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The effect of some family characteristics on the relationship between mental symptoms and levels of serum serotonin and salivatory cortisol

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ABSTRACT

Aim: Psychological symptoms (PSs) are also seen in healthy individuals. The aim of this study is to examine some familial features in the relationship between PSs and serum serotonin (5-HT) and salivary cortisol (CTS) levels in healthy subjects.

Materials and Method: Sociodemographic data form and psychiatric symptom screening questionnaire (SCL-90-R) were given to 320 healthy individuals (156 males, 164 females) aged 18-65 without any mental illness. Blood and saliva samples were duly taken and evaluated by ELISA method. Informed consent and local ethics committee approval were obtained from the participants before starting the study. Statistical analyzes were done with SPSS 15.0 program. Descriptive statistical data (number, percentage, mean, standard deviation, minimum and maximum), independent sample t-test, One-way ANOVA test, Pearson Correlation analysis were used in the analyzes. For statistical significance, $p<.05$ was accetted significant.

Results: The mean age of the participants was 29.19±8.41. According to family characteristics, PSs were found to be higher in those whose parents were separated, whose parents had a low educational level, and those with a family history of psychiatric illness. Depressive symptoms were statistically significantly higher in those whose families were separated. Somatization, anxiety, obsessive symptoms, depressive symptoms, hostility and additional symptoms were statistically significantly higher in those with a family history of psychiatric illness. Although it was not statistically significant, the 5-HT levels were highest in those living in an extended family, those whose parents lived together, those whose parents were primary school graduates, and those who did not have a family history of psychiatric disease. CTS levels were statistically significantly higher in those who did not have a family history of psychiatric disease. There was a negative correlation between 5-HT and CTS levels and PSs excluding additional symptoms. There was a positive correlation between 5-HT and CTS levels.

Conclusion: It was concluded that familial characteristics have an effect on the relationship between psychological symptoms and serotonin and cortisol levels in healthy individuals, but these characteristics alone are not effective in this relationship. There is a need for studies investigating other stressor factors that are thought to be effective in the relationship between mental symptoms and serotonin and cortisol levels.

Keywords: Family characteristic, psychological symptom, healthy subject, serotonin, cortisol

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INTRODUCTION

The two most frequently focused biomarkers in the etiology of mental disorders and the emergence of psychological symptoms (PSs) are serotonin (5-HT) and cortisol (CTS). Fluctuations in 5-HT levels and the diurinal rhythm of CTS play an important role in the formation of these symptoms. 5-HT is a monoamine neurotransmitter that regulates mood level, sleep-wake behavior and appetite in the central nervous system, and regulates various physiological functions (gastrointestinal system, cardiovascular system, immune system, endocrine system, etc.) in the periphery (1). Deficiencies in the serotonergic system, may cause various mental disorders, including anxiety disorders (2), depression (3), obsessive compulsive disorder (4), schizophrenia (5), mood disorders and autism (6)

Changes in the activity of the hypothalamo-pituitary-adrenal axis, especially hypercortisolemia, are associated with depression. In addition, generalized anxiety disorder, panic disorder, and phobias may be associated with increased and prolonged activation of the hypothalamo-pituitary-adrenal axis (HPAA). In social phobias, normal basal CTS levels and hypersensitivity of the adrenal cortex can be observed during psychosocial stressors. Early stressful life events may predispose individuals to develop psychopathology

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by causing changes in the stress response and thus in the HPAA during adulthood (7). In a study conducted by Walker et al. (8) in young adults, CTS levels were followed for one year in those who met the criteria for psychosis risk, and they found that individuals who developed psychosis had significantly higher CTS levels than the control group who were not at risk. CTS levels were also found to be high in anxiety disorders (9), depression (10) and specific phobias (11).

In recent studies, it has been stated that the interaction between 5-HT and CTS levels has an important place in the etiology of mental disorders (12). Chronic CTS excess in the brain can also lead to 5-HT deficiency due to decreased availability of tryptophan, the substrate for 5-HT production. Moreover, it reduces the density and reactivity of 5-HT receptors (13). Currently used antidepressants not only affect neurotransmitters and activate amine receptors, but also normalize the HPAA activity, reduce cortisol-releasing hormone levels and therefore adrenocorticotropic hormone and cortisol (14).

In addition to the effects of 5-HT and CTS, sociodemographic characteristics such as age, gender, educational status, occupational status, marital status, medical and mental illness burden also play a role in the etiology of mental disorders. Independent of these stressors, familial factors can be effective in the emergence of mental disorders and PSs.

The family is essential in providing a support system for individuals to overcome the difficulties they face. Family processes include many interactions that occur family life, such as supporting each other, sharing love, communicating, problem solving, aggression, and neglecting one another. These processes occur in family systems, and the cognition, emotions, genetics, and physiology of family members are inextricably intertwined with these processes (15). On the other hand, various stressor factors such as family type, education level of parents, and a family history of mental illness may cause PSs and mental disorders in individuals. In a study by Park et al. (16), it was stated that the children of mothers with less than secondary school education had a higher risk of developing depression in early adulthood than those whose mothers had more education, and this was not related to father education. The French longitudinal study suggested that low level of parental education not only causes mental health problems such as anxiety and depression in childhood, but also continues to affect mental health in adulthood (17). It has been reported that a family history of psychiatric illness is associated with generalized anxiety disorder (18), depression (19), and psychotic disorders (20).

In the light of this information, it is seen that randomized controlled studies on mental symptoms mostly focus on anxiety and depressive symptoms. In addition to these symptoms, PSs such as somatic symptoms, obsessive symptoms, and psychotic symptoms can also be seen in healthy individuals. In our study, PSs were evaluated according to the PSs (somatization, anxiety, depression, obsession, interpersonal relationships, psychotic symptoms, paranoid symptoms, hostility, phobic symptoms and additional symptoms) included in the Symptom Check-List-90-R (SCL-90-R; 21,22).

In most of the literature, studies on 5-HT, CTS and stressors, which are claimed to play a role in the etiology of mental disorders and the emergence of PSs, have been examined as sample group, patient and health control groups. The main feature of these studies is that they reveal the changes in the patient groups compared to the healthy control group. The results of these studies focused significantly on the patient group. Therefore, changes in 5-HT and CTS levels in healthy individuals and in the levels of PSs due to stressors have often been neglected due to the original design of the studies. The effects of the stressor factors that play a role in the emergence of these symptoms in healthy individuals have not been emphasized much. Likewise, studies on this subject are limited in number. In addition, among these stressors, familial factors have a very important role in the development of healthy individuals, interpersonal relationships and the emergence of mental symptoms. We developed the hypotheses of our study in order to fill the gap in this regard. According to these hypotheses, in this study, we aimed to determine whether there is a relationship between PSs and 5-HT levels, and whether there is a relationship between PSs and CTS levels, and whether familial characteristics are effective in the relationship between PS and 5-HT levels, and whether familial characteristics are effective in the relationship between PSs and CTS levels, and whether there is a relationship between serotonin and cortisol levels, in healthy subjects.

MATERIAL AND METHOD

The study was carried out with the permission of Clinical Researches Ethics Committee of Ankara Keçiören Training and Research Hospital (Date: 11.07.2012, Decision No: B.10.4.İSM.4.06.68.49). The healthy individuals included in the study were informed about the study and their written consent was obtained. All procedures were performed in accordance with ethical rules and the principles of the Declaration of Helsinki.

This study was carried out with 320 participants aged between 18-65 years, between December 2012 and March 2013 at the Gülhane Military Medical Academy Mental Health and Diseases Clinic. This cross-sectional and

descriptive study included healthy personnel working in various units of the Gülhane Military Medical Academy and without any psychiatric disorders or psychiatric complaints, and healthy subjects who examined to the mental health and diseases polyclinic for various reasons and did not receive any psychiatric diagnosis.

The selection of the participants was made using the purposive sampling method. Before the study, the sample size was obtained by calculating the number of people to be included in the study. Accordingly, the number of people to be included in the study was determined as 313. The sample of the study was 320 people, and when this number was reached, the data collection process was terminated. As a result of an interview with a specialist psychiatrist, those whose physical and cognitive health level is suitable to answer the applied forms, those who volunteer to participate in the research, and those who do not have a chronic medical disease (hypertension, heart disease, systemic disease such as endocrinological, neurological, physical therapy, etc.), and those who do not use drugs (birth control pills, hormonal drugs, etc.) that affect psychotropic and cortisol levels, and non-pregnant, non-premenstrual period and non-menstrual period women were included in the study. Volunteer participants were briefed about the study by the researchers and a questionnaire was applied by face-to-face interview technique. After filling out the data forms, they were checked by a specialist psychiatrist to ensure that there were no missing or erroneous data, and the participants were asked to answer the missing parts. Thus, it was ensured that there were no missing and incorrect data. Individuals who did not agree to participate in the study were excluded from the study.

Participants were asked not to eat after 22.00 pm, as blood would be drawn the next morning. Regarding the collection of saliva samples, necessary warnings were given to the participants that they should not brush their teeth in the morning the next day, that the smoking participants should not smoke, that they could only drink water and not take any liquid food. Blood and saliva samples were taken the next day.

Data Collection Utensils

Sociodemographic data form: The information form was developed by the researchers to determine the sociodemographic characteristics of individuals (age, education level, marital status, family type, mother's education level, father's education level, mother-father cohabitation status, and psychiatric illness in the family).

The Symptom Check-List-90-R (SCL-90-R): It is a 90-item self-assessment scale developed by Derogatis (21) that provides a five-point Likert-type measurement between "not at all" and "too much". Each item is scored between 0-4. This scale, which measures psychiatric symptoms and stress response, consists of nine subscales and one additional scale: Somatization, anxiety, obsession, depression, interpersonal sensitivity, paranoid thought, psychotism, hostility, phobic anxiety. Turkish adaptation studies of SCL-90-R were performed by Dağ et al. (22). Although the cut-off score varies from researcher to researcher, it is generally accepted as 1. The Cronbach α internal consistency coefficient of the scale was 0.97, and the test-retest reliability coefficients were between 0.65-0.87 according to the subscales, found to be .90 in total. Construct validity and criterion-related validity of the scale were also studied.

Collection and Analysis of Samples

Blood samples taken from the brachial vein were put in an EDTA blood tube and centrifuged at 2500 rev for 8 minutes. After centrifugation, approximately 2 cc plasma sample from the "buffer", where platelets are concentrated, was transferred to capped Epandorf tubes with a Pasteur pipette. Participants were asked to chew sugar-free gum for 3-4 minutes to increase salivation and then spit 8-10 times (approximately 2 cc) into sterile urine collection cups. Saliva samples collected in the urine collection cup were transferred to capped Epandorf tubes with another Pasteur pipette. The names of the participants were written on the capped tubes from which both samples were taken, and the samples were stored in the refrigerator at - 80°C until the target sample number was reached. When this number was reached, they were analyzed in the biochemistry laboratory of the hospital. Serotonin and cortisol levels were measured by ELISA method.

Statistical Analyzes

Descriptive statistical data were given as numbers, percentages, mean, standard deviation, minimum and maximum. The correspondence of the continuous data to the normal distribution was made by examining the skewness and kurtosis values. Values between -1.50 and +1.50 for skewness and kurtosis were evaluated as normal distribution (23). In the analysis of normally distributed data, independent sample t-test was used to compare two groups, and one-way ANOVA test was used to compare multiple groups. Pearson correlation coefficients was prefered to evaluate the relationship between variables. For statistical significance, $p<.05$ was accepted as significant at the 95% confidence interval.

RESULTS

In the study, in which 320 healthy individuals participated, the mean age of the participants was determined as 29.19±8.41. 51.2% (n=164) of the participants were female, 55.0% (n=176) were 13-16 years educated, 54.4% (n=174) were single. Some data on familial characteristics are given in **Table 1**.

Table 1. The cases of socio-demographics characteristics and familial characteristics

Parameter	Frequency (n=320)	Percent (%)
Sex		
Men	156	48.8
Women	164	51.2
Age		
18-30 years	179	55.9
31-40 years	105	32.8
41 years and upper	36	11.3
Years of Education		
5-8 years	28	8.8
9-12 years	43	13.4
13-16 years	176	55.0
17 years and/or more	73	22.8
Marital status		
Married	139	43.4
Single	174	54.4
Divorced	7	2.2
Income		
High	68	21.3
Middle	211	65.9
Low	41	12.8
Family type		
Nuclear family	263	82.2
Extended family	37	11.6
Living apart from family	20	6.3
Cohabitation of parents		
Parents live together	267	83.4
Parents live separately	53	16.6
Father's education status		
Illiterate	22	6.9
Primary school	174	54.4
High school and upper	124	38.8
Mother's education status		
Illiterate	53	16.6
Primary school	206	64.4
High school and upper	61	19.1
Family history of psychiatric illness		
Yes	41	12.8
No	279	87.2

According to familial characteristics, PSs were found to be higher in those whose mothers and fathers were separated, those whose parents had a low education level, and those with a family history of psychiatric disorder. Depressive symptoms were found to be statistically significantly higher in those with separated families, and somatization, anxiety, obsessive symptoms, depressive symptoms, hostility, and additional symptoms in those with a family history of psychiatric disorder. PSs levels were statistically the highest in the participants whose parents had a low education level (**Table 2**).

According to the familial characteristics of the participants in the study, the 5-HT levels were found to be highest in those living in an extended family, those whose parents lived together, those whose parents were primary school graduates, and those who did not have a family history of psychiatric illness, although it was not statistically significant (**Table 3**). It was determined that the CTS levels were statistically significantly higher in those who did not have a family history of psychiatric disorder.

Table 3. Distributions of serotonin and cortisol levels according to familial characteristics of the participants

	n=320	Serotonin	Cortisol
Family type† ($\bar{x}$±SD)			
Nf	263	201.11±150.73	5.73±2.12
Ef	37	242.41±133.30	6.26±2.35
Lf	20	223.70±147.87	6.05±1.54
F		1.381	1.161
p*		>.050	>.050
Cohabitation of parents ($\bar{x}$±SD)			
Pl-t	267	212.91±150.01	5.87±2.14
Pl-s	53	179.06±140.91	5.54±2.06
t		1.515	1.035
p*		>.050	>.050
Father's Education Status† ($\bar{x}$±SD)			
Illiterate	22	220,41±174,42	6.21±2.48
Prim.sch.	174	203,18±147,26	5.73±2.04
H. sch/upp.	124	210,76±147,32	5.85±2.17
F		.185	.558
p*		>.050	>.050
Mother's Education Status ($\bar{x}$±SD)			
Illiterate	53	216.58±153.67	6.14±2.11
Prim.sch.	206	199.04±146.87	5.72±2.11
H. sch/upp.	61	227.13±151.44	5.84±2.20
F		.916	.811
p*		>.050	>.050
Family history of psychiatric illness ($\bar{x}$±SD)			
Yes	41	176.63±149.02	5.12±1.62
No	279	211.81±148.57	5.92±2.17
t		-1.415	-2.803
p*		>.050	.007

*p<.05. $\bar{x}$=Mean, S.D.=Standard Deviation, $\chi 2$=Chi-Square value, t=Independed Samples T-test value, F=Oneway ANOVA value, Nf=Nuclear family, Ef=Extended family, Lf=Living apart from family, Pl-t=Parents live together, Pl-s=Parents live separately, Prim.sch.=Primary school, H. sch/upp.=High school and upper.

According to the results of Pearson correlation coefficients, a statistically significant negative correlation between 5-HT levels and PSs excluding additional symptoms was determined in **Table 4**. There was a statistically significant negative correlation between CTS levels and PSs excluding additional symptoms. There was a statistically significant positive correlation between the 5-HT and CTS levels of the participants.

Table 2. Distributions of psychiatric symptom sub-dimension mean scores according to familial characteristics of the participants

PSYCHIATRIC SYMPTOMS												
	n=320	**Somatization**	**Anxiety**	**Obsession**	**Depression**	**Interpersonal sensitivity**	**Psychotism**	**Paranoid idea**	**Hostility**	**Phobic symptoms**	**Additional symptoms**	**GSI**
Family type† ($\bar{x}$±SD)												
Nf1	263	.61±.56	.48±.54	.91±0.66	.71±.67	.74±.70	.34±.47	.66±.64	.55±.60	.21±.40	.64±.64	.60±.52
Ef2	37	.67±.49	.51±.46	.92±.59	.67±.52	.72±.46	.41±.30	.81±.50	.67±.60	.27±.26	.78±.66	.64±.40
Lf3	20	.59±.69	.55±.73	.99±.74	.89±.90	.83±.94	.55±.75	.88±1.00	.62±.83	.30±.46	.87±.74	.72±.73
F		2.017	1.601	.228	.395	.825	7.021	5.065	2.159	7.130	4.188	.588
p*		>.050	>.050	>.050	>.050	>.050	>.050	>.050	>.050	>.050	>.050	>.050
Cohabitation of parents ($\bar{x}$±SD)												
Pl-t	267	.58±.52	.48±.51	.89±.62	.68±.65	.72±.67	.34±.45	.67±.64	.57±.62	.21±.37	.65±.64	.59±.49
Pl-s	53	.78±.72	.55±.67	1.08±.78	.90±.79	.86±.78	.45±.57	.79±.73	.56±.57	.29±.50	.77±.70	.73±.62
t		-1.818	-.707	-1.685	-2.114	-1.320	-1.435	-1.215	.024	-1.065	-1.269	-1.522
p*		>.05	>.05	>.05	.035	>.05	>.05	>.05	>.05	>.05	>.05	>.05
Paternal education status† ($\bar{x}$±SD)												
Illiterate4	22	.95±.70	.70±.71	1.20±.60	.95±.81	1.14±.82	.65±.62	1.11±.84	.70±.65	.33±.47	.94±.85	.87±.66
Prim.sch.5	174	.62±.57	.53±.55	.94±.66	.77±.70	.79±.71	.40±.48	.73±.63	.64±.66	.26±.42	.70±.64	.65±.52
H. sch/upp.6	124	.55±.51	.39±.48	.84±.64	.60±.60	.61±.61	.21±.41	.56±.62	.44±.52	.16±.30	.57±.61	.51±.46
F		6.740	8.968	7.756	6.281	12.826	19.033	15.968	8.795	9.481	6.949	6.066
p*		.010	.016	.044	.027	.001	<.001	.001	.014	.042	.029	.003
S/d		4-5, 4-6	4-6, 5-6	4-5, 4-6	4-6, 5-6	4-5, 4-6, 5-6	4-5, 4-6, 5-6	4-5, 4-6,5-6	4-6, 5-6	4-6, 5-6	4-6, 5-6	4-6, 5-6
Maternal education status ($\bar{x}$±SD)												
Illiterate7	53	.73±.64	.55±.63	1.04±.66	.88±.76	.93±.78	.51±.52	.91±.76	.65±.58	.27±.39	.81±.70	.74±.59
Prim.sch.8	206	.65±.57	.53±.53	.94±.65	.73±.65	.77±.68	.37±.49	.70±.62	.60±.64	.25±.41	.71±.66	.63±.51
H. sch/upp.9	61	.40±.39	.29±.46	.76±.63	.52±.62	.50±.59	.21±.34	.50±.61	.37±.52	.12±.26	.39±.46	.42±.44
F		5.811	5.152	3.008	4.387	6.170	5.772	5.542	3.907	3.025	7.605	6.337
p*		.003	.006	.050	.013	.002	.003	.004	.021	.050	.001	.002
S/d		7-9, 8-9	7-9, 8-9	7-9	7-9	7-9, 8-9	7-9, 8-9	7-9	7-9, 8-9	-	7-9, 8-9	7-9, 8-9
Family history of psychiatric illness ($\bar{x}$±SD)												
Yes	41	.84±.75	.73±.74	1.12±.75	.97±.80	.90±.76	.48±.56	.84±.72	.91±.77	.36±.56	.94±.77	.80±.62
No	279	.58±.53	.45±.50	.89±.64	.68±.65	.72±.68	.34±.46	.67±.64	.52±.57	.21±.36	.63±.62	.58±.50
t		2.108	2.351	2.146	2.548	1.510	1.444	1.538	3.096	1.728	2.454	2.477
p*		.041	.023	.033	.011	>.050	>.050	>.050	.005	>.050	.018	.014

*p<.05. $\bar{x}$=Mean, SD=Standard Deviation, χ2=Chi-Square value, t=Independed Samples T-test value, F=Oneway ANOVA value, S/d=Significant difference, Nf=Nuclear family, Ef=Extended family, Lf=Living apart from family, Pl-t=Parents live together, Pl-s=Parents line separately, Prim.sch.=Primary school, H. sch/upp.=High school and upper.

Table 4. The relationship between the participants' mean scores of psychological symptoms sub-dimensions and serotonin and cortisol levels

	1	2	3	4	5	6	7	8	9	10	11	12
1. Global symptom index	-											
2. Somatization	.825**	-										
3. Anxiety	.909**	.802**	-									
4. Obsession	.872**	.677**	.744**	-								
5. Depression	.925**	.708**	.834**	.804**	-							
6. Interpersonal sensitivity	.889**	.652**	.749**	.789**	.821**	-						
7. Psychotism	.872**	.646**	.790**	.744**	.790**	.789**	-					
8. Paranoid idea	.843**	.621**	.719**	.718**	.794**	.795**	.778**	-				
9. Hostility	.792**	.655**	.739**	.634**	.714**	.684**	.657**	.708**	-			
10. Phobic symptoms	.769**	.661**	.816**	.612**	.689**	.642**	.703**	.582**	.534**	-		
11. Additional symptoms	.831**	.729**	.736**	.674**	.767**	.688**	.692**	.662**	.646**	.609**	-	
12. Serotonin	-.181**	-.209**	-.184**	-.136*	-.209**	-.134*	-.168**	-.176**	-.145**	-.116*	-.095	-
13. Cortisol	-.174**	-.156**	-.177**	-.133*	-.194**	-.146**	-.147**	-.160**	-.098	-.187**	-.086	.487**

*p<.05.

DISCUSSION

Psychiatric symptoms can be seen in individuals with mental disorders as well as in healthy individuals. However, these symptoms may not be as pronounced as in a mental disorder and may not affect their level of functioning. For this reason, the PSs levels in healthy individuals have been neglected in most of the studies. On the other hand, serotonin and cortisol are the two most emphasized biomarkers in the emergence of PSs. In addition to these, stressor factors also play a role in this process. In this study, the effect of some family characteristics of healthy individuals on the relationship between PSs and 5-HT and CTS cortisol levels was investigated.

According to the findings of our study, PSs were found to be higher in those whose parents were separated, those whose parents had a low educational level, and those with a family history of psychiatric disorder. In addition, depressive symptoms were found to be higher in those whose parents were separated than those whose parents lived together. Parental separation, or parental divorce, has a long-term impact on individuals' mental health, family relationships, and education. Sands et al. (24) found a significant relationship between parental divorce and depression in adult children; stated that this relationship was not related to anxiety levels. However, they were unable to prove that the length of time the divorces occurred had any effect on this relationship. When exposed to chronic stress such as parental separation, it has been suggested that there is a loss of spines and a dendritic reduction in the hippocampus and medial amygdala, while dendrites enlarge in the basolateral amygdala due to hypothalamo-pituitary-adrenal axis imbalance and structural and functional changes in the amygdala and hippocampal regions. (25). Disruptions in frontoamygdal connectivity have been associated with a variety of mental health problems, including depression (26) and anxiety (27). The findings of our study support these results, which show that there is a relationship between PSs and parental divorce experience in those whose parents are separated.

Psychological symptom levels of those whose parents were illiterate were found to be higher than those with primary and high school education or higher. In a study by Park et al. (16), it was stated that the children of mothers with less than secondary school education had a higher risk of developing depression in early adulthood than those whose mothers had more education, and this was not related to father education. In a study conducted in France, it was suggested that low level of parental education not only causes mental health problems such as anxiety and depression in childhood, but also continues to affect mental health in adulthood (17). On the other hand, it has been reported that the children of university graduate parents are more likely to have positive psychological health than children of non-university graduate parents (28). The findings of our study, in line with these findings, indicate that parent education plays an important role in the emergence of PSs.

Another finding of our study is that somatization, anxiety, obsession, depression, anger-hostility, phobic symptoms, additional symptom levels and GSI levels were significantly higher in patients with a family history of psychiatric disoredr. In studies, having a family history of psychiatric disorder has been associated with generalized anxiety disorder (18), depression (19), and psychotic disorders (20). On the other hand, it has been stated that positive family history and model learning do not play an important role in the development of psychogenic non-epileptic seizures (29). Serretti et al. (30) pointed out that there was no difference in general depressive symptoms between patients with and without major depression in their family. Although there are conflicting data in the literature, the findings of our study support the view that the presence of a psychiatric disorder in the family is a risk factor for the emergence of PSs.

In our study, it was found that 5-HT levels were highest in those with extended families, those whose parents lived together, those whose parents were primary school graduates, and those who did not have a family history of psychiatric disorder, and this result was not statistically significant. In a recent review study, it was declared that 5-HT plays a positive moderator role between negative childhood experiences such as functional disorders at home (parental incarceration, divorce, parental substance abuse and maternal physical abuse) and the risk of depression, and may also be effective in poor treatment outcomes in adulthood (31). Muck-Seler et al. (32) reported that platelet 5-HT concentration was higher in schizophrenic patients than in depressed patients or healthy controls, and it was lower in depressed patients compared to healthy controls and schizophrenic patients. In recent studies, it has been suggested that there is no difference between platelet 5-HT levels between patients with depressive symptoms and healthy individuals (33,34). Although the findings of our study show that 5-HT levels are affected by familial stressors, they do not provide sufficient evidence.

Another finding of our study is that the salivary CTS levels in patients with a family history of psychiatric disorder are significantly lower than those without a family history of the disease. Yıldırım et al. (20) found that CTS levels in wakefulness were higher in schizophrenia patients compared to their first-degree relatives, and CTS levels in first-degree relatives compared to healthy controls. In another study, it was reported that patients with newly diagnosed bipolar disorder had higher hair CTS levels than their unaffected first-degree relatives and healthy controls (35). CTS levels were found to be lower in the sons of fathers who had behavioral disorders in childhood and later developed antisocial personality disorder, compared to fathers who did not develop any axis 1 disorder or antisocial personality disorder (36). In a study conducted with patients with major depression, it was emphasized that there was no difference between the CTS levels of the patients and their unaffected first-degree relatives (19). The findings of our study suggest that CTS may play a role in pathological processes in individuals with genetic predisposition. In addition, these findings may contribute to the view that CTS levels, which are high at the beginning of the disease, may decrease during the long-term disease process, as they adapt to the stress load arising from the disease as a result of changes in the function of the HPAA.

In our study, a negative and significant relationship was found between 5-HT levels and somatization, anxiety, obsession, depression, interpersonal sensitivity, psychoticism, paranoid symptom, anger-hostility, phobic symptom and GSI subscale scores. Decreased 5-HT levels may cause PSs to occur in mental disorders such as anxiety disorders (2), depression (3), obsessive-compulsive disorder (4), schizophrenia (5), mood disorders and autism (6). In a recent study, a negative correlation was found between platelet 5-HT levels and impulsivity levels (37). The findings of our study support the findings in the literature.

Another finding of our study is that there is a negative and significant relationship between CTS cortisol levels and somatization, anxiety, obsession, depression, interpersonal sensitivity, psychoticism, paranoid symptom and phobic symptom and GSI subscale scores. It has been reported that the blood levels of CTS, which is a stress hormone, are high in patients with anxiety disorder (9), depression (10), psychotic disorder (8) and specific phobia (11) while it does not differ in those with social phobia (38). Muck-Seler et al. (32) found that plasma CTS levels increased significantly in both schizophrenia patients and depressed patients when compared to the values in healthy controls. The fact that CTS levels were low in individuals with PSs in our study supports the view that CTS level alone was not effective in the emergence of PSs.

In our study, a positive and significant relationship was found between 5-HT and CTS levels. Affecting the hippocampal region as a result of prolonged exposure to stressors can cause modulation of various neural pathways, including serotonergic input from the Raphe nucleus (39). Muck-Seler et al. (32) suggested that there was a significant correlation between platelet 5-HT and plasma CTS concentrations in healthy controls, but they stated that there was no such relationship in schizophrenia or depressed patients. On the other hand, CTS may be effective in the emergence of PSs such as depressive symptoms by affecting 5-HT levels (40). Evidence for an interaction between 5-HT and CTS in the occurrence of other PSs other than anxiety and depressive symptoms is insufficient. The findings of our study confirm the interaction between 5-HT and CTS.

Our work has some strengths. First, we believe that this is the first study to examine the effects of certain familial factors on the PSs and their relationship with 5-HT and CTS levels in a healthy population in Turkey. Secondly, SCL-90-R and two biomarkers (5-HT and CTS) that are effective in the etiology of mental disorders were used together instead of other diagnostic tests. Thus, the use of the SCL-90-R made it possible to evaluate not only depression and anxiety in healthy individuals, but also the GSI as well as other PSs such as somatization, obsessive symptoms, interpersonal sensitivity, anger-hostility, phobic anxiety, psychotic symptoms and additional psychological symptoms. Third, by considering the relationship between PSs and 5-HT and CTS levels

separately, we show that although PSs are highly correlated with these two components, they may actually have different effects and require different prevention and intervention strategies. Finally, we show that it is critical to acknowledge cross-context variability in the relationship between familial factors and adult mental health outcomes.

There are some limitations in our study. First, a cross-sectional design was applied and therefore no cause-effect relationship could be determined between the research variables. Secondly, it is considered to be partially sufficient in terms of sample size. Since it is a descriptive study, the sample size was kept large. Third, while self-report measures are used for familial characteristics and PSs, the gold standard for psychiatric diagnosis is a structured/semi-structured clinical interview. Fourth, few studies have examined associations between PSs and 5-HT and CTS levels, making it difficult to compare these results in our study with other studies. Fifth, it was limited to collecting a single blood sample, which did not take into account the circadian rhythm of CTS secretion. Finally, it is unclear whether the level of 5-HT in the plasma reflects the level in the brain (41), but some studies have shown that circulating 5-HT is related to brain tissue serotonin (42).

CONCLUSION

Psychological symptoms diverged from person to person, place of residence, socio-cultural characteristics, work life and stressful events. It can be said that familial characteristics, the effect of serotonin and cortisol, as well as assorted life events, personal characteristics and the reactions of individuals to these events are potent in the emergence of these symptoms. Evaluating the relationship between psychological symptoms, which are highly related to these two biomarkers, and serotonin and cortisol levels separately may require different prevention and intervention strategies due to different effects. More research is needed on how these determinants affect serotonin and cortisol levels.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Clinical Researches Ethics Committee of Ankara Keçiören Training and Research Hospital (Date: 11.07.2012, Decision No: B.10.4.İSM.4.06.68.49)

Informed Consent: All patients signed the free and informed consent form.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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