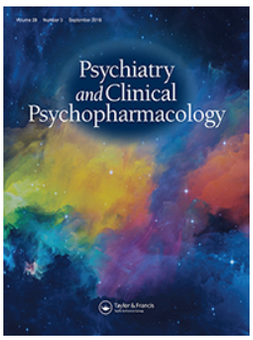

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Miray Çetinkaya, Özden Şükran Üneri & Zeynep Göker

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Serum oxytocin and vasopressin levels in children with social anxiety disorder and the effects of parent characteristics

Miray Çetinkaya[a], Özden Şükran Üneri[b] and Zeynep Göker [b]

[a]Department of Child and Adolescant Psychiatry, Dr. Sami Ulus Maternity and Child Health Training Hospital, Ankara, Turkey; [b]Department of Child and Adolescant Psychiatry, Ankara Child Health and Hematology/Oncology Training and Research Hospital, Ankara, Turkey

ABSTRACT

OBJECTIVES: We aim to determine serum oxytocin, vasopressin levels and examine parent characteristics in children diagnosed with social anxiety disorder (SAD).

METHODS: Thirty four children diagnosed with SAD and 34 mothers were compared with a healthy control group (21 control children and their mothers) in this case–control study. Assessment performed via State-Trait Anxiety Inventory (STAI), Symptom Checklist-90 (SCL-90), Parental Attitude Research Instrument (PARI), Beck Depression Inventory (BDI), Liebowitz Social Anxiety Scale (LSAS) and Social Anxiety Scale for Children-Revised (SASC-R). Serum samples collected for detection of oxytocin and vasopressin levels.

RESULTS: The distribution range of vasopressin levels were found statistically higher in control group than SAD group ($p = 0{,}002$). Additionally results showed no statistically significant differences according to the mean levels of serum oxytocin and vasopressin between groups. The scores of STAI-C, SASC-R and democratic attitudes/egalitarianism subscales of PARI were found significantly higher in children with SAD. Similarly we reported that mean scores of SCL-90 scale, LSAS and SCL-90 subscales were higher in mothers of patients group.

CONCLUSIONS: Although significantly lower distribution range of vasopressin levels was found in SAD patients, mean oxytocin and vasopressin levels were not associated with SAD etiology. Additionally psychopathologies particularly anxious behaviour in mothers may contribute SAD development in early period of childhood.

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KEYWORDS
Social anxiety disorder; oxytocin; vasopressin; parent characteristics

1. Introduction

Social anxiety disorder, also known as social phobia, is an intensely fear of being embarrassed and humiliated by others. Fear and avoidance of social encounters or performance situations mostly associated with impaired social interactions, academic performance and interpersonal relationships in individuals with SAD. Social anxiety disorder most commonly begins during early childhood or adolescence and typically follows an unremitting course. Additionally comorbid conditions such as major depression, alcohol abuse commonly occur among individuals without treatment [1,2].

Persons with social anxiety disorder may avoid public speaking or other performance situations, meeting new people, eating or drinking while someone watches [3]. Among children fear of class participation, reading aloud, speaking in class, interacting with teachers, playing games with other children and taking tests or exams are also common [4]. Social avoidance behaviour is the main factor that associated with SAD severity and intensified with age [5]. The SAD prevalence is 3.9% among elementary and secondary school students in our society and reported two times more in girls than in boys [6].

The attachment styles, rural life, socioeconomic status and adverse life events as well as presence of psychotic disorders in parents and features of upbringing children seem to have marked influence on SAD etiology [7–9]. Hypercritical and poor communicated parents' children have higher risk of SAD occurrence [10]. Therefore focusing on parents in diagnostic and therapeutic process may contribute to reduction of SAD risk [11].

Recently, roles of arginin vasopressin (AVP) and oxytocin have evaluated in the SAD etiology. It is well-known that anxiety decreases by increasing the level of oxytocin in the central nervous system in conditions such as giving birth, sexual intercourse [12]. On the contrary, AVP enhances liability to depression and anxiety [13]. It has been also observed that both neuropeptides levels changed in the psychopathologies such as depression, social anxiety disorder and post traumatic stress disorder [14].

Therefore both oxytocin and vasopressin are appear to be regulators of anxiety, social functioning, stress-coping and they have prominent impact on emotional and social behaviours. Particularly oxytocin has been associated with social interactions, interpersonal

CONTACT Miray Çetinkaya makinci@gmail.com Department of Child and Adolescant Psychiatry, Dr. Sami Ulus Maternity and Child Health Training Hospital, Ankara, Turkey

relationships and parenting [15]. Thus we aimed to determine serum oxytocin, vasopressin levels and examine the parent characteristics in children and adolescents diagnosed with social anxiety disorder.

2. Materials and methods

2.1. Sample

This study was performed with the Institutional Review Board protocol approval date 11/02/2014 and number 2014/011 in Ankara Children's Hematology Oncology Training and Research Hospital, Department of Child and Adolescent Psychiatry between February 2014 and September 2014. In this case–control study 38 children with parents applied to the outpatient clinics of Ankara Children's Hematology Oncology Training and Research Hospital. Of these, one did not meet the DSM-IV-TR criteria for SAD, and three did not complete the required questionnaires. Thirty four children (> 7 years-old) who were newly diagnosed with SAD according to the DSM-IV-TR criteria and their mothers have compared with a healthy control group (21 control children and their mothers) in present study. The healthy control group without any psychiatric disorders were randomly selected from individuals (> 7 years-old) who were applied to the Child and Adolescent Psychiatry department of the Ankara Children's Hematology Oncology Training and Research Hospital. Exclusion criteria for both case and control group were accompanying serious physical disorders, mental retardation and administration of psychotropic drugs within at least 3 months. All participants were able to read and write. Children and parents were enrolled in this study after obtainment of written informed consent.

2.2. Measures

Socio-demographic questionnaire: Includes socio-demographic data such as age, sex, education history, medical history, socio-economic level, and place of residence, as well as information including education history of parents, drugs used, and family type.

State-Trait Anxiety Inventory for Children (STAI-C): The STAI is a brief self-report assessment designed to measure and differentiate between anxiety as a trait and a state by Spielberger [16]. The study for the validity and reliability in Turkish was conducted by Ozusta [17]. The STAI consist of two sub-scale of 40 items each. The first questionnaire measures state anxiety (how one feels at the moment), the second, trait anxiety (how one generally feels). Each scale scored between 20 and 80. Higher scores indicates higher anxiety state. We utilized STAI to determine the presence and level of anxiety in children.

Social Anxiety Scale for Children-Revised (SASC-R): SASC-R is a 10-item self-report measure designed by La Greca and revised to 18 items scale in 1993 [18]. The validity and reliability study of the Turkish version was carried out by Demir et al. [19]. 'Fear of Negative Evaluation From Peers' and 'Social Avoidance' were evaluated via this scale. SASC-R outcome scores range from 18 to 90 [20]. We used SASC-R to assess the presence and level of social anxiety in children.

Parental Attitude Research Instrument (PARI): This instrument which evaluates parental attitudes toward child-rearing, developed by Schaeper and Bell [21]. The Turkish reliability and validity study of the scale was conducted by Le Compte et al. in 1978 [22]. Form consists of 60 statements that combined with 5 sub-scales (Over protective motherhood, democratic act and equality, refusing being housewife, spouse incompatibility and pressure/discipline). PARI outcome scores range from 1 to 4. Higher scores indicates higher contents of related sub-scale's features.

Beck Depression Inventory (BDI): The BDI is a self-report which contains 21 items, each with a response set of four statements describing the severity of depressive symptoms over the past 2 weeks along a continuum from 0 (absent or mild) to 3 (severe). A total score is computed by summing the scores across items (range 1⁄4 0–63). The cut-off point for the scale was accepted as 17 [23]. We used BDI to diagnose depression in parents.

The Symptom Checklist-90-Revised (SCL-90-R): SCL-90-R is a 90-item self-report symptom inventory developed by Derogatis in 1973 to measure psychological symptoms and psychological distress [24]. The Turkish reliability and validity study of the scale was conducted by Kılıç in 1991 [25]. The SCL-90-R assesses psychological distress in terms of nine primary symptom dimensions and three summary scores termed global scores. The principal symptom dimensions are labelled somatization, obsessive-compulsive, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation and psychoticism. The global measures are referred to as the global severity index, the positive symptom distress index, and the positive symptom total. Global measures outcome scores range from 0 to 4. We used SCL-90 to determine the symptom load of the parents.

Liebowitz Social Anxiety Scale (LSAS): The LSAS is a clinician-administered instrument that assesses both fear and avoidance across a number of social situations. The validity and reliability study of the Turkish version was carried out by Soykan et al. [26]. The scale consists of 24 items each depicting different social situations and further divided into two subscales for scoring, including social interaction (11 items) and performance situations (13 items). The fear scale ratings range from 0 (no fear) to 3 (severe fear) [27]. We used LSAS to evaluate fear and avoidance in social interaction in children.

Schedule For Affective Disorders and Schizophrenia for School Aged Children – Present and Lifetime Version

(K-SADS-PL-Turkish Version): An interview form that created by Chambers et al. in order to detect past and current psychopathologies in children and adolescents according to DSM-III-R (APA 1987) and DSM-IV-TR (APA 1994) diagnostic criteria. The form has three sections as "introduction", "diagnosis" and "general evaluation". Severity of symptoms is rated as "absent", "subthreshold" and "threshold" [28,29]. The study for the validity and reliability in Turkish was conducted by Gokler et al. [30].

2.3. Biochemical measurements

Ten millilitre of blood specimens were collected to determine serum vasopressin and oxytocin levels from all participants. Samples were stored at –80°C until the assay date. According to the manufacturer's instructions after some incubation and washing procedure, serum vasopressin and oxytocin levels were measured by using an enzyme immune assay technique in polystyrene microelisa plates (Awareness-Chromate 4300). The inter- and intra-assay coefficients of variation for oxytocin were 3.4% and 4.8%, respectively; for AVP were 4.6% and 14.5%, respectively.

2.4. Statistical analysis

All the data were analyzed with SPSS (Statistical Package for the Social Sciences) software for Windows Version 17.0. Comparison of the data with normal distribution was made with Student t test and ANOVA. For the continuous variables that were not normally distributed, the Mann Whitney U test and Kruskal–Wallis test were conducted to compare between groups. Comparisons between multiple groups were made with Chi-square test. P-Values of < 0.05 were considered statistically significant.

3. Results

The SAD patients included in this study were 14 (41.2%) male and 20 (58.8%) female, control group was 3 (14.3%) male and 18 (85.7.8%) female. Mean age of the participants detected in SAD group ($n = 34$) was 11 years 9 months ± 2 years 8 months, in control group group ($n = 21$) was 11 years ± 2 years 9 months. The number of female participants in control group was statistically higher than SAD group ($p < 0,05$). No significant differences found between SAD group and healthy control group according to mean age, mean scores of school achievement scores, number of sister/brothers and total intelligence scores of WISC-R.

The distribution ranges of vasopressin were 79.98–340.67 pg/ml in SAD group and 23.40–796.88 pg/ml in control group. The distribution range of vasopressin levels were found statistically higher in control group than SAD group ($p = 0,002$). The mean level of serum vasopressin was 233,80 pg/ml in SAD group and 294.81 pg/ml in control group. There were no statistically significant differences found according to the mean values of serum vasopressin levels between groups ($p = 0,634$). Additionally the mean level of serum oxytocin was 51,60 pg/ml in SAD group and 131.87 pg/ml in control group. There were also no statistically significant differences found according to the mean and the distribution range of serum oxytocin levels between groups (p-values = 0.171, 0.128 respectively) (Table 1).

The 52.9% of mothers ($n = 34$) in SAD group and % 81 ($n = 21$) of mothers in control group were physically and mentally healthy. Physically and mentally unhealthy mothers were found significantly higher in patient group than control group ($p < 0.05$). Besides there were no significant differences found between SAD group and healthy control group according to fathers medical conditions. Additionally no significant differences observed between parents of SAD group and healthy control group according to mean age, education status and socioeconomic status. Primary caregivers was the mothers among 88.2% ($n = 30$) of children in SAD group and %81 ($n = 17$) of children in control group and no significant differences found between groups according to primary caregivers.

The trait anxiety STAI scores in SAD patients were statistically higher (40.8±8.6) when compared to control group (35.4±6.8). Besides the sub-scale of state anxiety scores showed no significant differences between groups. The SASC-R scores in SAD patients were also found statistically higher (52.3±15.5) when compared to control group (40.5±11.4). We determined 12 years as cut-off value for this scale to make evaluation according to age and results showed that the scores of SAD group was statistically higher than control group in children older than 12 years. In addition gender differences had no impact on scores of scales (Table 2).

There were no significant differences found between groups according to the both state/trait anxiety scores of STAI and BDI scores in participant mothers. The mean positive symptom total scores of the SCL-90-R sub-scale were statistically higher in mothers of SAD group (1.03±0.59) when compared to control group (0.71±0.46). Similarly the somatization, depression,

Table 1. Comparison of serum oxytocin and vasopressin levels between groups.

Laboratory (pg/ml)	SAD Group	Control Group	p-value
Oxytocin			
Mean±Sd	51.60±100.53	131.87±192.87	0.171
Range (min-max)	5.90–535.71	10.43–570.15	0.128
Vasopressin			
Mean±Sd	233.80±65.15	294.81±223.15	0.634
Range (min-max)	79.98–340.67	23.40–796.88	0.002*

*$p < 0.05$ statistically significant, **Sd** = Standard deviation, **SAD** = Social Anxiety Disorder.

Table 2. Distribution of SASC-R mean scores according to age and gender.

	SASC-R Scores		p-value
	SAD Group (Mean±Sd)	Control Group (Mean±Sd)	
Gender			
Female	49.05±15.63	40.28±11.89	0.064
Male	56.40±14.83	42.00±9.64	0.131
Age			
<12 years	48.17±13.22	42.00±13.40	0.213
≥12 years	56.94±16.94	38.13±7.24	0.007*

*$p < 0.05$ statistically significant, **Sd** = Standard deviation, **SAD** = Social Anxiety Disorder, **SASC-R** = Social Anxiety Scale for Children-Revised.

Table 3. Comparison of SCL-90-R scores in mothers.

Sub-scale	SAD Group (Mean ±Sd)	Control Group (Mean±Sd)	p-value
Somatization	1.27±0.84	0.72±0.57	0.011*
Anxiety	0.79±0.55	0.55±0.51	0.103
Obsessive-compulsive	1.27±0.70	0.92±0.54	0.061
Depression	1.20±0.65	0.80±0.55	0.022*
Interpersonal sensitivity	1.24±0.75	0.76±0.69	0.022*
Psychoticism	0.70±0.53	0.32±0.37	0.006*
Paranoid ideation	1.21±0.63	0.74±0.57	0.007*
Hostility	0.91±0.76	0.74±0.53	0.372
Phobic anxiety	0.47±0.58	0.34±0.40	0.374
Additional scale	1.09±0.79	0.79±0.61	0.145
Total	1.03±0.59	0.71±0.46	0.036*

*$p < 0.05$ statistically significant, **Sd** = Standard deviation, **SAD** = Social Anxiety Disorder, **SCL-90** = Symptom Checklist-90.

Table 4. Comparison of the LSAS scores in participant mothers.

Sub-scale	SAD Group (Mean ±Sd)	Control Group (Mean ±Sd)	p-value
Anxiety	48.30±12.48	35.90±10.70	<0.001*
Avoidance	48.63±12.25	39.71±15.47	0.022*
Total	97.0±22.2	75.8±23.6	0.001*

*$p < 0.05$ statistically significant, **Sd** = Standard deviation, **SAD** = Social Anxiety Disorder, **LSAS** = Liebowitz Social Anxiety Scale.

interpersonal sensitivity, psychoticism and paranoid ideation scores of SCL-90-R sub-scales were statistically higher in mothers of SAD group than control group (Table 3).

The total scores of LSAS scale were significantly higher in mothers of patients group (97.0±22.2) than control group (75.8±23.6) ($p = 0{,}001$). Additionally the scores of both anxiety and avoidance sub-scales in SAD patients were also found statistically higher than control group (p-values = 0<001, 0.022, respectively) (Table 4). In addition 'Democratic act and equality' scores of PARI sub-scales were statistically higher in SAD group than control group (Table 5).

Table 5. Comparison of the PARI scores in mothers.

Sub-scale	SAD Group (Mean±Sd)	Control Group (Mean±Sd)	p-value
Over protective motherhood	47.7±7.4	43.9±8.0	0.087
Democratic act and equality	28.5±2.9	26.5±3.0	0.017*
Refusing being housewife	26.5±4.8	24.6±6.9	0.235
Spouse incompatibility	14.9±2.7	14.8±4.2	0.905
Pressure/discipline	39.5±5.5	36.8±6.2	0.101

*$p < 0.05$ statistically significant, **Sd** = Standard deviation, **SAD** = Social Anxiety Disorder, **PARI** = Parental Attitude Research Instrument.

4. Discussion

More recently personal and parental features were widely examined in children diagnosed with SAD in published data. Particularly an association between impaired social interactions and serum vasopressin/oxytocin status has been demonstrated in clinical studies [3,13].

SAD have been reported more frequently in children with female gender [31,20]. A study in our country showed that SAD occurrence was 2 or 3 times more prevalent in female gender [6]. The high frequency of male gender obtained from our study could be a possible effect of our cross-sectional examination. Additionally we enrolled new diagnosed participants without administration of psychotropic drugs at least 3 months in this study. Moreover the SAD onset is commonly occur in adolescences, thus mean age of our sample found to be consistent with published data [32].

Oxytocin has been documanted a potential biomarker of emotional distress and impaired social interactions in depressive patients in published data [33]. In a case–control study Gorka et al. administrated intranasal oxytocin in patients with generalized social anxiety disorder, results suggest that oxytocin simultaneously dampens amygdala reactivity and enhances amygdala functional connectivity in patients with SAD [34]. In another case–control study with total number of 67 patients diagnosed with bipolar disorder Turan et al. have documented significantly higher serum oxytocin levels in the manic episode and depressive episode patients than control group after treatment. Therefore researchers concluded that oxytocin may be a trait marker in bipolar disorder [35]. In another study researches reported that no significant differences found between participants whom given a task involving interpersonal trust and control group according to serum oxytocin levels [36]. Striepens and colleagues provided evidence that a behaviourally effective dose of intranasal oxytocin elevated cerebrospinal fluid (+60%) and blood (+250%) oxytocin concentrations in humans but that the kinetics in these compartments were considerably different [37]. On the contrary Hoge et al. reported no significant differences in oxytocin levels between 24 patients with generalized SAD and 22 healthy controls using an EIA [38]. In our study there were also no statistically significant differences found according to the mean and the distribution range of serum oxytocin levels between patient and control groups. It appears that published data about oxytocin levels in psychopathologies seems to be conflicting. Thus our findings found to be consistent with published data.

Assessment of a direct link between serum vasopressin levels and SAD has not been performed yet in children and adolescents. In a study after intranasal

administration of arginine vasopressin, healthy participants demonstrated reduced risk-taking and defensive behaviour [39]. Moreover the anxiety symptoms have been associated with above normal-plasma vasopressin levels in depressive patients [40]. In our study the distribution range of vasopressin levels were found statistically higher in control group than SAD group. These outcomes supports anxious characteristic of low arginine vasopressin levels and found consistent with our study.

SAD is associated with impaired peer and teacher interactions in school that result in lower academic performance [41]. A research on adolescences reported that SAD effected average scores of national university entry exam and semester grade negatively in USA [42]. Bayram Özdemir et al. associated shy behaviours with more depressive symptoms, poorer academic performance, less school liking, and higher school avoidance in a study conducted with 599 children from six public schools in Turkey [43]. In our study no significant differences found between SAD group and healthy control group according to mean value of school achievement scores. This could be possible effect of our limited number of sample and cultural differences of our society, moreover lack of related published data restricts interpretation.

Viana et al. have been reported that anxiety symptoms, particularly SAD, were more prevalent in patients ranged in age from 8 to 18 years among all patients group diagnosed with urticaria and the trait anxiety STAI scores were found statistically higher in those patients [44]. Additionally numerous researches have reported that SASC-R is a specific and reliable instrument for diagnosing SAD in children [45,46]. Similarly the STAI and SASC-R scores in SAD patients were found statistically higher when compared to control group in our study. Moreover we showed that the SASC-R scores of SAD group was statistically higher than control group in children older than 12 years. Supportively it has been highlighted that anxiety symptoms enhance in adolescence period in children diagnosed with SAD [47]. It has been also observed that anxiety and depression symptoms are more prevalent in children of physically or mentally unhealthy mothers [48]. Supportively, physically and mentally unhealthy mothers were found significantly higher in patient group in this study.

Contrary to our findings Mazefsky et al. reported that the mean scores of SCL-90-R sub-scales (anxiety, phobic anxiety and hostility) were found statistically higher in mothers of children diagnosed with autism spectrum disorders and comorbid anxiety [49]. In another study researches reported that the SCL-90-R mean scores were similar in mothers of children with anxiety [50]. Maternal over protective attitudes reported to have an effect on frequency of SAD in a study [51]. In our study the high scores of interpersonal sensitivity and psychoticism sub-scales have been associated with maternal over protective attitudes in mothers of patient group. Maternal anxiety and insecure attachment style in childhood may contribute SAD development [52]. In present study there were no significant differences found between groups according to the BDI scores in participant mothers. This finding has been associated with self-report feature of the BDI inventory.

Stevenson-Hinde et al. compared 55 SAD patients with 158 healthy participants including mothers and reported that the total mean scores and sub-scale scores of LSAS were found statistically higher in mothers of children with SAD [53]. Similarly Bayraktutan compared 36 SAD patients with 30 healthy participants and found statistically higher scores in both avoidance and anxiety sub-scales of LSAS than control group ($p = 0{,}0001$). Moreover researchers documented statistically significant decrease in both subscales' scores of LSAS after treatment ($p = 0{,}0001$) [54]. Supportively in our study the total scores of LSAS scale were significantly higher in mothers of patients group than control group. Additionally the scores of both anxiety and avoidance sub-scales in SAD patients were also found statistically higher than control group. Avoidance of social interactions and anxious behaviour in mothers may cause behavioural inhibition in children with SAD features in early period of childhood.

Although there are limited published data related to PARI instrument in mothers of children diagnosed with SAD, it is well-known that strict, anxious, refusing and over protective motherhood have higher risk of SAD occurrence in children [55,56]. In our study 'Democratic act and equality' scores of PARI subscale was statistically higher in SAD group than control group. This outcome was related to absence of father's information as a caregiver in our study.

In conclusion, however oxytocin and vasopressin levels have not been associated with SAD etiology, the distribution range of vasopressin levels were found statistically higher in control group in present study. In this respect further researches should be perform with larger study groups including evaluation of cortisol and cerebrospinal fluid AVP levels may contribute to diagnosis and treatment of SAD.

5. Limitations

In our study, we have examined limited number of samples and held a case–control evaluation not cross-sectional examination and attachment styles are beyond the scope of this study and they were not evaluated. Present study was lack of evaluation of father's information as a caregiver. Additionally majority of scales were based on a self-report instrument without stimulated recall procedures.

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Disclosure statement

No potential conflict of interest was reported by the authors.

ORCID

Zeynep Göker http://orcid.org/0000-0002-6489-3800

References

[1] Kessler RC, Berglund P, Demler O, et al. Lifetime prevalence and age-of-onset distributions of DSM-IV-TR disorders in the national comorbidity survey replication. Arch. Gen. Psychiatry. 2005;62(6):593–602.
[2] Rapee RM. Anxiety disorders in children and adolescents. nature, development, treatment and prevention. In: Rey JM, editor. IACAPAP e-Textbook of child and adolescent mental health. Geneva: International Association for Child and Adolescent Psychiatry and Allied Professions; 2014. p. 2–6.
[3] den Boer JA. Social anxiety disorder/social phobia: epidemiology, diagnosis, neurobiology, and treatment. Compr Psychiatry. 2000;41(6):405–415.
[4] Beidel DC, Turner SM, Morris TL. Psychopathology of childhood social phobia. J Am Acad Child Adolesc Psychiatry. 1999;38(6):643–650.
[5] Sumter SR, Bokhorst CL, Westenberg PM. Social fears during adolescence: Is there an increase in distress and avoidance? J Anxiety Disord. 2009;23 (7):897–903.
[6] Demir T, Eralp-Demir D, Ozmen E, et al. The validity and reliability of capa social anxiety scale in children and adolescents. Dusunen Adam J Psychiat Neurol Sci. 1999;12:23–30.
[7] Bosquet M, Egeland B. The development and maintenance of anxiety symptoms from infancy through adolescence in a longitudinal sample. Dev. Psychopathol.. 2006;18(2):517–550.
[8] Bandelow B, Torrente AC, Wedekind D, et al. Early traumatic life events, parental rearing styles, family history of mental disorders, and birth risk factors in patients with social anxiety disorder. Eur Arch Psychiatry Clin Neurosci. 2004;254(6):397–405.
[9] Grant BF, Hasin DS, Blanco C, et al. The epidemiology of social anxiety disorder in the United States: results from the national epidemiologic survey on alcohol and related conditions. J Clin Psychiatry. 2005;66 (11):1351–1361.
[10] Rapee RM, Heimberg RG. A cognitive-behavioral model of anxiety in social phobia. Behav Res Ther. 1997;35(8):741–756.
[11] Tyson KE, Cruess DG. Differentiating high-functioning autism and social phobia. J Autism Dev Disord. 2012;42(7):1477–1490.
[12] Hog EA, Lawson EA, Metcalf CA, et al. Plasma oxytocin immunoreactive products and response to trust in patients with social anxiety disorder. Depress Anxiety. 2012;29(11):924–930.
[13] Neumann ID, Landgraf R. Balance of brain oxytocin and vasopressin: implications for anxiety, depression, and social behaviors. Trends Neurosci.. 2012;35(11): 649–659.
[14] Kagerbauer SM, Martin J, Schuster T, et al. Plasma oxytocin and vasopressin do not predict neuropeptide concentrations in human cerebrospinal fluid. J Neuroendocrinol.. 2013;25(7):668–673.
[15] Hammock EA, Young LJ. Microsatellite instability generates diversity in brain and sociobehavioral traits. Science. 2005;308(5728):1630–1634.
[16] Spielberger CD, Gorsuch RL, Lushene RE. Manual for the state-trait anxiety inventory. Palo Alto (CA): Consulting Psychologists Press; 1983.
[17] Ozusta S. Turkish standardization, reliability and validity of state trait anxiety inventory for children (In turkish). Turk J Psychol. 1995;10:32–44.
[18] La Greca AM, Stone WL. Social anxiety scale for children-revised: factor structure and concurrent validity. J Clin Child Psychol. 1993;22(1):17–27.
[19] Demir T, Karacetin G, Demir DE, et al. Prevalence and some psychosocial characteristics of social anxiety disorder in an urban population of turkish children and adolescents. Eur Psychiatry. 2013;28(1):64–69.
[20] Binelli C, Muñiz A, Sanches S, et al. New evidence of heterogeneity in social anxiety disorder: defining two qualitatively different personality profiles taking into account clinical, environmental and genetic factors. Eur Psychiatry. 2015;30(1):160–165.
[21] Schaefer ES, Bell RQ. Development of a parental attitude research instrument. Child Dev. 1958;29(3):339–361.
[22] LeCompte G, LeCompte A, Özer S. Three socioeconomic level childrearing attitudes of mothers in Ankara: A scale adaptation. Türk Psikoloji Dergisi. 1978;1:5–8. (In Turkish).
[23] Hisli N. Beck depresyon envanterinin universite ogrencileri icin gecerliligi, guvenilirligi. (A reliability and validity study of beck depression inventory in a university student sample). J Psychol 1989;7:3–13.
[24] Derogatis LR, Lipman RS, Covi L. SCL-90: an outpatient psychiatric rating scale, preliminary report. Psychopharmacol Bull. 1973;9(1):13–28.
[25] Kılıç M. Belirti tarama listesi (Scl. 90-R) Nin geçerlilik Ve güvenirliği. Türk Psikolojik Danışma ve Rehberlik Dergisi. 2016;1(2):45–52.
[26] Soykan Ç, Özgüven HD, Gençöz T. Liebowitz social anxiety scale: the turkish version. Psychol Rep. 2003;93(3_suppl):1059–1069.
[27] Liebowitz MR. Social phobia. In: Anxiety. Vol. 22. Basel: Karger Publishers; 1987. p. 141–173.
[28] Chambers WJ, Puig-Antich J, Hirsch M, et al. The assessment of affective disorders in children and adolescents by semistructured interview: test-retest reliability of the schedule for affective disorders and schizophrenia for school-Age children, present episode version. Arch Gen Psychiatry. 1985;42(7):696–702.
[29] Kaufman J, Birmaher B, Brent D, et al. Schedule for affective disorders and schizophrenia for school-age children-present and lifetime version (K-SADS-PL): initial reliability and validity data. J Am Acad Child Adolesc Psychiatry. 1997;36(7):980–988.
[30] Gökler B, Ünal F, Pehlivantürk B, et al. Reliability and validity of schedule for affective disorders and schizophrenia for school Age children-present and lifetime version-turkish version (K-SADS-PL-T)-. Turk J Child Adol Mental Health. 2004;11(3):109–116.

[31] Ranta K, Kaltiala Heino R, Rantanen P, et al. Social phobia in Finnish general adolescent population: prevalence, comorbidity, individual and family correlates, and service use. Depress Anxiety. 2009;26 (6):528–536.
[32] Knappe S, Beesdo-Baum K, Fehm L, et al. Social fear and social phobia types among community youth: differential clinical features and vulnerability factors. J Psychiatr Res. 2011;45(1):111–120.
[33] Parker KJ, Kenna HA, Zeitzer JM, et al. Preliminary evidence that plasma oxytocin levels are elevated in major depression. Psychiatry Res. 2010;178(2): 359–362.
[34] Gorka SM, Fitzgerald DA, Labuschagne I, et al. Oxytocin modulation of amygdala functional connectivity to fearful faces in generalized social anxiety disorder. Neuropsychopharmacology. 2015;40(2):278–286.
[35] Turan T, Uysal C, Asdemir A, et al. May oxytocin be a trait marker for bipolar disorder? Psychoneuroendocrinology. 2013;38(12):2890–2896.
[36] Christensen JC, Shiyanov PA, Estepp JR, et al. Lack of association between human plasma oxytocin and interpersonal trust in a prisoner's dilemma paradigm. PLoS one. 2014;9(12):e116172.
[37] Striepens N, Kendrick KM, Hanking V, et al. Elevated cerebrospinal fluid and blood concentrations of oxytocin following its intranasal administration in humans. Sci Rep. 2013;3:3440.
[38] Hoge EA, Pollack MH, Kaufman RE, et al. Oxytocin levels in social anxiety disorder. CNS Neurosci Ther. 2008;14(3):165–170.
[39] Patel N, Grillon C, Pavletic N, et al. Oxytocin and vasopressin modulate risk-taking. Physiol. Behav. 2015;139:254–260.
[40] Goekoop JG, De Winter RP, de Rijk R, et al. Depression with above-normal plasma vasopressin: validation by relations with family history of depression and mixed anxiety and retardation. Psychiatry Res. 2006;141(2):201–211.
[41] Motoca LM, Williams S, Silverman WK. Social skills as a mediator between anxiety symptoms and peer interactions among children and adolescents. J Clin Child Adol Psychol. 2012;41(3):329–336.
[42] Strahan EY. The effects of social anxiety and social skills on academic performance. Pers Individ Dif. 2003;34(2):347–366.
[43] Bayram Özdemir S, Cheah CS, Coplan RJ. Processes and conditions underlying the link between shyness and school adjustment among turkish children. Brit J Dev Psychol. 2017;35(2):218–236.
[44] Viana AG, Rabian B, Beidel DC. Self-report measures in the study of comorbidity in children and adolescents with social phobia: research and clinical utility. J Anxiety Disord. 2008;22(5):781–792.
[45] Hergüner S, Kılıç G, Karakoc S, et al. Levels of depression, anxiety and behavioural problems and frequency of psychiatric disorders in children with chronic idiopathic urticaria. Br J Dermatol. 2011;164(6):1342–1347.
[46] Epkins CC. A comparison of two self-report measures of children's social anxiety in clinic and community samples. J Clin Child Adolesc Psychol. 2002;31(1): 69–79.
[47] Burstein M, He JP, Kattan G, et al. Social phobia and subtypes in the national comorbidity survey–adolescent supplement: prevalence, correlates, and comorbidity. J Am Acad Child Adolesc Psychiatry. 2011;50 (9):870–880.
[48] Annunziato RA, Rakotomihamina V, Rubacka J. Examining the effects of maternal chronic illness on child well-being in single parent families. J Dev Behav Pediatr. 2007;28(5):386–391.
[49] Mazefsky CA, Conner CM, Oswald DP. Association between depression and anxiety in high-functioning children with autism spectrum disorders and maternal mood symptoms. Autism Res. 2010;3(3):120–127.
[50] Esbjørn BH, Pedersen SH, Daniel SI, et al. Anxiety levels in clinically referred children and their parents: examining the unique influence of self reported attachment styles and interview based reflective functioning in mothers and fathers. Brit J Clin Psychol. 2013;52 (4):394–407.
[51] Brumariu LE, Kerns KA. Mother–child attachment and social anxiety symptoms in middle childhood. J Appl Dev Psychol. 2008;29(5):393–402.
[52] Eapen V, Ghubash R, Salem MO, et al. Familial predictors of childhood shyness: A study of the United Arab Emirates population. Public Health Genomics. 2005;8 (1):61–64.
[53] Stevenson-Hinde J, Shouldice A, Chicot R. Maternal anxiety, behavioral inhibition, and attachment. Attach Hum Dev. 2011;13(3):199–215.
[54] Bayraktutan, M. Social anxiety disorder in patients with empathy skill, alexithymia, depression, anxiety levels and sympathetic skin response relationship and effects of medical treatment [unpublished master thesis]. Pamukkale Universty Faculty of Medicine Department of Psychiatr; 2014.
[55] Fang A, Hoge EA, Heinrichs M, et al. Attachment style moderates the effects of oxytocin on social behaviors and cognitions during social rejection: applying a research domain criteria framework to social anxiety. Clin Psychol Sci. 2014;2(6):740–747.
[56] Knappe S, Beesdo-Baum K, Fehm L, et al. Characterizing the association between parenting and adolescent social phobia. J Anxiety Disord. 2012;26(5):608–616.