristics of affective temperaments of parents should be examined as a part of exploration of suicidal thoughts in schizophrenic patients.

Affective temperament characteristics of relatives of patients with schizophrenia are associated with the course of the disease. Suicidality in schizophrenia is related with relatives' affective temperaments and patients' own positive symptom scores. The relationship between suicidal thoughts and depressive temperament is highlighted in this study.

REFERENCES

1. World Health Organization. *Preventing suicide: a global imperative*. Geneva:World Health Organization;2014.
2. Brown S. *Excess mortality of schizophrenia. A meta-analysis*. *Br J Psychiatry* 1997;171:502-508.
3. Palmer BA, Pankratz VS, Bostwick JM. *The lifetime risk of suicide in schizophrenia: a reexamination*. *Arch Gen Psychiatry* 2005;62:247-253.
4. Dutta R, Murray RM, Hotopf M, Allardyce J, Jones PB, Boydell

- J. Reassessing the long-term risk of suicide after a first episode of psychosis. *Arch Gen Psychiatry* 2010;67:1230-1237.
5. Perenyi A, Forlano R. *Suicide in schizophrenia*. *Neuropsychopharmacol Hung* 2005;7:107-117.
 6. Rihmer Z, Gonda X, Torzsa P, Kalabay L, Akiskal HS, Eory A. *Affective temperament, history of suicide attempt and family history of suicide in general practice patients*. *J Affect Disord* 2013;149:350-354.
 7. Chang WC, Chen ES, Hui CL, Chan SK, Lee EH, Chen EY. *The relationships of suicidal ideation with symptoms, neurocognitive function, and psychological factors in patients with first-episode psychosis*. *Schizophr Res* 2014;157:12-18.
 8. Hawton K, Sutton L, Haw C, Sinclair J, Deeks JJ. *Schizophrenia and suicide: systematic review of risk factors*. *Br J Psychiatry* 2005;187:9-20.
 9. Popovic D, Benabarre A, Crespo JM, Goikolea JM, González-Pinto A, Gutiérrez-Rojas L, et al. *Risk factors for suicide in schizophrenia: systematic review and clinical recommendations*. *Acta Psychiatr Scand* 2014;130:418-426.
 10. Lee BD, Park JM, Lee YM, Moon E, Jeong HJ, Chung YI, et al. *Heritability and familiarity of temperament and character dimensions in Korean families with schizophrenic linkage disequilibrium*. *Clin Psychopharmacol Neurosci* 2016;14:203-209.
 11. Schwartz-Stav O, Apter A, Zalsman G. *Depression, suicidal behavior and insight in adolescents with schizophrenia*. *Eur Child Adolesc Psychiatry* 2006;15:352-359.
 12. Mauri MC, Paletta S, Maffini M, Moliterno D, Altamura AC. *Suicide attempts in schizophrenic patients: clinical variables*. *Asian J Psychiatr* 2013;6:421-427.
 13. Subotnik KL, Nuechterlein KH, Asarnow RF, Fogelson DL, Goldstein MJ, Talovic SA. *Depressive symptoms in the early course of schizophrenia: relationship to familial psychiatric illness*. *Am J Psychiatry* 1997;154:1551-1556.
 14. Palmer CJ Jr. *Suicide attempt history, self-esteem, and suicide risk in a sample of 116 depressed voluntary inpatients*. *Psychol Rep* 2004;95:1092-1094.
 15. Kawamura K, Kawamura N, Kumazawa Y, Kumagai J, Fujimoto T, Tanaka T. *Brain-derived neurotrophic factor/tyrosine kinase B signaling regulates human trophoblast growth in an in vivo animal model of ectopic pregnancy*. *Endocrinology* 2011;152:1090-1100.
 16. Karam EG, Itani L, Fayyad J, Hantouche E, Karam A, Mneimneh Z, et al. *Temperament and suicide: A national study*. *J Affect Disord* 2015;184:123-128.
 17. Çorapçıoğlu A, Aydemir Ö, Yıldız M, Esen A, Köroğlu E. *The Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I): The Clinician version [DSM-IV Eksen-I Bozuklukları İçin Yapılandırılmış Klinik Görüşme]*. Ankara:Hekimler Yayın Birliği;1999.
 18. Akiskal HS, Placidi GF, Marenmani I, Signoretta S, Liguori A, Gervasi R, et al. *TEMPS-I: delineating the most discriminant traits of the cyclothymic, depressive, hyperthymic and irritable temperaments in a nonpatient population*. *J Affect Disord* 1998;51:7-19.
 19. Akiskal HS, Akiskal KK, Haykal RF, Manning JS, Connor PD. *TEMPS-A: progress towards validation of a self-rated clinical version of the Temperament Evaluation of the Memphis, Pisa, Paris, and San Diego Autoquestionnaire*. *J Affect Disord* 2005;85:3-16.
 20. Vahip S, Kesebir S, Alkan M, Yazici O, Akiskal KK, Akiskal HS. *Affective temperaments in clinically-well subjects in Turkey: initial psychometric data on the TEMPS-A*. *J Affect Disord* 2005;85:113-125.
 21. Kay SR, Fiszbein A, Opler LA. *The positive and negative syndrome scale (PANSS) for schizophrenia*. *Schizophr Bull* 1987;13:261-276.
 22. Kostakoglu AE, Batur S, Tiryaki A, Gögüş A. *[Reliability and validity of the Turkish version of the Positive and Negative Syndrome Scale (PANSS)]*. *Türk Psikoloji Dergisi* 1999;14:23-32. Turkish.
 23. Ventura J, Reise SP, Keefe RS, Hurford IM, Wood RC, Bilder RM. *The Cognitive Assessment Interview (CAI): reliability and validity of a brief interview-based measure of cognition*. *Schizophr Bull* 2013;39:583-591.
 24. Guy W. *ECDEU assessment manual for psychopharmacology*. Rockville, MD.:U.S. Dept. of Health, Education, and Welfare, Public Health Service, Alcohol, Drug Abuse, and Mental Health Administration, National Institute of Mental Health, Psychopharmacology Research Branch, Division of Extramural Research Programs;1976.
 25. Bosgelmez S, Yıldız M, Yazici E, Inan E, Turgut C, Karabulut U, et al. *Reliability and validity of the Turkish version of cognitive assessment interview (CAI-TR)*. *Klinik Psikofarmakol Bülteni* 2015;25:365-380.
 26. Kaneda Y. *Depression and suicide risk in patients with schizophrenia during the treatment by second generation antipsychotic agents: A mini-review*. *Clin Psychopharmacol Neurosci* 2007;5:14-18.
 27. Rihmer Z, Akiskal KK, Rihmer A, Akiskal HS. *Current research on affective temperaments*. *Curr Opin Psychiatry* 2010;23:12-18.
 28. Wang T, Zhang X, Li A, Zhu M, Liu S, Qin W, et al. *Polygenic risk for five psychiatric disorders and cross-disorder and disorder-specific neural connectivity in two independent populations*. *Neuroimage Clin* 2017;14:441-449.
 29. Yoo T, Kim SW, Kim SY, Lee JY, Kang HJ, Bae KY, et al. *Relationship between suicidality and low self-esteem in patients with schizophrenia*. *Clin Psychopharmacol Neurosci* 2015;13:296-301.
 30. Grunebaum MF, Oquendo MA, Harkavy-Friedman JM, Ellis SP, Li S, Haas GL, et al. *Delusions and suicidality*. *Am J Psychiatry* 2001;158:742-747.
 31. Teraishi T, Hori H, Sasayama D, Matsuo J, Ogawa S, Ishida I, et al. *Relationship between lifetime suicide attempts and schizotypal traits in patients with schizophrenia*. *PLoS One*

2014;9:e107739.

32. Harkavy-Friedman JM, Kimhy D, Nelson EA, Venarde DF, Malaspina D, Mann JJ. *Suicide attempts in schizophrenia: the role of command auditory hallucinations for suicide. J Clin*

Psychiatry 2003;64:871-874.

33. Gurak K, Weisman de Mamani A. *Risk and protective factors, perceptions of family environment, ethnicity, and schizophrenia symptoms. J Nerv Ment Dis* 2016;204:570-577.