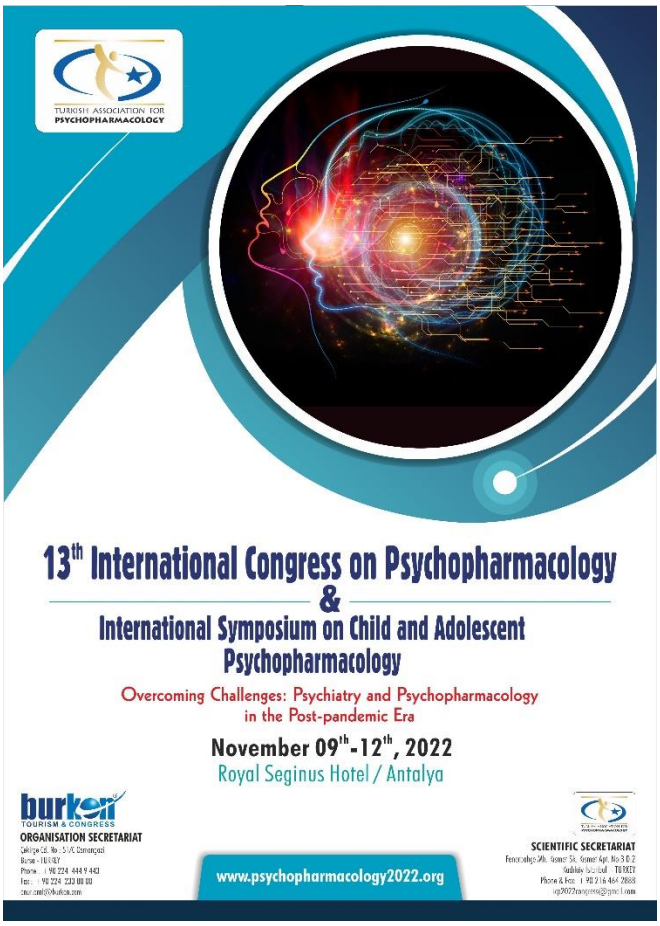

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ICP 2022 Outstanding Research Award Nominees Brief Reports

INVITATION

It is our great pleasure to announce that the Turkish Association for Psychopharmacology (TAP)'s 13th International Congress on Psychopharmacology & International Symposium on Child and Adolescent Psychopharmacology (ICP 2022) will be held on November 09-12, 2022 in Antalya, Turkey.

13th ICP & 9th ISCAP Organizing Committee

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Outstanding Research Award Nominees Brief Reports

13th International Congress on Psychopharmacology &
9th International Symposium on Child and Adolescent Psychopharmacology

[Abstract:0014] [Others]

0014 - Application of theta burst transcranial magnetic stimulation to the left dorsolateral prefrontal cortex in a depressed patient with previous history of aneurysm coiling procedure: a case report

Merve Setenay İris

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BACKGROUND: Major depressive disorder (MDD) is a highly prevalent and challenged condition often associated with significant morbidity and mortality where only one third of patients achieve remission after the first antidepressant treatment. Depression that does not respond to two or more different antidepressant drugs at adequate dosage and duration, which has been termed as treatment-resistant depression, has a significantly lower likelihood of responding to another antidepressant Lithium and lamotrigine augmentation, Ketamine infusion therapy and TMS are some of the tretament options in resisstant depression. Recent studies with ketamine have demonstrated a rapid onset (2–24 hours postinfusion) of antidepressant effect. However, the effect is relatively short-lived. A once-weekly dosing interval is unlikely to maintain the response, at least initially, because the duration of the effect after a single-dose infusion is less than one week . On the other hand it may cause some side effects such as dissociative/perceptual changes and hypertension. As another safe and non-invasive treatment in medication resisstant depressive disorder TMS can be considered. TMS is also safe to use even in pregnant women. It is effective and is approved by FDA in 2008 for Major Depressive Disorder.There are different protocols for TMS treatment. Repetitive transcranial magnetic stimulation (rTMS) has been established as an effective and evidence-based treatment in resisstant depression. On the other hand, Theta burst stimulation (TBS) is also a novel pattern of applying TMS shown to induce significant and long-lasting effects in the prefrontal cortex. In one study, Bilateral Neuronavigated TBS-20Hz TMS brought more than two-thirds of treatment refractory depressed patients to remission. However, because it lowers the epileptic threshold the patients should be evaluated carefully in terms of intracranial lesions, presence of shunts, cochlear implants, eye implants, vascular stent in the neck and intracranial area. The risk of seizures in TMS is reported to be <1 in 30,000. The presence of intracranial aneurysm clips is considered to be a relative contraindication for TMS treatment. However, recent research has shown that non-ferromagnetic aneurysm clips may not significantly move or heat up. Here we want to discuss a case to whom we applied TMS although she had a history of Cranial Aneursym Coiling Procedure.

METHODS: We used a 3 Tesla Magnetic field ALTMS device to provide deeper magnetic stimulation. Before the TMS protocol was appropved by neurosurgeons we used 0.5 mg/kg ketamine infusion therapy as a single session which provided important contribution to the treatment. We used a theta burst 3600 pulse accelarated protocol (two times a day , each session with 6 hours apart). We applied Beck anxiety and Beck depression scales to measure the improvement.

The reliability of the Beck Depression Inventory was examined by Hisli et. Al by item analysis and halving techniques, and these correlation coefficients were found to be r=.80 and r=.74. The validity of the scale was tried to be determined by the co-validation method and the MMPI-D Scale was used. The Pearson correlation coefficient between the two scales was found to be r=.50.

The reliability of the Beck Anxiety Inventory was examined by Gümüş Avcı in 1995 ; internal consistency, split-half reliability and test-retest reliability coefficients were examined. Cronbach's alpha value was calculated as r=.94, split-half reliability coefficient r=.94, and test-retest reliability coefficient r=.71. In order to examine the validity, the correlation coefficients between BAI and STAI were examined; A correlation coefficient of r=.61 with STAI-TX and r=.59 with STAI-TX-2 was determined .

CASE: A 50 year old female patient was admitted to our outpatient clinic with depressive complaints started after lithium discontinuation due to renal injury. She had been using antidepressant treatment since 27 years. Her first complaints had started when her husband was passed away in a traffic accident. She had a son who was 1 year old during this accident and had to raise him alone. She constanly had anxiety of loosing her child in some traffic accident. She had a gastritis problem and a brain anuerysm history. She was hospitalised in 2005 in Cerrahpaşa University Faculty of Medicine. Since this date she had been using lithium treatment. Other medications she use were duloxetine 60 mg/day, quetiapine XR 100 mg/day and lamotrigine 200 mg/day. After the discontinuation of lithium her apetite was decreased, she had feelings of worthlessness, unhappiness and her energy level was low. She described anhedonia and passive suisicidal ideation. She had used alprozalam, venlafaxine, sertraline before and did not respond. She had a history of Cerebral Aneurysm Coiling Procedure sixteen years ago. Although her resistant symptoms continiued nothing other than drug arrangement was planned. So TMS treatment was not applied although she had requested from her doctor. So she wanted to try her chance in our clinic. In first admission Beck Anxiety Scale score was 24 and Beck Depression Scale score was 32. In Psychiatric examination, her mood was depressive, her affect was anxious. She had ruminative negative thoughts about not being able to get well again. She had lost 2-3 kilograms because her appetite was decreased. She had passive suicidal thoughts but she was collabrating. We arranged her medication as Lamotrigine 250 mg/day, vortioxetine 10 mg/day, olanzapine 5 mg/day and made 1 session of Ketamine Infusion Therapy while we requested MRI and neurosuragical counsaltation in terms of TMS applicability. Because the patient was able to have an MRI it was understood that magnetic field was safe for the patient. So, after the counsaltation it was decided that the patient was suitable for TMS treatment. Accelareted Theta Burst TMS treatment is started to the left Dorso lateral Prefrontal Cortex. A total of 30 sessions (2 sessions per day) was made.

RESULTS: The patient improved significantly after the treatment and no side effects were detected. In psychiatric evaluation she was feeling better, her mood and affect were elevated, her appetite was increased, her energy level was improved and her anxiety was diminished. The depression and anxiety scales were repeated. After the treatment, the Beck Anxiety Score was diminsihed to 10 and Beck Depression score was diminished to 10 points, she only had mild symptoms. Her symptoms did not completely disappear probably resulting from the stressor her son was planning get married and move to another city.

During the follow up, some of the patient's depressive symptoms reocurred after her son's engagement party. She had anhedonia and agitation symptoms. She came to the out patient clinic with feelings of hopelessness and anxiety. Her apetite was decreased and she had difficulties in maintaining her social relationships because of intoleration. As she also was benefited from ketamine infusion therapy, a weekly ketamine infusion treatment was planned, her medications were rearranged and a total of four ketamine infusion sessions were made. After the first infusion therapy she quickly recovered and at the end her symptoms were significantly improved and functionality was increased. Currently, she is under full remission.

CONCLUSION: Depression disrupts functionality critically an even may cause suiscidal ideation. Classical antidepressant medications may not always be sufficient for some patients and mood stabilizers may cause certain side effects. Treatments like TMS is a good option in these cases. However, some of these patients may have undergone certain brain operations. In such cases neurosurgical consaltation can be needed. Recently, coils suitable fo MRI are used in brain aneurysm coiling operations. If the identity of the clip is known (that is, confirmed in the medical record with the physician who implanted it), it can be checked and if suitable TMS can be used according to literature. Shellock has provided a valuable resource documenting the magnetic properties of nearly all known medical devices. If a clip is listed as "Safe" for MRI, and because MRI also has a powerful magnetic effect, patients suitable for MRI can also be appropriate candidates for TMS treatment.

Because depression is a highly prevalent and challenged condition, multidirectional approaches are crucial. Primum non nocere should definetely be our first rule. Thus investigating proper treatment options is important. In this case, if we did not try and examine the applicability of TMS and ketamine therapy, the patient would probably continue

to suffer from this condition. So, we may say that not giving the necessary treatment to the patient is as critical as causing direct harm to the patient.
LIMITATIONS: Because this is a single case report it is impossible to draw definite conclusions about tms applicability in this group of patients, but there are some cases like ours in the literature who successfully managed to accomplish the treatment. Our difference is also making accelareted sessions (2 sessions in one day 6 hours apart). Different protocols may be tried in order to achieve the best outcome.
Also, because of the traumatic life events in the patient's life long term psychotherapy might be needed in such a patient, however due to her prejudices this option could not be tired. A multidirectional approach would be ideal in such cases for long term remission rates.

Key Words: brain aneursym coiling procedure , ressistant depression, TMS

REFERENCES

1) Gümüş Avcı, M. (1995). Beck Anksiyete Ölçeği'nin Geçerlik Ve Güvenirlik Çalışması (Yayınlanmamış Yüksek Lisans Tezi). Ege Üniversitesi, İzmir.
2) Hisli, N. (1989). Beck Depresyon Envanterinin Üniversite Öğrencileri İçin Geçerliği, Güvenirliği. Psikoloji Dergisi, 7(23), 3-13.
3) Pridmore S, Lawson F. Transcranial magnetic stimulation and movement of aneurysm clips. Brain Stimul. 2017 Nov-Dec;10(6):1139-1140. doi: 10.1016/j.brs.2017.08.009. Epub 2017 Sep 13. PMID: 28941752.
4) Stillman M., Chandonnet N., Davis L., Buzan R., Wirecki T. Deep transcranial magnetic stimulation in patients with intracranial aneurysm clips: a case report and guidelines for clinicians in: Poster presented at the clinical TMS society 7th annual meeting. Canada, VancouverFebruary 2019
5) Taylor Rohan et al. Transcranial magnetic stimulation (TMS) safety: a practical guide for psychiatrists. Australas Psychiatr. 2018; 26: 189-192 https://doi.org/10.1177/1039856217748249
6) Shellock., Frank G., Reference manual for magnetic resonance safety, implants, and devices. Biomedical Research Publishing Group, 2018
7) Stubbeman WB., Zarrabi B., Bastea S., Ragland V., Khairkhah R. Bilateral neuronavigated 20Hz theta burst TMS for treatment refractory depression: An open label study. Brain Stimulation .Volume 11, Issue 4, July–August 2018, Pages 953-955.

[Abstract:0017] [Psychopharmacology]

0017 - Risperidone for the treatment of retentive fecal incontinence in children and adolescents: a randomize clinical trial

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ABSTRACT
BACKGROUND: Functional retentive overflow incontinence (Retentive FI) is the most common cause of fecal soiling in children. Based on the clinical experiences, patients with retentive FI and comorbid psychiatric disorders, were accelerated in their treatment of fecal incontinence when they were being treated with Risperidone

for their psychiatric comorbidities, therefore this study was conducted to evaluate the effect of Risperidone in the treatment of Retentive FI in children and adolescents.
METHOD: In this double-blind randomized clinical trial, 170 patients aged 4-16 years eligible for the study were randomly divided into two groups receiving Risperidone (n=70) and placebo (n=70). About half of these patients had newly diagnosed psychiatric disorders and were drug naïve, this was considered in their division. Participants received a daily dose of 0.25-0.5 mg every 12 hours of Risperidone syrup (intervention group) or maltodextrin (placebo group) for 12 weeks. Sociodemographic data including age, sex, weight, height, BMI and BMI z-score (equivalent BMI-for-age percentile), and socioeconomic status were recorded. nocturnal fecal incontinence, diurnal fecal incontinence and painful defecations information was collected from subjects.
RESULTS: 136 participants (69 on Risperidone and 67 on placebo) completed the intervention. Mean age of participant in the intervention and placebo groups were 7.2±2.4 years and 8.0±3.1 y, respectively. The mean number of nocturnal fecal incontinence (P_{trend}=0.39), diurnal fecal incontinence (P_{trend}=0.48) and painful defecations for participants with and without psychiatric comorbidities were not significantly different between the groups (P=0.49, P=0.47, respectively). While, a significant interaction was observed between time duration and psychiatric comorbidities (P <0.001) for diurnal fecal incontinence after treatment with Risperidone.
CONCLUSION: Based on our findings in this study, Risperidone, used commonly for psychiatric disorders in children and adolescents, may be useful in the treatment of retentive fecal incontinence in the presence of psychiatric comorbidities, and along with other interventions.

Keywords: Retentive Fecal Incontinence, Risperidone, Pediatric, Encopresis, Atypical antipsychotics, Fecal Soiling

INTRODUCTION

According to DSM-5 (Diagnostic and Statistical Manual of Mental Disorders-Fifth Edition), encopresis is defined as voluntary or involuntary passage of stool in inappropriate places such as underwear, in a child with a developmental age of four years or older, after rule out of organic causes (1). There are two types of encopresis, with and without constipation and overflow incontinence (2). Functional retentive overflow incontinence (Retentive FI), also known as encopresis with constipation and overflow incontinence, is the most common cause of fecal soiling in children. 1.5% of children 7 to 8 year old have this problem, and it is three times more common in boys. (3) Patients often recover significantly, 30-50% in a year and about 50-75% after five years. (4). This disorder can lead to feelings of embarrassment and guilt in patients and can make them victims of bullying (5, 6). Studies have shown that in 30 to 50% of cases, there are psychiatric disorders, especially attention deficit hyperactivity disorder (ADHD), oppositional defiant disorder (ODD), mood and anxiety disorders, and poor school performance in children with fecal incontinence. (3, 5, 7, 8). The biopsychosocial perspective conceptualizes underlying causes and course of fecal incontinence, and therefore, a comprehensive approach to evaluation and treatment is required (9).
Clinical experience shows that treatment of underlying psychiatric disorders, along with treatment of fecal incontinence, helps to better advance the treatment plan. In the comprehensive approach to the treatment of fecal incontinence, psychopharmacotherapy is recommended in some texts, and Imipramine, methylphenidate, and Atomoxetine, have been found to be effective in treating non-retentive FI (10-12).
In the clinical experience of the psychiatrist in charge of this article, children and adolescents with retentive FI and comorbid psychiatric disorders, were accelerated in their treatment of encopresis when they were being treated with Risperidone for their psychiatric comorbidities, although various studies have suggested that atypical antipsychotic drugs may cause fecal incontinence(13). Risperidone, an atypical antipsychotic, is commonly used to treat many psychiatric disorders in all age groups, and exhibits its action as a serotonergic and dopaminergic receptor antagonist (14). Therefore, this randomized clinical trial was conducted to evaluate the effect of Risperidone in the treatment of retentive FI in children and adolescents.

METHODS:

Study design

In this double-blind randomized clinical trial, pediatric patients referred to the gastrointestinal clinic of two children's hospitals in Tehran were considered over a period of six months. To determine the sample size based on studies on the effect of Risperidone on mood and behavior symptoms, and also the expert opinions in the field of pediatric gastroenterology and child and adolescent psychiatry, the effectiveness of conventional therapies in the treatment of retentive FI in the short term, and the effectiveness of Risperidone in the treatment of retentive FI comorbid with psychiatric disorders was estimated at 25% and 50%, respectively. Using the percentage of treatment of fecal incontinence in both groups, and with a significant level of 95%, with the type I of error probability level of 5% ($\alpha = 0.05$), the type II error probability level of is 20% ($\beta = 0.20$, power = 80%) and assuming 10% of the possible loss, the sample size in each group 70 people, and a total of 140 people were identified as follow:

$$m = \frac{\left\{ z_{1-\alpha/2}\sqrt{\left[(1+\varphi)\overline{p}\,\overline{q}\right]} + z_{1-\beta}\sqrt{\left[\varphi p_1 q_1 + p_2 q_2\right]} \right\}^2}{\varphi \delta^{2}_{plan}}$$

Patients' selection

Inclusion criteria were willingness to cooperate and signing the informed consent form after full knowledge of the objectives and method of the study, age 4-18 years, and diagnosis of Retentive Fecal Incontinence (Retentive FI) according to ROME-IV diagnostic criteria. Exclusion criteria were having any histories of cardiovascular, hepatic, renal and metabolic diseases, morbid obesity, use of medications for psychiatric disorders, pregnant and lactating adolescents, smoking (more than one cigarette in the last week or more than 200 cigarettes in a lifetime), have any previous allergies to Risperidone, and noncompliance with medication.

Psychiatric and gastrointestinal assessments were performed by a child and adolescent psychiatrist using K-SADS, and a pediatric gastroenterologist using ROME-IV, respectively. Sociodemographic data including age, sex, weight, height, BMI and BMI z-score (equivalent BMI-for-age percentile), and socioeconomic status were recorded.

Randomization

136 children and adolescents aged 4-16 years who meet the inclusion criteria were randomly divided into two groups receiving Risperidone and placebo. The flow diagram for the trial is shown in Figure 1. About half of these patients had newly diagnosed psychiatric disorders (with mild to moderate intensity) and were drug naïve and this was considered in their division. Considering that BMI Z-score and psychiatric disorders can have a great impact on the results of the study, to ensure the uniform distribution of these variables in the groups, random allocation by Stratified Randomization and using the Permuted block randomization method with quadruple and binary blocks were used. Based on the sample size of 136 subjects, the quadruple block or double block were produced using the online site (www.sealedenvelope.com). These codes were inserted on the packages by the company receiving the supplements and placebos. Upon each person entering the study, based on the sequence generated, the drug package in which the code is recorded was assigned to the parents. Also, the random sequence generated during the study was unpredictable. The admission rate of patients after the intervention period was calculated using the following formula, and patients whose admission rate is less than 80% were excluded from the study. Acceptance rate = number of packages received at the beginning of the study/number of packages consumed at the end of the study * 100.

Interventions (pharmacological and non-pharmacological)

Participants received a daily dose of 0.25-0.5 mg every 12 hours of Risperidone syrup (intervention group) or maltodextrin (placebo group) for 12 weeks. Due to the double-blindness of the study, before starting the study, sets of packs containing Risperidone and placebo were prepared by someone other than the researchers, and the placebo syrup was similar in appearance to Risperidone syrup, therefore, none of the participants and researchers knew which of the two groups received Risperidone or placebo. The drugs were given to the parents at the beginning of the study,

and they were asked to bring empty packages of cans at the end of 3 months to check the acceptance of the intervention. In addition to polyethylene glycol, all the participants received family counseling and education for withholding behaviors and related behavioral interventions including regular toileting, use of diaries to track stooling, and reward systems for successful evacuations. Non-pharmacological interventions for psychiatric comorbidities, including cognitive behavioral therapy, social skills training, parent management training (PMT), and family therapy were performed by a child and adolescent mental health professional.

Statistical analysis

Quantitative variables were reported as mean (standard deviation) and qualitative variables were reported as numbers (percentage). To compare the mean of quantitative outcomes between the two groups, independent T-Test were used to compare the results between baseline and end of the intervention. Chi-square test or Fisher's exact test were used to compare qualitative factors between the two groups. The effect of Risperidone on quantitative variables was investigated by two-way repeated measure ANOVA and post-adaptation covariance test for possible confounding factors. SPSS software version 16 was used to obtain statistical analyses, and significant levels for all tests were considered as P-value <0.05. Intention-to-treat (ITT) analysis was performed as well.

Ethical considerations

This study was approved by the research ethics committee of Shahid Beheshti University of Medical Sciences, Tehran, Iran (IRCT20200203046352N1). This randomized controlled trial has been registered in Iranian Registry of Clinical Trials with IRCT number of This prospective randomized controlled trial has been registered in Iranian Registry of Clinical Trials with IRCT number of IRCT20181117041683N1.

RESULTS: 136 participants (69 on Risperidone and 67 on placebo) completed the intervention. Demographic characteristics in each group are shown in **Table 1**. Mean age of participant in the intervention and placebo groups were 7.2±2.4 years and 8.0±3.1 y, respectively. No statistically significant differences were observed in weight, height, BMI Z-score and BMI (kg/m^2) among the groups at baseline. While the number of girls between groups (girls in placebo=17(36.2%) and intervention =30(63.8%)) was different significantly. 34 subjects in Risperidone group and 35 in placebo group had psychiatric comorbidities and there was no statistically significant difference between the two groups regarding psychiatric comorbidity (P=0.43).

Table 2, shows gastrointestinal manifestations of participants at baseline. Values for constipation, fissures, hard stool, and compact feces were not significantly different among groups (P>0.05). While the percentage of hemorrhoids in patients with psychiatric disorders was significantly different between groups (P = 0.025).

values for the mean number of nocturnal fecal incontinence (P_{trend}=0.39), diurnal fecal incontinence (P_{trend}=0.48) and painful defecations for participants with and without psychiatric comorbidities were not significantly different between the groups (P=0.49, P=0.47, respectively).When comparing changes in the number of diurnal and nocturnal fecal incontinence in terms of the presence of psychiatric comorbidities, a significant interaction was observed between time and psychiatric comorbidities (P <0.001) for diurnal fecal incontinence (**Table3**).

DISCUSSION: In pediatric patients with fecal incontinence, psychiatric comorbidities especially ADHD and ODD have been reported more frequently, (5, 7, 8) and some studies showed that comorbid internalizing and externalizing psychiatric disorders are a predictor of poor outcome in children with fecal incontinence (15, 16). Based on the clinical experiences, in addition to educational, psychological and behavioral interventions for patients with fecal incontinence and comorbid psychiatric disorders, psychopharmacologic interventions have sometimes been effective in this multidisciplinary treatment program. (5, 10-12, 17) Atypical antipsychotics are prescribed for various psychiatric disorders such as psychotic, mood, anxiety, tic, obsessive-compulsive, and disruptive behavior disorders (18). The reason for using Risperidone as one of the atypical antipsychotics in our study was efficacy in symptom reduction in many child and adolescent psychiatric disorders. (18) To our knowledge, this is the first double-blind randomized clinical trial performed with Risperidone for the treatment of retentive fecal incontinence in a clinical setting. According to the results of our study, in the presence of psychiatric comorbidities, Risperidone added to other traditional interventions significantly reduced the frequency of fecal incontinence during the day (P <0.001). With gradual discontinuation of Risperidone at the end of the third month of study, fecal soiling gradually increased

during the next three months of follow-up. Risperidone has high affinity for dopamine D2 and serotonin 5-HT2A, adrenergic α1- and α2- and histaminergic H1 receptors, and moderate affinity for serotonin 5-HT1C, 5-HT1D, and 5-HT2A receptors (18). It is not clear whether the mechanism of action of Risperidone on retentive FI is central or peripheral. Dopamine inhibits colonic movements and prolongs gastrointestinal transit time (19, 20) and the efficacy of Risperidone as a dopamine antagonist in retentive FI may be due to this fact. (18). Also, Risperidone has possible analgesic effect (21).

In reviewing the literature, a relationship between atypical antipsychotics and fecal incontinence has been mentioned. In a systematic review in 2021, Arasteh et al. pointed out that atypical antipsychotic drugs can cause fecal incontinence, which may be due to α1-adrenergic blockade, sedative effects, and blockage of the pudendal reflexes (13). Among atypical antipsychotic medications, Risperidone has less sedation (22). In our study the most common adverse effects observed with Risperidone were overweight and mild sedation. There are studies in support of Imipramine, Methylphenidate, and Atomoxetine, which suggest that these medications may be helpful in treating fecal incontinence (10-12). Imipramine is a Tricyclic Antidepressant and has an anticholinergic effect similar to Loperamide by reducing gastrointestinal motility and increasing sphincter tone. In some texts it is mentioned that Imipramine can be useful in treating non-retentive FI, but due to cardiovascular complications, Tricyclic Antidepressants should not be prescribed as usual (5, 11). In a 2013 case report, Yılmaz and Akça noted that Methylphenidate leads to recovery from fecal incontinence(12) and in a 2012 study, Huang and Chien showed that inhibition of gastric emptying and intestinal transit induced by amphetamine is due to an effect on the dopaminergic system (via D1 and D2 receptors) and to some extent adrenergic receptors. Golubchik and Weizman in an article in 2013 pointed out that direct impact of methylphenidate, imipramine, and atomoxetine, on self-organizing skills, impulse control, and executive functioning, may enable children to recognize and respond to internal cues for defecation, helping them in the treatment process.(12, 17)

The effects of Atomoxetine in the treatment of fecal incontinence have been reported in the literature, however, constipation is a side effect of Atomoxetine, such as risperidone, and administration of Atomoxetine to patients with ADHD and comorbid fecal incontinence can improve or worsen fecal incontinence. (10, 18, 23, 24)

These findings may shed light on the effects of the central nervous system medications on the gastrointestinal tract, (25) and given the high comorbidity of psychiatric disorders with fecal incontinence, it may be necessary to develop a comprehensive treatment plan, considering the benefits of psychopharmacotherapy.

CONCLUSION: Due to the high prevalence of psychiatric comorbidities in retentive FI, a comprehensive psychiatric evaluation is recommended, especially when there is a suspicion of mood and behavior disorders and attentional problems. Based on our findings in this study, Risperidone, used commonly for psychiatric disorders, may be useful in the treatment of fecal incontinence in the presence of psychiatric comorbidities, and along with other interventions. Future studies should be conducted multicenter with large sample size to provide evidence-based results.

Conflict of interest/funding: None

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REFERENCES

1. von Gontard A. DEVELOPMENTAL DISORDERS. 2012.
2. Dade P. Encyclopedia of child behavior and development. Reference Reviews. 2011.
3. Martin A, Volkmar FR, Bloch MH. Lewis's Child and Adolescent Psychiatry: A Comprehensive Textbook: Wolters Kluwer; 2017.
4. Loening-Baucke V. Encopresis. Current Opinion in Pediatrics. 2002;14(5):570-5.
5. Koppen I, Von Gontard A, Chase J, Cooper C, Rittig C, Bauer S, et al. Management of functional nonretentive fecal incontinence in children: Recommendations from the International Children's Continence Society. Journal of pediatric urology. 2016;12(1):56-64.

6. Blum NJ, Taubman B, Nemeth N. During toilet training, constipation occurs before stool toileting refusal. Pediatrics. 2004;113(6):e520-e2.
7. Cox DJ, Morris Jr JB, Borowitz SM, Sutphen JL. Psychological differences between children with and without chronic encopresis. Journal of Pediatric Psychology. 2002;27(7):585-91.
8. Çoban ÖG, Önder A, Adanır AS. Psychiatric comorbidities of children with elimination disorders. Archives de Pédiatrie. 2021;28(1):59-63.
9. Culbert TP, Banez GA. Integrative approaches to childhood constipation and encopresis. Pediatric Clinics of North America. 2007;54(6):927-47.
10. Hergüner S, Hergüner A. Atomoxetine for encopresis in 2 children with attention-deficit/hyperactivity disorder. Journal of clinical psychopharmacology. 2012;32(2):302-3.
11. Gavanski M. Treatment of non-retentive secondary encopresis with imipramine and psychotherapy. Canadian Medical Association Journal. 1971;104(1):46.
12. Yılmaz S, Akça ÖF. Effectiveness of methylphenidate in the treatment of encopresis whether or not attention-deficit/hyperactivity disorder symptoms are present. Journal of Child and Adolescent Psychopharmacology. 2013;23(9):632-3.
13. Arasteh A, Mostafavi S, Vahed SZ, Montazeri SSM. An association between incontinence and antipsychotic drugs: A systematic review. Biomedicine & Pharmacotherapy. 2021;142:112027.
14. Ereshefsky L, Lacombe S. Pharmacological profile of risperidone. The Canadian Journal of Psychiatry/La Revue canadienne de psychiatrie. 1993.
15. Montgomery DF, Navarro F. Management of constipation and encopresis in children. Journal of Pediatric Health Care. 2008;22(3):199-204.
16. van Wering HM, Tabbers MM, Benninga MA. Are constipation drugs effective and safe to be used in children?: a review of the literature. Expert opinion on drug safety. 2012;11(1):71-82.
17. Golubchik P, Weizman A. Attention-deficit hyperactivity disorder, methylphenidate, and primary encopresis. Psychosomatics. 2009;50(2):178-.
18. Sadock BJ, Sadock VA, Ruiz P. Kaplan and Sadock's Comprehensive Textbook of Psychiatry: Wolters Kluwer Health; 2017.
19. Sanger GJ. Chronic constipation: improved understanding offers a new therapeutic approach. The Journal of Physiology. 2016;594(15):4085.
20. Winge K, Rasmussen D, Werdelin L. Constipation in neurological diseases. Journal of neurology, neurosurgery, and psychiatry. 2003;74(1):13.
21. Fishbain DA, Cutler R, Lewis J, Cole B, Rosomoff RS, Rosomoff H. Do the second-generation “atypical neuroleptics” have analgesic properties? A structured evidence-based review. Pain Medicine. 2004;5(4):359-65.
22. Eugene AR, Eugene B, Masiak M, Masiak JS. Head-to-Head Comparison of Sedation and Somnolence Among 37 Antipsychotics in Schizophrenia, Bipolar Disorder, Major Depression, Autism Spectrum Disorders, Delirium, and Repurposed in COVID-19, Infectious Diseases, and Oncology From the FAERS, 2004–2020. Frontiers in pharmacology. 2021;12:295.
23. Yektas Ç, Cansiz MA, Tufan AE. Increased frequency of encopresis in a child diagnosed with attention deficit/hyperactivity disorder and encopresis after atomoxetine use: a case report. Clinical Neuropharmacology. 2016;39(4):212-3.
24. Türkoglu S, Bilgiç A, Uzun N. Effectiveness of atomoxetine in the treatment of children with encopresis. Journal of Clinical Psychopharmacology. 2015;35(5):622-3.
25. Huang W-J, Chien EJ, Yeh J-Y, Chen J-J, Chiao Y-C, Wang PS, et al. The roles of dopamine receptor and adrenoreceptor on the inhibition of gastric emptying and intestinal transit by amphetamine in male rats. Chin J Physiol. 2012;55(4):259-66.

[Abstract:0018] [Psychotherapy]

0018 - Indirect stuttering treatment in preschool children

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OBJECTIVE: Almost everyone has come across someone with stuttering. This person may be someone you see on the road, that you do not know at all or you have just met, or they may be
very close to you, such as your friend, spouse, child, or relative. As you see the effort they make when they speak, you too experience their distress - through your mirror neurons - your
body becomes tense, and you burn with empathy, a willingness to help. I was one of them.
Years ago, I was a psychiatric assistant when my daughter started stuttering when she was 2.5
years old. after my daughter stuttering, my curiosity and questions increased as I researched. What made me think the most was this: If a physical- organic cause caused this disease, why was not there stuttering in some cases? For example, why didn't a person stutter when alone, and when talking to children, animals, people he felt comfortable with or singing? Even though my daughter's problem was over, maybe this was the source of my endless interest in stuttering. Thanks to the curiosity and interest we develop a new treatment technique of stuttering.
This study is about how parents who have stuttering children can indirectly correct their children's speech using a technique they can actively use. I know well the helplessness and panic I see in parents who have stuttering in their children; because I experienced it too. Sending them home with a tool is a fantastic feeling. I am happy to overcome with such an easy method, and in every case, I see this improves, this happiness is riveted.
Therefore, the purpose of this study is to give a brief introduction to a new treatment technique of stuttering. We named it the "stuttering vaccine" because it is a method to prevent stuttering from occurring. In this study, firstly the theoretical background of stuttering and its main characteristics such as causes, consequences, prevalence, and treatment practices, etc. are summarized. Then, the development process of stuttering vaccine technique, the application of its by two specific protocols, an assessment and intervention tool are presented. Furthermore, the use of stuttering vaccine in psychotherapy are presented through two different case examples. Finally, a brief information letter called "Stuttering Vaccine" that the therapists can give to families is presented. Our target audience is 2-6 years old, which is the age at which stuttering is most common.
METHODS: The stuttering vaccine technique is an utterly indirect method; permanent learning is aimed through implicit memory. In learning through implicit memory, the person is not aware that he or she is learning about a situation or event. In other words, learning occurs without conscious awareness. Stuttering occurs with the locking (spasm) of the vocal cords and the act of forcing to resolve this spasm, and we emphasized that speed stress is the only cause of this speech disorder in very young children. There is only one way to unlock this lock; speaking slowly, clearly, and by spelling.
The stuttering vaccine technique; is based on our spelling of parents' speeches to their stuttering children to speak slowly and clearly. Thus, it is aimed that the child will learn the technique permanently by imitating (through mirror neurons) and unconsciously (implicit memory). It is based on the assumption that this response, which is intended to be transformed into a habit, will be used automatically when the vocal cords contract. (SEE Protocol to be applied in 2-6-year-old stuttering).
We know that stuttering is followed by improvement and repetition in children. With this slow speech, which will become a habit, the child who can resolve the spasm, who can speak fluently, will use it as long as he/she needs it. He/she will continue his/her fluent speech with spelling instead of stuttering when he/she is stuck.

RESULTS: The "stuttering vaccine" technique was used in psychotherapy in two different cases. According to the first case (4 yrs.), he gained fluency within a week because of "stuttering vaccine" technique. When he started to speak fluently, the family had neglected the principles of maintenance treatment. This boy's stuttering recurred about a year later. Parents who called were asked to use the technique without seeing the child for the examination and were told to bring the child if it did not pass. Speaking did not reoccur in this sibling, who was recovered quickly and is now 10-11 years old.

The mother of these children was talking very fast. The severely stuttering client was seen with his family. Spelling practices were done with the parents, and they were asked to shoot videos. It was observed in the short videos that the parents used the technique correctly. Within a few days, it was observed that the child's stuttering decreased, and the stuttering took less time. In the video shot at the end of the 10th day, it was observed that the child spoke fluently, although it was observed that the parents neglected the spelling. At the end of the first month, the child was speaking entirely fluently.

Regarding to second case (5 yrs.), he had been stuttering for a year, and it never passed. A year ago, her parents argued, and his father did not come home for two months. During this period, the child started nursery, cried a lot, and they could only take her there for eight days. After one month, her stuttering started. At home, they treated the child as she was sick and in a protective manner. Her uncle stuttered at the age of 10-12, and it lasted for one year. Everyone in the house was talking very fast.

The client was seen with her family. Spelling practices were done with the parents, and they were asked to shoot videos. In the videos, the family was successful in speaking by spelling the first few days. It was observed that the duration of the child's stuttering decreased in a few days. In the video taken in the 1st week, it was observed that the parents stopped spelling because the child started to speak fluently, and they were asked to continue spelling. However, in the next video, it was observed that family members were using spelling at an extremely rapid pace or not at all. The child still spoke fluently, but it was observed that occasional stuttering continued. They did not come to the 1st-month control, and the family, who was contacted by phone, was advised to follow the continuation steps to avoid recurrence.

The application will bring the highest success rate in children who are newly born or who have a stuttering habit in their family and surroundings. The longer a habit has been used, the learning consolidates, and the harder it is to improve.

Early diagnosis and treatment for all physical and mental diseases; means more effective, more comfortable, and cheaper treatment. Just as we are vaccinating to avoid getting sick, we can vaccinate our children to prevent the occurrence of stuttering. For this reason, the fact that parents and people who are taking care of children speak slowly and clearly with children by prolonging the word, that is, by spelling, helps the child to learn to speak in this way. Overcoming speed stress, which is almost the only stress in young children, will not cause stuttering. When stuttering occurs in the speech, the child will speak slowly and continue to speak fluently.

Without realizing the speed of the other person's speech, we get carried away. This situation is more pronounced in children. When we speak slowly and clearly with young children who stutter, they imitate us, and their conversations become fluent. For this reason, we recommend those who are taking care of children to talk to the child and each other in this manner. This form of treatment is indirect. The child is not pressured to speak slowly. His/her speech is not corrected. Learning through imitation, the child will learn to speak slowly and fluently by imitating you after a while. Continuous, as long as there is stuttering, and when it disappears, frequent clear speech and occasional spelling will provide preventive treatment.

DISCUSSION: The main aim of the current study was to prevent the emergence of stuttering at these ages and treat the stuttering by “stuttering vaccine”. According to the case examples, the stuttering vaccine both prevents stuttering and ends the stuttering that starts in a short time. The method will be seen to be very easy and very useful when applied. The first thing to do; never correct the child's speech. In other words, the child's speech will not be interfered with in any way. Secondly, it will be spoken slowly, piece by piece, with a little low voice and spelling when talking to the child.

Controlled studies are needed to compare all these recommended techniques with other treatments applied in children aged 2-6 years and older adults. Besides, studies can be designed to use all three of these techniques (speaking by spelling, slowing down actions, watching videos with reduced speed by 50%) in problems other than stuttering, for example, in the control group with and without an anxiety disorder. The effects of slowing down and acceleration (accelerating movements, speaking, and watching videos with a 50% increase in speed) on the person's stress level, physical and emotional tension can be investigated. For this, the autonomic nervous system (sympathetic fight-flight, parasympathetic sedative) can be measured indirectly by measurements of pulse and skin resistance (GSR: Galvanic skin resistance). Thus, it will open the way for these techniques to be used in different situations. Finally, future directions for its use to treat stuttered children and adolescents are discussed. We hope that this book will benefit families, children, adults, and therapists who feel helpless and suffer from stuttering and bring a bright eye. In addition, suggestions are given for field workers and researchers in the light of the relevant literature.

[Abstract:0029] [Specific learning disabilities]

0029 - Evaluation of p300 and spectral resolution in children with attention deficit hyperactivity disorder and specific learning disorder

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OBJECTIVE: Attention Deficit Hyperactivity Disorder (ADHD) and Specific Learning Disorder (SLD), causing academic difficulties and impairment in functionality, are two neurodevelopmental disorders with frequent seen together. It has been reported that non-invasive nature and high temporal resolution of the P300 technique have the potential to reveal cortical functioning in children with SLD and/or ADHD[1,2]. On the other hand, it has been suggested that the auditory processing problems emphasized in the etiopathogenesis of learning disabilities are not limited to temporal processing, and that spectral (frequency) processing is also impaired[3]. The spectral resolution, which evaluates spectral processing, has been associated with the listener's ability to parse frequency information in a complex signal such as speech, distinguish between quiet and loud speech sounds, and thus understand speech in noisy listening environments[4]. It has been thought that understanding speech in noise plays an essential role in children's academic success at school. As far as we know, there is no study in literature evaluating P300 and spectral resolution in ADHD and SLD. This study aims to examine the relationship between functional impairment levels, auditory performance skills, auditory spectral resolution, P300 amplitude, and latency in children with ADHD, SLD, and ADHD+SLD.

MATERIALS AND METHODS

Participants: Our study included patients with the diagnosis of SLD, ADHD, and ADHD+SLD between the ages of 7-12 who were treated in Cerrahpaşa Child Psychiatry Outpatient Clinic between October 2021-April 2022, and age*gender matched healthy controls. Informed written consent was obtained from parents, along with verbal assent from the participating children, in accordance with the Declaration of Helsinki. This study was approved by Istanbul University-Cerrahpasa, Cerrahpasa Medical Faculty Ethics Committee (04.08.2021-152549). The study statistics were performed on four groups, 15 SLD, 17 ADHD, 15 ADHD+SLD, and 15 healthy control(Figure 1).

Questionnaire measures: All children were evaluated with the clinical opinion of an experienced clinician based on DSM-5, and a semi-structured interview was applied. Parents filled out the Sociodemographic data form, Destructive Behavior Disorders Screening Scale according to Turgay-DSM-IV, and Weiss Impairment Functioning Scale Parent Form (WFIRS-P). Mathematics, Reading, Writing Scale (MOYA) is a likert-type scale and consists of 47 questions. Parents also completed the Children's Auditory Performance Rating Scale (CHAPS)[5] to differentiate Auditory Processing Disorder, which can be confused with clinical symptoms of ADHD and SLD. In total score "passing" range is +36 to -11, "risk" range is -12 to -130.

Experimental procedures

Spectral-temporally Modulated Ripple Test (SMRT): SMRT V.1.1.3 software(http://www.ear-lab.org/smrt.html) was loaded on a laptop computer, and the computer was calibrated by connecting it with an audiometer. The test was carried out in a quiet cabinet utilizing free-space speakers. Three stimuli, one of which was the target stimulus, were presented. The software reports scores in ripples per octave(RPO) at the end of the test[6].

ERP Acquisition: ERP recordings were performed with the NeuronSpectrum 5/P 19-channel digital EEG device. The ERPs were recorded from 19-scalp-electrode according to the international 10–20 electrode-system using Electro-Cap. An auditory oddball two-tone discrimination task was used to reveal auditory P300 potentials. ERP were calculated separately for both stimulus types (frequent/infrequent), and the data were cleaned in noise. EEG data analyzed with BrainVision Analyzer 2.1.

Statistical Analysis

The Statistical Package for the Social Sciences-21(SPSS) was used for data analysis. For comparison of the categorical data and continuous data, the Kruskal–Wallis test was used following the normality test (Shapiro–Wilk). The binary logistic regression analysis was used to predict CHAPS risk status. Multiple linear regression was used to predict P300 parietal region amplitudes.

In the ERP's statistics, the 270-600 ms time window for the peak latency results and the average amplitude values separately; stimulus types (non-target/target), location (anterior/middle/posterior), hemisphere (left/middle/right), and between 4 groups ANOVA analysis was applied for repeated measurements depending on the parameters. Significance levels were reported using the Greenhouse-Geisser correction and p values. For repeated measurements, post-hoc tests were performed in the Statistica. The significance level was determined as $p \leq 0.05$.

RESULTS: There was no correlation between study groups and SMRT($p=0.198$). According to the CHAPS scale, 52.9% (n=9) of the ADHD group, 53.3% (n=8) of the SLD group, 67.7% (n=10) of the ADHD+SLD group, and 6.7%(n=1) of the control group were at risk auditory performance(Table 2). In multiple regression analysis determining CHAPS risk status, WFIRS-P score increased risk by 141.1 (95%CI=3.240-6141.430) times.

The amplitude in the parietal region was found to be statistically higher than the frontal and central regions ($F(6,116)=3.798$, $p<0.01$). The amplitude values of ADHD, SLD, and comorbid patient groups were statistically lower than the control group ($p=0.046$, $p=0.037$, $p<0.001$). And the amplitude values of the comorbid patient group were statistically lower than the ADHD and SLD groups ($p=0.02$, $p=0.041$), $F(3,58)=10.626$, $p<0.001$. There was no significant difference between SLD and ADHD groups. There was a statistically difference between target and non-target stimulus amplitudes in the control, ADHD, and SLD groups, ($F(3,58)=5.249$, $p<0.01$), but no difference was found in the ADHD+SLD group ($p=0.064$)(Figure 2).

In the regression analysis of P300 parietal region amplitudes, only the presence of diagnosis has a statistical contribution($\beta=-3.072$; $p<0.001$).

DISCUSSION: Individuals diagnosed with SLD and/or ADHD are most frequently diagnosed with the complaint of academic failure in the first years of their formal education. In order to understand speech, as well as for learning, the auditory system must have a dynamic structure that moves fast in terms of spectral and temporal processing. Although SMRT is a reliable measure of spectral resolution ability, it also provides information about individuals' ability to understand speech[6]. A 2015 study investigated whether auditory processing underlies the phonological deficits of dyslexia. Speech and non-speech stimuli were given to 42 individuals. Individuals with dyslexia had

significantly lower temporal and spectral processing skills in both stimulus types than healthy individuals[7]. However, the spectral resolution has not been examined before in ADHD, SLD, and ADHD+SLD groups.

Although we used spectral and temporally modulated sound stimuli in our study, no difference in spectral resolution skills specific to ADHD and/or SLD was found. In previous studies, the spectral resolution was estimated using speech sounds. However, in our study, non-speech stimuli that are not specific to the Turkish language should be considered. Moreover, although previous studies have highlighted a general deficiency of auditory processing in SLD, our study indicates that there may be no difference in spectral processing in the SLD and/or ADHD group compared to healthy individuals. Auditory performance skills in the patient groups are lower than in the control group, and there is no difference in spectral resolution, which may be due to the difference in temporal processing from auditory processing skills. In addition, we suggest that patients with ADHD and/or SLD who have lower functional skills should be kept in mind may have low auditory processing skills even if their hearing tests are standard.

Oddball studies reveal the N200 and P300 components reflect stimulus discrimination and evaluation problems and that the P300 amplitude is the amount of attentional capacity allocated to a stimulus[8]. Since when the target stimulus arrives, the attentive performance of the tasks by the participants may cause an increase in P300 amplitude and a shortening in p300 latency compared to the non-target stimulus. In our study, the response amplitudes of the control, ADHD, and SLD groups to the target stimulus were higher than the non-target stimulus in all regions. However, this difference was not found for the comorbid patient group. This result may indicate that the comorbid patient group has difficulty processing the stimulus. In the regression analysis, the presence of a psychiatric diagnosis was the most important explainer of the p300 amplitude variance, affirming that the decrease in P300 amplitude in children with ADHD reflects the inability to perceive, learn, and remember stimuli[1].

In the ERP technique, the P300 amplitude has been generated by attention-based neural activity transmitting the signal to the temporal-parietal areas[8]. Although similar amplitude results were observed in the SLD and ADHD groups in the parietal region, the amplitudes of both groups were lower than the control group and higher than the ADHD+SLD group. This result also indicates that the P300 reflects a more general cognitive processing rather than attention skills and this processing capacity is lower in the comorbid patient group. It has been determined that those with ADHD+SLD have a more severe course than ADHD and SLD.

Our study group included an IQ score>70 but did not make any adjustments for IQ scores. There are comments that when IQ is used as a variable, it leads to over-corrected findings[9]. It was ensured that children with ADHD and ADHD+SLD used psychostimulants did not take medication for 48 hours before our evaluations to prevent the effects on the results. The effect of psychostimulants on spectral resolution and P300 may be the subject of future research.

As a result, in the presence of ADHD+SLD, functional impairment was highest, auditory performance was lowest, and parietal region amplitude values were lower than in other groups. This report indicates that more attention should be paid to ADHD+SLD group in follow-up and treatment.

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Keywords: Attention Deficit and Hyperactivity Disorder, P300, ERP, Spectral Resolution, SMRT, Specific Learning Disorder

REFERENCES

1. Hilger K, Sassenhagen J, Kühnhausen J, vd. Neurophysiological markers of ADHD symptoms in typically-developing children. Sci Rep. 2020;10(1):1–15. doi:10.1038/s41598-020-80562-0

2. Papagiannopoulou EA, Lagopoulos J. P300 event-related potentials in children with dyslexia. Ann Dyslexia. 2017;67(1):99–108. doi:10.1007/s11881-016-0122-6

3. Steinbrink C, Klatte M, Lachmann T. Phonological, temporal and spectral processing in vowel length

discrimination is impaired in German primary school children with developmental dyslexia. Res Dev Disabil. 2014;35(11):3034–3045. doi:10.1016/j.ridd.2014.07.049
4. Davies-Venn E, Nelson P, Souza P. Comparing auditory filter bandwidths, spectral ripple modulation detection, spectral ripple discrimination, and speech recognition: Normal and impaired hearing. J Acoust Soc Am. 2015;138(1):492–503. doi:10.1121/1.4922700
5. Baydan M, Aslan F, Yılmaz S. Children's Auditory Performance Scale: Turkish Validity and Reliability. Hacettepe Univ Fac Heal Sci J. 2020;7(1):32–40. doi:10.21020/husbfd.635851
6. Aronoff JM, Landsberger DM. The development of a modified spectral ripple test. J Acoust Soc Am. 2013;134(2):EL217–EL222. doi:10.1121/1.4813802
7. Christmann CA, Lachmann T, Steinbrink C. Evidence for a General Auditory Processing Deficit in Developmental Dyslexia From a Discrimination Paradigm Using Speech Versus Nonspeech Sounds Matched in Complexity. J Speech, Lang Hear Res. 2015;58(1):107–121. doi:10.1044/2014_JSLHR-L-14-0174
8. Johnstone SJ, Barry RJ, Clarke AR. Ten years on: A follow-up review of ERP research in attention-deficit/hyperactivity disorder. Clin Neurophysiol. 2013;124(4):644–657. doi:10.1016/j.clinph.2012.09.006
9. Dennis M, Francıs DJ, Cirino PT, Schachar R, Barnes MA, Fletcher JM. Why IQ is not a covariate in cognitive studies of neurodevelopmental disorders. J Int Neuropsychol Soc. 2009;15(3):331–343. doi:10.1017/S1355617709090481

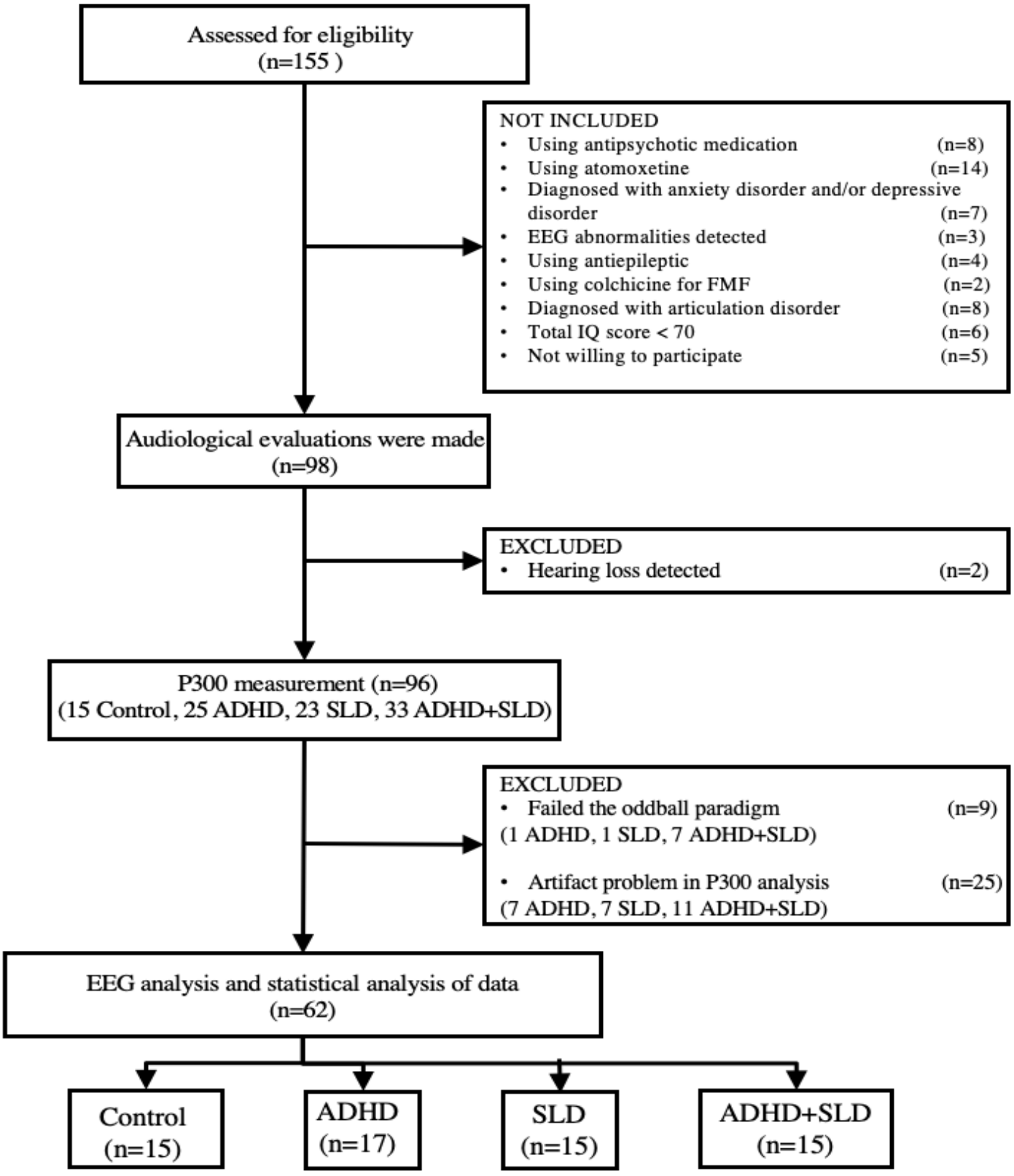

Figure 1. Flow chart

			Group								
			CONTROL		ADHD		SLD		ADHD+SLD		p
Gender	Boy	(N,%)	7	46.7	14	82.4	10	66.7	11	73.3	0.177
Age		(Median, IQR_{25-75})	10	(8 -11)	10	(9 -11)	10	(9 -11)	9	(8 -10)	0.279
Height (cm)		(Median, IQR_{25-75})	135	(130 -143)	138	(132 -147)	137	(131 -150)	132	(130 -142)	0.603
Weight (kg)		(Median, IQR_{25-75})	33	(29 -40)	34	(30 -40)	33	(29 -45)	34	(28 -39)	0.791
Hand preference	right	(N,%)	15	100.0	14	82.4	15	100.0	12	80.0	
	left	(N,%)	0	0.0	3	17.6	0	0.0	2	13.3	0.197
	both	(N,%)	0	0.0	0	0.0	0	0.0	1	6.7	
Mental illness in family	no	(N,%)	12	80.0	15	88.2	13	86.7	10	66.7	0.414
	yes	(N,%)	3	20.0	2	11.8	2	13.3	5	33.3	
Medical conditions in family	no	(N,%)	12	80.0	11	64.7	14	93.3	13	86.7	
	yes	(N,%)	3	20.0	6	35.3	1	6.7	2	13.3	0.198
Marital Status	Together	(N,%)	15	100.0	14	82.4	15	100.0	14	93.3	
	Separated	(N,%)	0	0.0	3	17.6	0	0.0	0	0.0	0.076
	Death	(N,%)	0	0.0	0	0.0	0	0.0	1	6.7	

Table 1. Descriptive statistics for socio-demographic and clinical characteristics

X^2 test

Kruskal Wallis Test

ADHD: Attention and Hyperactivity Disorder, SLD: Specific Learning Disorder

Table 2. Turgay, MOYA, WFIRS-P, CHAPS, and SMRT score comparisons between 4 group

		Control[1]	ADHD[2]	SLD[3]	ADHD+SLD[4]		
		Median (IQR_{25-75})	Median (IQR_{25-75})	Median (IQR_{25-75})	Median (IQR_{25-75})	p	Intergroup comparison
TURGAY ADHD score		6 (2 -14)	30 (25 -36)	10 (7 -17)	32 (23 -38)	**<0.001**	4=2>3=1
MOYA		64 (53 -91)	109 (98 -122)	129 (117 -156)	143 (128 -165)	**<0.001**	2>1, 3>1, 4>1, 4>2
WFIRS-P		0.1 (0.1 -0.2)	0.5 (0.3 -0.7)	0.3 (0.3 -0.6)	0,5 (0.4 -0.8)	**<0.001**	4=3=2>1
SMRT		7 (6.2 -7.6)	6.5 (4.9 -7.5)	6.5 (5.6 -7.3)	4 (2.2 -7.2)	0.198	NS
CHAPS		14 (-4 -23)	-19 (-29 -0)	-12 (-19 --4)	-16 (-33 --5)	**<0.001**	1>4, 1>2
Risk status at CHAPS	N(%)	1(6.7%)	9(52.9%)	8(53.3%)	10(66.7%)	**0.006**	

X^2 test

Kruskal Wallis Test

ADHD: Attention and Hyperactivity Disorder, SLD: Specific Learning Disorder, MOYA: Mathematics, Reading, Writing Scale, WFIRS-P: Weiss Impairment Functioning Scale Parent Form CHAPS: Children Auditory Performance Test, SMRT: Spectral -Temporally Modulated Ripple Test (SMRT) mean score

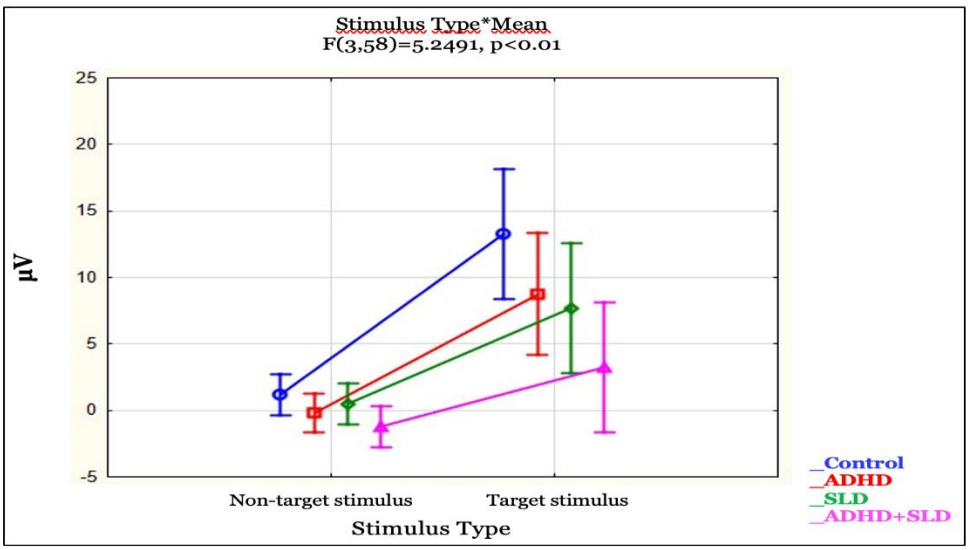

Figure 2. Group*stimulus type interaction in parietal region amplitudes

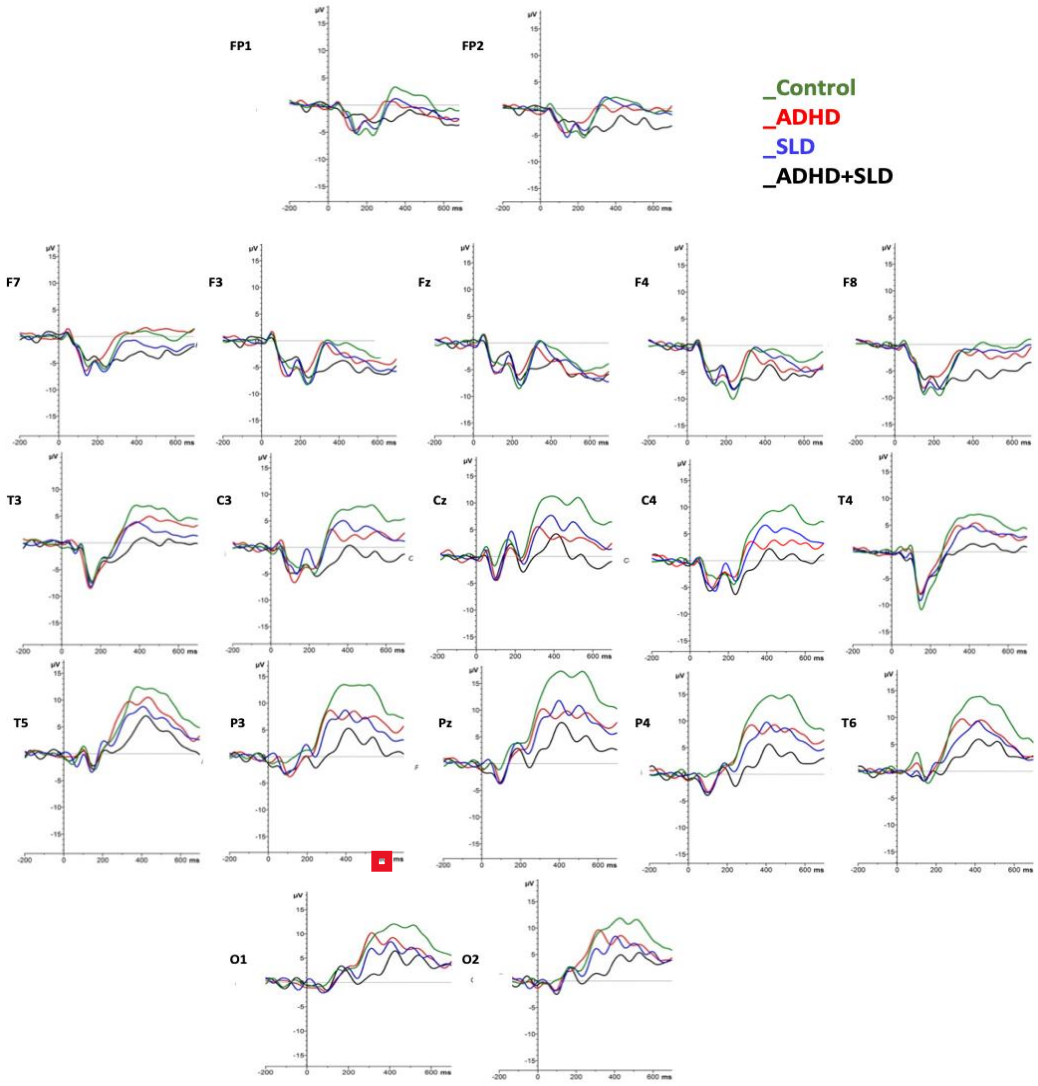

Figure 3. The effect of the target stimulus grand averages on the relevant channels according to the groups

[Abstract:0050] [Psychosomatic medicine- Liaison psychiatry]

0050 - The impact of anxiety and depressive symptoms on the quality of life of hemodialysis patients in a sample from somalia

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ABSTRACT

OBJECTIVE: The main objective of the present study was to determine the quality of life, depression, and anxiety levels in end-stage renal disease (ESRD) patients undergoing hemodialysis treatment and examine the impact of depression and anxiety on the quality of life of these patients in a sample from Somalia.

METHODS: A sample of 200 patients with ESRD who were undergoing hemodialysis treatment approximately two to three times a week were included. All participants were administered a Sociodemographic Data Form, Patient Health Questionnaire-9 (PHQ-9), Hospital Anxiety and Depression Scale (HADS), and World Health Organization Quality of Life (WHO-QOL-BREF). Subjects on hemodialysis for less than 3 months prior to the study date were excluded.

RESULTS: Of the ESRD patients, 200 patients, aged between 18-68 years (mean=52.29; SD=14.13) consented and participated in the study. 58.5% of the participants were men, 84% of them had a chronic kidney disease duration of 1-5 years, and 88.5% of them had a hemodialysis duration of 1-5 years. Overall quality of life dimension of the WHO-QOL-BREF was significantly correlated with PHQ-9 Total (r_s=-0.409, p<0.01), HADS-A (r_s=-0.314, p<0.01), and HADS-D scores (r_s=-0.432, p<0.01). Physical health dimension was significantly correlated with PHQ-9 Total (r_s=-0.647, p<0.01), HADS-A (r_s=-0.396, p<0.01), and HADS-D scores (r_s=-0.612, p<0.01). Psychological health dimension was significantly correlated with PHQ-9 Total (r_s=-0.566, p<0.01), HADS-A (r_s=-0.477, p<0.01), and HADS-D scores (r_s=-0.694, p<0.01). Social Relationships dimension was significantly correlated with PHQ-9 Total (r_s=-0.239, p<0.01), HADS-A (r_s=-0.242, p<0.01), and HADS-D scores (r_s=-0.291, p<0.01). Environment dimension was significantly correlated with HADS-A (r_s=-0.183, p<0.01) and HADS-D scores (r_s=-0.276, p<0.01). Hierarchical regression analyses revealed that family income (β=0.234, t=-3.829, p=0.000), PHQ-9 Total (β=-0.202, t=-2.403, p=0.017), and HADS-D scores (β=-0.278, t=-3.310, p=0.001) were significant predictors of overall QoL. Age (β=-0.228, t=-4.234, p=0.000), PHQ-9 scores (β=-0.377, t=-5.164, p=0.000), and HADS-D scores (β=-0.336, t=-4.616, p=0.000) were significant predictors of Physical Health dimension. Family income (β=0.152, t=3.054, p=0.003), HADS-A scores (β=-0.261, t=-4.073, p=0.000), and HADS-D scores (β=-0.509, t=-7.456, p=0.000) were significant predictors of Psychological well-being. Age (β=-0.311, t=-4.851, p=0.000), gender (β=0.211, t=3.333, p=0.001), family income (β=0.192, t=3.047, p=0.003), and HADS-D scores (β=-0.254, t=-2.924, p=0.004) were significant predictors of Social Relationships dimension. Family income (β=0.218, t=3.375, p=0.001) and HADS-D scores (β=-0.368, t=-4.131, p=0.000) were significant predictors of Environmental well-being.

CONCLUSIONS: This present study has highlighted the associated factors with poor QoL and impact of anxiety and depression on QoL. PHQ-9 Total and HADS-Depression scores were significant predictor of Overall QoL and Physical Health. HADS-Anxiety and HADS-Depression scores were significant predictors of Psychological well-being. Evaluation of anxiety and depression levels in conjunction with quality of life should be an integral part of the hemodialysis treatment.

Keywords: End-stage renal disease, hemodialysis, anxiety, depression, quality of life

INTRODUCTION: End-stage renal disease (ESRD) is a major public health problem due to associated adverse health consequences and associated mortality and morbidity due to chronic disease and need for frequent and intensive care that is burdensome for the patients. Average prevalence of CKD in Africa is 6.5%, ranging from 4.9% in Uganda to 17.6% in Mauritius. Although CKD prevalence in Somalia has been reported as 5.14 (95%CI 4.76-5.56), the exact number of treated ESRD patients who are undergoing hemodialysis treatment is unknown and understudied. Only 18 African countries have a center-based hemodialysis service that involves treatment of three times a week for 3-4 hours. In addition, home hemodialysis was not generally available in any countries in Africa, as opposed to 13% of countries worldwide. [International Society of Nephrology, Global Kidney Health Atlas 2019]. Despite developments in ESRD therapy, patients continue to have poor quality of life [Sathvik et al., 2008]. Anemia and neurological abnormalities are among the adverse health consequences of ESRD in addition to a worsening of physical functioning and a decline in mental health [O'Callaghan, 2009]. Hemodialysis patients have been reported to have a reduced quality of life as a result of factors such as decreased working ability, which results in financial dependence to others, inability to care for one's family, and lack of ability to involve in active social life. These elements may lead to psychiatric problems such as anxiety disorder, depression, and decrease in neurocognitive functioning [Sarnak et al., 2013]. Major depressive disorder was reported to be one of the most common psychiatric disorders in ESRD patients receiving hemodialysis [Teles et al., 2014]. According to a tertiary care institution study, hemodialysis patients in Nigeria had a prevalence of depression as 34.5% [Amira et al., 2011], compared to African American hemodialysis patients, who had a 27 percent [Weisbord et al., 2007]. Another study from Sudan reported depression rate as 72% in ESRD patients [Kaballo et al., 2010]. Low compliance with prescribed medications, inadequate diet, and marital issues were reported as risk factors for depression in ESRD patients [Kimmel and Peterson, 2008].

Psychological issues in ESRD patients have been understudied in Africa, and to the best of our knowledge, there is no data on this subject in Somalia. In this present study, we aimed to determine the quality of life, depression, and anxiety levels in end-stage renal disease (ESRD) patients undergoing hemodialysis treatment and examine the impact of depression and anxiety on the quality of life of these patients in a sample from Somalia.

METHODS: The study design was cross-sectional and was conducted at the hemodialysis unit of Mogadishu Somalia-Turkey Recep Tayyip Erdogan Research and Training Hospital in Mogadishu, Somalia. The participants were 200 (83 women, 117 men) patients who were undergoing hemodialysis treatment approximately two to three times a week. Hemodialysis patients for less than 3 months prior to the study date were not included in the study. The study protocol was approved by the Hospital's Ethics Review Board (MSTH/10161, Date: 05/09/2022). All participants were administered a sociodemographic data form, Patient Health Questionnaire-9 (PHQ-9), Hospital Anxiety and Depression Scale (HADS), and World Health Organization Quality of Life (WHO-QOL-BREF).

Patient Health Questionnaire-9 (PHQ-9). The PHQ-9 is a 9-items scale that measures the depressive thoughts and feelings in individuals over the previous two weeks. The PHQ-9 is a 4-point Likert scale with a range from 0 to 3. Zero for "not at all" responses and 3 for "nearly every day" responses. Scores range from 0 to 27.

Hospital Anxiety and Depression Scale (HADS). The HADS: It is a 14-items self-report screening scale with 7-items each for depression (HADS-D subscale) and anxiety (HADS-A subscale).

World Health Organization Quality of Life (WHOQOL-BREF). The WHOQOL-BREF is a shorter form of the WHOQOL-100 was administered. It assessed four domains of QoL; namely, physical, psychological, social, and environmental. Items on this measure were scored on a 5-point Likert scale. The scores range from 1 (low) to 5 (high) with increasing scores from 1 to 5 denoting higher QoL.

Statistical Analysis

All statistical analyses were performed by using SPSS (Armonk, NY: IBM Corp.) version 26.0. Categorical variables were analyzed and presented as frequencies and percentages. The continuous variables were presented as means and standard deviations. Preliminary analyses were conducted to ascertain the normality of the data. Since the data was non-normally distributed, Spearman's Rank Order Test was used for correlation analyses. Hierarchical regression

analyses were conducted to examine the association between the anxiety and depression level and quality of life parameters.

RESULTS: The average age of 200 participants in the study was 52.3 with a standard deviation of 14.13 and it ranged from 18 to 68. The sample consisted 83 women (41.5 %) and 117 men (58.5%) undergoing hemodialysis treatment. The majority of the participants in the study were married (n=139, 69.5%) and 6% were single (n=12), and the remaining participants (n=49, 24.5%) were either divorced or widowed. The majority of the participants in the study were illeterate (n=137, 68.5%), and 84% of the participants have a duration of CKD of 1-5 years, 88.5% had a duration of HD of 1-5 years. In 58.5% of participants, hypertension was reported as the cause of CKD and in 20% of the participants diabetes mellitus was reported as the cause of CKD.

The mean PHQ-9 Total scores was 6.01 (SD 3.39), the mean HADS-Anxiety total scores was 2.79 (SD 3.07), the mean HADS-Depresion Total scores was 6.07 (SD 3.19), the mean overall quality-general health was 70.44 (SD 16.40), the mean overall quality-general health was 70.44 (SD 16.40), the mean Physical Health was 49.83 (SD 17.17), the mean Psychological was 70.31 (SD 13.12), the mean Social Relationships was 29.95 (SD 16.66), and the mean Environmental domain was 66.00 (SD 11.45). In terms of PHQ-9 scale; 86.5% of the participants reported no symptoms of depression and 13.5% of the participants reported mild to moderate symptoms of depression. In terms of HADS-Anxiety scale; 92.5% of the participants reported no symptoms of anxiety and 7% of the participants reported mild to moderate symptoms of anxiety, and only 0.5% reported severe symptoms of anxiety. In terms of HADS-Depression scale; 62.5% of the participants reported no symptoms of depression and 37.5% of the participants reported mild to moderate symptoms of depression.

Age was significantly correlated with Physical Health, Psychological, Social Relationships, and Environment dimensions of WHOQOL-BREF (r_s=-0.257, p<0.01; r_s=-0.147, p<0.05; r_s=-0.332, p<0.01; r_s=-0.153, p<0.05, respectively). Gender was significantly correlated with Social Relationships of WHO-BREF (r_s=0.237, p<0.01). Overall QoL was negatively correlated with PHQ-9 Total (r_s=-0.409, p<0.01), HADS-Anxiety (r_s=-0.314, p<0.01), and HADS-Depression (r_s=-0.432, p<0.01). Physical Health dimension was negatively correlated with PHQ-9 Total (r_s=-0.647, p<0.01), HADS-Anxiety (r_s=-0.396, p<0.01), and HADS-Depression (r_s=-0.612, p<0.01). Psychological dimension was negatively correlated with PHQ-9 Total (r_s=-0.566, p<0.01), HADS-Anxiety (r_s=-0.477, p<0.01), and HADS-Depression (r_s=-0.694, p<0.01). Social Relationships dimension was negatively correlated with PHQ-9 Total (r_s=-0.239, p<0.01), HADS-Anxiety (r_s=-0.242, p<0.01), and HADS-Depression (r_s=-0.291, p<0.01). Environment dimension was negatively correlated with HADS-Anxiety (r_s=-0.183, p<0.01), and HADS-Depression (r_s=-0.276, p<0.01). PHQ-9 Total scores significantly correlated with HADS-Anxiety (r_s=0.516, p<0.01), and HADS-Depression (r_s=0.716, p<0.01). HADS-Anxiety scores significantly correlated with HADS-Depression (r_s=0. 606, p<0.01). Family Income significantly correlated with Overall QoL (r_s=0. 193, p<0.01). Duration of CKD significantly correlated with physical health (r_s=-0. 197, p<0.01), Psychological (r_s=-0. 205, p<0.01), PHQ-9 Total (r_s=0. 221, p<0.01), HADS-Anxiety (r_s=0.143, p<0.01), and HADS-Depression (r_s=0.250, p<0.01). Duration of Hemodialysis significantly correlated with Duration of CKD (r_s=0. 834, p<0.01), Physical Health (r_s=-0. 171, p<0.05), PHQ-9 Total (r_s=0. 168, p<0.05), and HADS-Depression (r_s=0.192, p<0.01).

Family income (β=0.234, t=3.829, p=0.000), PHQ-9 Total scores (β=-0.202, t=-2.403, p=0.017), and HADS-Depression scores (β=0.278, t=-3.310, p=0.001) were significant predictors of Overall QoL Age (β=-0.228, t=-4.234, p=0.000), PHQ-9 Total scores (β=-0.377, t=-5.164, p=0.000), and HADS-Depression scores (β=-0.336, t=-4.616, p=0.000) were significant predictors of Physical Health scores. Family income (β=0.152, t=3.054, p=0.003), HADS-Anxiety scores (β=-0.261, t=-4.073, p=0.000), and HADS-Depression scores (β=-0.509, t=-7.456, p=0.000) were significant predictors of Psychological well-being. Age (β=-0.311, t=-4.581, p=0.000), gender (β=0.211, t=3.333, p=0.001), family Income (β=0.192, t=3.047, p=0.003), and HADS-Depression scores (β=-0.254, t=-2.924, p=0.004) were significant predictors of Social Relationships scores. Family income (β=0.218, t=3.375, p=0.001) and HADS-Depression scores (β=-0.368, t=-4.131, p=0.000) were significant predictors of Environmental well-being.

DISCUSSION: In this present study; using HADS-Depression scale, more than one third (37.5%) of the participants reported mild to moderate symptoms of depression and by using PHQ-9 scale, 13.5% of the participants reported

mild to moderate symptoms of depression. The prevalence of depression in our study was relatively lower than in other studies, which have reported depression prevalence among ESRD patients ranging from 34.5% to 72% with different scales used across different African populations [Amira et al., 2011; Kaballo et al., 2010; Ganu et a., 2018]. Seven percent of the participants reported mild to moderate symptoms of anxiety. The prevalence of anxiety reported in our study was smaller than WHO reports (15%) for the general population and the National Co-morbidity Survey (18%) [Wang and Chen, 2012]. We believe these differences are due to cultural differences and/or psychological resilience affected by religiosity/ spirituality in Somali HD patients.

A negative and moderate correlation was found between the Overall QoL and PHQ-9 Total, HADS-Anxiety, and HADS-Depression levels. A negative and strong correlation was found between the Physical Health dimension and PHQ-9 Total, HADS-Anxiety, and HADS-Depression levels. A negative and strong correlation was found between the Psychological dimension and PHQ-9 Total, HADS-Anxiety, and HADS-Depression levels. A negative and weak correlation was identified between Social Relationships and PHQ-9 Total, HADS-Anxiety, and HADS-Depression. A negative and weak correlation was identified between Environment dimension and HADS-Anxiety and HADS-Depression. These findings strengthened the hypothesis that the QoL decreases as the presence of anxiety and depressive symptoms increases, negatively affecting different aspects of the patients' life. PHQ-9 Total scores strongly correlated with HADS-Depression. HADS-Anxiety scores strongly correlated with HADS-Depression scores. A negative and weak correlation was identified between Family Income and Overall QoL. Both duration of CKD and duration of Hemodialysis negatively and weakly correlated with Physical Health and Psychological dimensions, positively with PHQ-9 Total, HADS-Anxiety, and HADS-Depression. Duration of Hemodialysis positively correlated with Duration of CKD, negatively with Physical Health, positively with PHQ-9 Total, and positively with HADS-Depression. As the duration of CKD and Hemodialysis increase, presence of anxiety and depressive symptoms were increasing. These findings were consistent with previous reports [Ganu et al., 2018; Ottaviani et al., 2016].

Our study revealed that family income was a significant predictor of Overall QoL, Psychological, Social Relationships, and Environmental well-being. This was intuitive since most of our HD patients had no jobs or funds and they could only afford hemodialysis sessions provided that a significant portion of the payment was covered as pro bono by the hospital. PHQ-9 Total scores and HADS-Depression scores were significant predictor of Overall QoL and Physical Health. Having higher depression scores were associated with poorer QoL. Similarly, HADS-Anxiety and HADS-Depression scores were significant predictors of Psychological dimension scores. HADS-Depression scores were significant predictors of Social Relationships and Environmental well-being.

In conclusion, this present study has highlighted the associated factors with poor QoL and impact of anxiety and depression on QoL. Our study emphasizes the role and strength of the HADS as a secreening tool to identify, monitor, and follow-up anxiety and depression. A multidisciplinary team consisted of psychiatric nurses, psychologists, and psychiatrists should provide a more integrated and holistic treatment to hemodialysis patients.

REFERENCES

1. Bello AK, Levin A, Lunney M, Osman MA, et al. (2019). Global Kidney Health Atlas: A report by the International Society of Nephrology on the Global Burden of End-stage Kidney Disease and Capacity for Kidney Replacement Therapy and Conservative Care across World Countries and Regions. International Society of Nephrology, Brussels, Belgium.

2. Sathvik BS, Parthasarathi G, Narahari MG, Gurudev KC. An assessment of the quality of life in hemodialysis patients using the WHOQOL-BREF questionnaire. Indian J Nephrol. 2008 Oct;18(4):141-9.

3. O'Callaghan C. The renal system at a glance. John Wiley & Sons; 2016 Jul 28.

4. Sarnak MJ, Tighiouart H, Scott TM, Lou KV, Sorensen EP, Giang LM, Drew DA, Shaffi K, Strom JA, Singh AK, Weiner DE. Frequency of and risk factors for poor cognitive performance in hemodialysis patients. Neurology. 2013 Jan 29;80(5):471-80.

5. Teles F, Azevedo VF, Miranda CT, Miranda MP, Teixeira Mdo C, Elias RM. Depression in hemodialysis patients: the role of dialysis shift. Clinics (Sao Paulo). 2014 Mar;69(3):198-202.
6. Amira O. Prevalence of symptoms of depression among patients with chronic kidney disease. Niger J Clin Pract. 2011 Oct-Dec;14(4):460-3.
7. Weisbord SD, Fried LF, Unruh ML, Kimmel PL, Switzer GE, Fine MJ, Arnold RM. Associations of race with depression and symptoms in patients on maintenance haemodialysis. Nephrol Dial Transplant. 2007 Jan;22(1):203-
8. Kaballo BG, Idris M, Alhaj HI, Gadour MO. Psychological disorders and quality of life among Sudanese dialysis patients and renal transplant recipients. Sudan Journal of Medical Sciences. 2010;5(1).
9. Kimmel PL, Peterson RA. Depression in end-stage renal disease patients treated with hemodialysis: tools, correlates, outcomes, and needs. Semin Dial. 2005 Mar-Apr;18(2):91-7.
10. Wang LJ, Chen CK. The psychological impact of hemodialysis on patients with chronic renal failure. Renal Failure-the Facts. 2012 May 23;13:220.
11. Ottaviani AC, Betoni LC, Pavarini SC, Gramani Say K, Zazzetta MS, Orlandi FD. Association between anxiety and depression and quality of life of chronic renal patients on hemodialysis. Texto & Contexto-Enfermagem. 2016 Aug 18; 25(3):e00650015.

Table 1. Correlations between Quality of Life dimensions and demographics and scales

	1	2	3	4	5	6	7	8	9	10	11
Overall WHOQOL-BREF	1										
Physical Health	0.371**	1									
Psychological	0.490**	0.588**	1								
Social Relationships	0.239**	0.464**	0.311**	1							
Environment	0.339**	0.224**	0.506**	0.209**	1						
PHQ-9 Total	-0.409**	-0.647**	-0.566**	-0.339**	-0.131	1					
HADS-Anxiety	-0.314**	-0.396**	-0.477**	-0.242**	-0.183**	0.516**	1				
HADS-Depression	-0.432**	-0.612**	-0.694**	-0.291**	-0.276**	0.716**	0.606**	1			
Family Income	0.193**	0.001	0.065	0.100	0.160*	0.099	0.071	0.085	1		
Duration of CKD	-0.038	-0.197**	-0.205**	-0.123	-0.060	0.221**	0.143*	0.250**	-0.027	1	
Duration of HD	0.030	-0.171*	-0.137	-0.122	-0.014	0.168*	0.099	0.192**	-0.53	0.834**	1

Note. *p<0.05; **p<0.01
WHOQOL-BREF: World Health Organization Quality of Life
PHQ9: Patient Health Questionnaire Version 9
HADS-Anxiety: Hospital Anxiety and Depression Scale - Anxiety Dimension
HADS-Depression : Hospital Anxiety and Depression Scale - Depression Dimension
CKD: Chronic Kidney Disease
HD: Hemodialysis

Table 2. The hierarchical regression analyses

Model	Independent variable	B	t	p	F	df	R^2	Model p
1	Family Income	0.234	3.829	0.000	22.924	3, 191	0.306	<0.001
	PHQ-9 Total score	-0.202	-2.403	0.017				
	HADS-Depression	-0.278	-3.310	0.001				
2	Age	-0.228	-4.234	0.000	44.862	3, 191	0.480	<0.000
	PHQ-9 Total score	-0.377	-5.164	0.000				
	HADS-Depression	-0.336	-4.616	0.000				
3	Family Income	0.152	3.054	0.003	64.896	3, 191	0.542	<0.000
	HADS-Anxiety	-0.261	-4.073	0.000				
	HADS-Depression	-0.509	-7.456	0.000				
4	Age	-0.311	-4.851	0.000	5.745	3, 191	0.259	<0.001
	Gender	0.211	3.333	0.001				
	Family Income	0.192	3.047	0.003				
	HADS-Depression	-0.254	-2.924	0.004				
5	Age	-0.161	-2.441	0.016	10.906	3, 191	0.188	<0.000
	Family Income	0.218	3.375	0.001				
	HADS-Depression	-0.368	-4.131	0.000				

Model 1: Dependent variable Overall QOL Score
Model 2: Dependent variable Physical Health Score
Model 3: Dependent variable Psychological Score
Model 4: Dependent variable Social Relationships Score
Model 5: Dependent variable Environment Score
PHQ9: Patient Health Questionnaire Version 9
HADS-Anxiety: Hospital Anxiety and Depression Scale - Anxiety Dimension
HADS-Depression: Hospital Anxiety and Depression Scale - Depression Dimension

[Abstract:0051] [Psychosomatic medicine- Liaison psychiatry]

0051 - The perceived social support and quality of sleep of hemodialysis patients in a sample from somalia

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ABSTRACT
OBJECTIVE: Perceived social support and sleep quality are important determining factors in the quality of life of end-stage renal disease (ESRD) patients undergoing hemodialysis treatment. The main objective of the present study is to examine the relationship between perceived social support and quality of sleep and determine the predictors of sleep quality in hemodialysis patients in a sample from Somalia.
METHODS: A sample of 200 patients with ESRD who were undergoing hemodialysis treatment approximately two to three times a week were included. All participants were administered a Sociodemographic Data Form, the

Multidimensional Scale of Perceived Social Support (MSPSS), the Insomnia Severity Index (ISI), and Pittsburgh Sleep Quality Index (PSQI). Patients on hemodialysis for less than 3 months prior to the study date were excluded.
RESULTS: Of the ESRD patients, 200 patients, aged between 18-68 years (mean=52.29; SD=14.13) consented and participated in the study. Sixty-three subjects (31.5%) reported poor sleep quality defined as a Total PSQI score > 5. Fifty-nine subjects (29.5%) reported clinically significant insomnia defined as a Total ISI score > 7. ISI Total was significantly correlated with MSPSS Friends (rs=-0.195, p<0.01), MSPSS Total (rs=-0.159, p<0.05). PSQI Total negatively correlated with MSPSS Friends (rs=-0.294, p<0.01), and MSPSS Total (rs=-0.222, p<0.01). Hierarchical regression analyses revealed that MSPSS Friends (β=-0.261, t=-3.545, p=0.000), MSPSS Total scores (β=-0.167, t=-2.253, p=0.025) were significant predictors of ISI Total. MSPSS Family (β=0.142, t=2.007, p=0.046), MSPSS Friends (β=-0.286, t=-3.926, p=0.000), and MSPSS Total scores (β=-0.183, t=-2.487, p=0.014) were significant predictors of PSQI Total. MSPSS Family was significant predictor of Subjective Sleep Quality (β=0.142, t=1.988, p=0.046). MSPSS Friends was significant predictor of Sleep Latency (β=-0.227, t=-3.082, p=0.002). Family Income (β=0.149, t=2.107, p=0.036), MSPSS Family (β=0.156, t=2.248, p=0.026), MSPSS Friends (β=-0.250, t=-3.492, p=0.001), and MSPSS Total scores (β=-0.171, t=-2.364, p=0.019) were significant predictors of Sleep Duration. Duration of CKD (β=0.396, t=3.162, p=0.002), Duration of HD (β=-0.306, t=-2.441, p=0.016), and MSPSS Friends (β=-0.167, t=-2.256, p=0.025) were significant predictors of Sleep Disturbance. MSPSS Friends (β=-0.277, t=-3.748, p=0.000) and MSPSS Total (β=-0.195, t=-2.626, p=0.009) were significant predictors of Daytime Dysfunction.
CONCLUSIONS: this present study has highlighted the associated factors with poor sleep and impact of perceived social support on quality of sleep. Overall, our results show the value of family as a principal support system in Somali culture. Understanding the relationship between social support and sleep quality in hemodialysis patients will provide guidance to the healthcare providers, social services, and family members about the significance of social support and should be an integral part of the hemodialysis treatment.

Keywords: End-stage renal disease, hemodialysis, social support, quality of sleep

INTRODUCTION: Several studies have shown that sleep was disturbed in ESRD patients undergoing hemodialysis treatment [Novak et al., 2006; Koch et al., 2009, Shayamsunder et al., 2005]. Underlying causes of sleep disturbances was reported to be multifactorial including electrolyte imbalances, uremia, eythropoetin deficiency-related anemia, circadian rhytm disturbances due to melatonin release etc. [Novak et al., 2006; Koch et al., 2009, Shayamsunder et al., 2005]. Hemodialysis patients can also have a reduced quality of life as a result of sleep disturbances, which results in daily functioning, inability to care for one's family due to daytime sleepiness, and lack of ability to be actively involved in social life.

Social support refers to the intricate network in which an individual might receive and provide help and have emotional needs met [Cohen et al., 2007]. Social support is the individual's relationships with others creating a sense of physical and psychological well-being and has been shown to have a profound impact on the daily life of the hemodialysis patients [Cohen et al., 2007; Kim et al., 2018]. Social support is often provided by family members, friends and significant others and supposedly constitute cognitive, emotional, and materials support to the individual [Cohen et al., 2007]. Although the need for examining the social support has been emphasized in hemodialysis patients, to the best of our knowledge, no studies have examined this relationship and predictive capacity of social support on quality of sleep as a measure of quality of life. This is also the first study in Africa to examine this crucial relationship.

In this present study, we aimed to examine the relationship between perceived social support and quality of sleep and determine the predictors of sleep quality in hemodialysis patients in a sample from Somalia.

METHODS: The study design was cross-sectional and was conducted at the hemodialysis unit of Mogadishu Somalia-Turkey Recep Tayyip Erdogan Research and Training Hospital in Mogadishu, Somalia. The participants were 200 (83 women, 117 men) patients who were undergoing hemodialysis treatment approximately two to three times a week. Hemodialysis patients for less than 3 months prior to the study date were not included in the study.

The study protocol was approved by the Hospital's Ethics Review Board (MSTH/10515, Date: 05/30/2022). All participants were administered a sociodemographic data form, Pittsburgh Sleep Quality Index (PSQI), Insomnia Severity Index (ISI), and Multidimensional Scale of Perceived Social Support (MSPSS).

The Pittsburgh Sleep Quality Index (PSQI). The PSQI is self-administered questionnaire that assesses quality of sleep during the previous month and contains 19 self-rated questions and 5 questions rated by a bed partner or roommate yielding seven components: subjective sleep quality, sleep latency, sleep duration, sleep efficiency, sleep disturbance, use of sleep medications and daytime dysfunction. Each component is scored from 0 to 3, yielding a global PSQI score between 0 and 21, with higher scores indicating lower quality of sleep.

The Insomnia Severity Index (ISI). The ISI is a 7-item self-reported questionnaire about a person's sleep experiences over the past 2 weeks. The dimensions evaluated are the severity of sleep onset, sleep maintenance, early morning awakening problems, sleep dissatisfaction, interference of sleep difficulties with daytime functioning, noticeability of sleep problems by others, and distress caused by sleep difficulties.

The Multidimensional Scale of Perceived Social Support (MSPSS). The MSPSS is a 12-item measure that assesses three dimensions of social support: support from significant others, family, and friends. The questions of each dimension expressing "support" are rated on a 7-point Likert scale from 1 = very strongly disagree to 7 = very strongly agree. Higher scores indicate greater perceived social support.

Statistical Analysis

All statistical analyses were performed by using SPSS (Armonk, NY: IBM Corp.) version 26.0. Categorical variables were analyzed and presented as frequencies and percentages. The continuous variables were presented as means and standard deviations. Preliminary analyses were conducted to ascertain the normality of the data. Depending on distribution of the data parametric and non-parametric tests were performed. Since the data was non-normally distributed, Spearman's Rank Order Test was used for correlation analyses. Hierarchical regression analyses were conducted to examine the association between perceived social support and quality of sleep parameters. A p-value less than 0.05 was considered statistically significant.

RESULTS: The average age of 200 participants in the study was 52.3 with a standard deviation of 14.13 and it ranged from 18 to 68. The sample consisted of women (41.5 %) and 117 men (58.5%) hemodialysis patients. Sixty-three subjects (31.5%) reported poor sleep quality defined as a Total PSQI score > 5. Fifty-nine subjects (29.5%) reported clinically significant insomnia defined as a Total ISI score > 7. The mean PSQI total scores was 4.39 (SD 4.73), the mean ISI total scores was 5.81 (SD 7.65), the mean MSPSS Family scores was 6.55 (SD 0.81), the mean MSPSS Friends was 2.72 (SD 1.87), the mean MSPSS Significant Others was 1.09 (SD 0.55), the mean MSPSS Total was 3.45 (SD 0.76).

ISI Total was significantly correlated with MSPSS Friends (r_s=-0.195, p<0.01), MSPSS Total (r_s=-0.159, p<0.05), and PSQI Total (r_s=0.083, p<0.05). PSQI Total negatively correlated with MSPSS Friends (r_s=-0.294, p<0.01), and MSPSS Total (r_s=-0.222, p<0.01). MSPSS Total significantly correlated with MSPSS Family (r_s=0.481, p<0.01), MSPSS Friends (r_s=0.892, p<0.01), and Family Income (r_s=0.212, p<0.01). MSPSS Family significantly correlated with MSPSS Friends (r_s=0.145, p<0.05), Family Income (r_s=0.231, p<0.01), and Duration of CKD (r_s=-0.140, p<0.01). MSPSS Friends significantly correlated with Age (r_s=0.177, p<0.05), and Family Income (r_s=0.177, p<0.05). MSPSS Significant Others significantly correlated with MSPSS Family (r_s=-0.132, p<0.63).

In hierarchical regression analyses; MSPSS Friends was significant predictor of ISI Total (β=-0.261, t=-3.545, p=0.000). MSPSS Total scores was significant predictor of ISI Total (β=-0.167, t=-2.253, p=0.025). 11.5% of variability in PSQI Total scores and 8.5% increase in predictive capacity was accounted for inclusion of MSPSS Significant Others, MSPSS Family, and MSPSS Friends subscores [F(3, 191)=6.110, p=0.001]. MSPSS Family was significant predictor of PSQI Total (β=0.142, t=2.007, p=0.046). MSPSS Friends was significant predictor of PSQI Total (β=-0.286, t=-3.926, p=0.000). MSPSS Total scores was significant predictor of PSQI Total (β=-0.183, t=-2.487, p=0.014). MSPSS Family was significant predictor of Subjective Sleep Quality (β=0.142, t=1.988, p=0.048). MSPSS Friends was significant predictor of Subjective Sleep Quality (β=-0.294, t=-3.999, p=0.000). MSPSS Total scores was significant predictor of Subjective Sleep Quality (β=-0.174, t=-2.335, p=0.021). MSPSS Friends was

significant predictor of Sleep Latency (β=-0.227, t=-3.082, p=0.002). Family Income was significant predictor of Sleep Duration (β=0.149, t=2.107, p=0.036). MSPSS Family was significant predictor of Sleep Duration (β=0.156, t=2.248, p=0.026). MSPSS Friends was significant predictor of Sleep Duration (β=-0.250, t=-3.492, p=0.001). MSPSS Total scores was significant predictor of Sleep Duration (β=-0.171, t=-2.364, p=0.019). Age was significant predictor of Sleep Efficiency (β=0.144, t=2.000, p=0.047). Gender was significant predictor of Sleep Efficiency (β=-0.173, t=-2.453, p=0.015). Duration of CKD was significant predictor of Sleep Disturbance (β=0.396, t=3.162, p=0.002). Duration of HD was significant predictor of Sleep Disturbance (β=-0.306, t=-2.441, p=0.016). MSPSS Friends was significant predictor of Sleep Disturbance (β=-0.167, t=-2.256, p=0.025). MSPSS Friends was significant predictor of Daytime Dysfunction (β=-0.277, t=-3.748, p=0.000). MSPSS Total was significant predictor of Daytime Dysfunction (β=-0.195, t=-2.626, p=0.009).

DISCUSSION: This study examined the relationship between social support and quality of sleep in a sample of Somali hemodialysis patients. Thirty-two percent of our HD patients were poor sleepers, which was remarkably lower than previous reports [Tel et al., 2007; Novak et al., 2006; Pai et al., 2007]. Thirty percent of patients reported clinically significant insomnia defined as a Total ISI score > 7. Thse results were counter-intuitive due to the fact that our hemodialysis unit has a nocturnal HD shift beginning at 10 PM up to 2 AM in the morning. While mean MSPSS Friends, MSPSS Significant Others, MSPSS Total scores were lower than the original scale American sample, MSPSS Family scores were higher than the original scale sample. Majority of the patients reported high Family support, low Friends and Significant Others support. There are no established population norms on the MSPSS. Norms would likely vary on the basis of culture and nationality, as well as age and gender. Overall, our results show the value of family as a principal support system in Somali culture.

A negative and weak correlation was found between the ISI Total and MSPSS Friends and MSPSS Total scores. A negative and weak correlation was found between the PSQI Total and MSPSS Friends and MSPSS Total scores. A positive and weak correlation was found between the MSPSS Total and Family Income. A positive and weak correlation was found between the MSPSS Family and Family Income. A negative and weak correlation was found between the MSPSS Family and Duration of CKD. As the duration of CKD increase, family support levels were decreasing. A positive and weak correlation was found between the MSPSS Friends and Family Income. A negative and weak correlation was found between the MSPSS Friends and age. As the patients' ages were increasing, friend support levels were decreasing. These findings were all intuitive and consistent with a previous study by Cohen et al. primarily in African-American hemodialysis patients [Cohen et al., 2007].

MSPSS Friends and MSPSS Total scores were significant predictors of ISI Total scores. MSPSS Family, MSPSS Friends, and MSPSS Total scores were significant predictors of PSQI Total scores. MSPSS Family, MSPSS Friends, and MSPSS Total scores were significant predictors of Subjective Sleep Quality. MSPSS Friends was significant predictor of Sleep Latency. Family Income, MSPSS Family, MSPSS Friends, and MSPSS Total scores were significant predictors of Sleep Duration. Age and Gender were significant predictors of Sleep Efficiency. Duration of CKD, Duration of HD, and MSPSS Friends were significant predictors of Sleep Disturbance. MSPSS Friends and MSPSS Total were significant predictors of Daytime Dysfunction. Our study revealed that MSPSS Total and MSPSS Friends scores were significant predictors of overall sleep quality. Duration of HD was significant predictor of Sleep Disturbance. These results were intuitive since most of our HD patients had no jobs or funds and they could only afford hemodialysis sessions using family as a principal financial resource.

In conclusion, this present study has highlighted the associated factors with poor sleep and impact of perceived social support on quality of sleep. This present study contributed to the limited research knowledge that examined the relationship between social support and quality of sleep of hemodialysis patients. Hemodialysis patients might benefit from receiving formal and informal social support such as support from family and friends. Healthcare professionals working in hemodialysis units should continuously assess patients' quality of sleep and monitor the level of social support to improve their treatment adherence. Healthcare policymakers should consider social support as a high priority area of work and research to enhance the management of hemodialysis patients.

REFERENCES

1. Anutrakulchai S, Mairiang P, Pongskul C, Thepsuthammarat K, Chan-On C, Thinkhamrop B. Mortality and treatment costs of hospitalized chronic kidney disease patients between the three major health insurance schemes in Thailand. BMC Health Serv Res. 2016 Sep 29;16(1):528.
2. Makusidi MA, Liman HM, Yakubu A, Isah MD, Abdullahi S, Chijioke A. Hemodialysis performance and outcomes among end stage renal disease patients from Sokoto, North-Western Nigeria. Indian J Nephrol. 2014 Mar;24(2):82-5.
3. Bello AK, Levin A, Lunney M, Osman MA, et al. (2019). Global Kidney Health Atlas: A report by the International Society of Nephrology on the Global Burden of End-stage Kidney Disease and Capacity for Kidney Replacement Therapy and Conservative Care across World Countries and Regions. International Society of Nephrology, Brussels, Belgium.
4. Sathvik BS, Parthasarathi G, Narahari MG, Gurudev KC. An assessment of the quality of life in hemodialysis patients using the WHOQOL-BREF questionnaire. Indian J Nephrol. 2008 Oct;18(4):141-9.
5. O'Callaghan C. The renal system at a glance. John Wiley & Sons; 2016 Jul 28.
6. Novak M, Shapiro CM, Mendelssohn D, Mucsi I. Diagnosis and management of insomnia in dialysis patients. Semin Dial. 2006 Jan-Feb;19(1):25-31.
7. Koch BC, Nagtegaal JE, Kerkhof GA, ter Wee PM. Circadian sleep-wake rhythm disturbances in end-stage renal disease. Nat Rev Nephrol. 2009 Jul;5(7):407-16.
8. Shayamsunder AK, Patel SS, Jain V, Peterson RA, Kimmel PL. Sleepiness, sleeplessness, and pain in end-stage renal disease: distressing symptoms for patients. Semin Dial. 2005 Mar-Apr;18(2):109-18.
9. Kim K, Kang GW, Woo J. The Quality of Life of Hemodialysis Patients Is Affected Not Only by Medical but also Psychosocial Factors: a Canonical Correlation Study. J Korean Med Sci. 2018 Apr 2;33(14):e111.
10. Tel H, Tel H, Esmek M. Quality of sleep in hemodialysis patients. Dialysis and Transplantation. 2007 Sep;36(9):479-84.
11. Pai MF, Hsu SP, Yang SY, Ho TI, Lai CF, Peng YS. Sleep disturbance in chronic hemodialysis patients: the impact of depression and anemia. Ren Fail. 2007;29(6):673-7.

Table 1. Correlations between percieved social support measures and demographics and scales

ISI Total	1					
PSQI Total	-0.803**	1				
MSPSS Total	-0.159*	-0.222**	1			
MSPSS Family	0.091	0.088	0.481**	1		
MSPSS Friends	-0.195**	-0.294**	0.892**	0.145*	1	
MSPSS Significant Others	-0.035	-0.007	0.060	-0.132	0.044	1
Age	0.088	0.127	-0.126	0.057	-0.167*	-0.124
Duration of CKD	0.115	0.136	-0.126	-0.140*	-0.102	0.028
Family Income	0.094	0.011	0.212**	0.231**	0.177*	-0.086

Note. *p<0.05; **p<0.01
ISI: Insomnia Severity Index
PSQI: Pittsburgh Sleep Quality Index
MSPSS: Multidimensional Scale of Perceived Social Support
CKD: Chronic Kidney Disease

Table 2a. The hierarchical regression analyses

Model	Independent variables	B	t	p	F	df	R^2	Model p
1	MSPSS Friends	-0.261	-3.545	0.000	5.018	3, 191	0.097	0.002
	MSPSS Total score	-0.167	-2.253	0.025				
2	MSPSS Family	0.142	2.007	0.046	6.110	3, 191	0.115	0.001
	MSPSS Friends	-0.286	-3.926	0.000				
	MSPSS Total score	-0.183	-2.487	0.014				

Model 1: Dependent variable ISI Total Score
Model 2: Dependent variable PSQI Total Score
MSPSS: Multidimensional Scale of Perceived Social Support

Table 2b. The hierarchical regression analyses of the PSQI dimensions

Model	Independent variables	B	t	p	F	df	R^2	Model p
1	MSPSS Family	0.142	1.988	0.048	6.302	3, 191	0.097	0.000
	MSPSS Friends	-0.294	-3.999	0.000				
	MSPSS Total score	-0.174	-2.335	0.021				
2	MSPSS Friends	-0.227	-3.082	0.002	3.640	3, 191	0.094	0.014
3	Family Income	0.149	2.107	0.036	5.755	3, 191	0.142	0.001
	MSPSS Family	0.156	2.248	0.026				
	MSPSS Friends	-0.250	-3.492	0.001				
	MSPSS Total score	-0.171	-2.364	0.019				
4	Age	0.144	2.000	0.047	1.780	3, 191	0.093	0.152
	Gender	-0.173	-2.453	0.015				
5	Duration of CKD	0.396	3.162	0.002	1.769	3, 191	0.086	0.154
	Duration of HD	-0.306	-2.441	0.016				
	MSPSS Friends	-0.167	-2.256	0.025				
6	MSPSS Friends	-0.277	-3.748	0.000	5.108	3, 191	0.087	0.002
	MSPSS Total score	-0.195	-2.626	0.009				

Model 1: Dependent variable Subjective Sleep Quality
Model 2: Dependent variable Sleep Latency
Model 3: Dependent variable Sleep Duration
Model 4: Dependent variable Sleep Effciency
Model 5: Dependent variable Sleep Disturbance
Model 6: Dependent variable Daytime Dysfunction
PSQI: Pittsburgh Sleep Quality Index
MSPSS: Multidimensional Scale of Perceived Social Support
CKD: Chronic Kidney Disease
HD: Hemodialysis

[Abstract:0061] [Addiction Psychiatry]

0061 - The relationship between somatization, emotional dysregulation and social media addiction in an adolescent outpatient sample

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Introduction: Rapid improvements in internet and smartphone technologies have been accompanied by substantial growth in the use of internet-based applications and platforms (Cheng & Li, 2014; Kuss & Griffiths, 2012; , Karila, & Billieus, 2014) . Consequently, potential health problems and risks resulting from overuse and dependency on using such technologies have been observed and defined. Social media addiction has been found to be associated with a host of emotional, relational, health, and performance problemsEcheburua & de Corral, 2010 Kuss & Griffiths, 2011 Marino, FinosnVieno, Lenzi, & Spada,2017 Therefore, we aimed to examine the relationship between social media addiction, psychological symptoms and emotional dysregulation in adolescents.

Methods: A total of twenty-eight adolescents (19 girls and nine boys, mean age: 14.54 years) admitted to the child and psychiatry clinic were included in the study. Their social media addiction, emotional regulation and psychopathology were evaluated

Social Media Addiction Scale Short Form For Adolescents: It was adapted into Turkish by Özgenel in 2019, between the ages of 11-18. The draft scale form is scored as a 5-point Likert-type scale (1-Never, 2-Rarely, 3-Sometimes, 4-Very Often, 5-Always). The scale has no reverse-scored items. Due to the scale consisting of nine items, a participant can get a minimum of 9 points and a maximum of 45 points

Brief Version of the Difficulties in Emotion Regulation Scale: *:* It was developed by developed by Gratz & Roemer, in 2004. The adaptation of the scale used to Turkish was prepared by Rugancı and gençöz (2010). The DERS covers six subscales, namely, lack of emotional awareness, lack of emotional clarity, non-acceptance of negative emotions, lack of strategy building, lack of control on impulsive behaviors, and inability to behave in accordance with goal sunder negative emotions

The DERS-16, and the Brief Symptom Inventory: The scale is a 16-item self-report measure, developed by Bjureberg et al. (2016) as a brief form of DERS (Gratz and Roemer 2004). The adaptation of the scale used to Turkish was prepared by Yiğit(2017) DERS-16 is used to evaluate various aspects of emotion regulation difficulties. It comprises five subscales, namely Clarity, Goals, Impulse, Strategies and Non-acceptance. As with DERS, the items in DERS-16 are rated on a 5-point Likert scale ranging from 1 (almost never) to 5 (almost always). Higher scores indicate greater emotion dysregulation

We used the Shapiro-Wilk test to analyze whether data were normally distributed. Descriptive statistics were presented as mean ± standard deviation or median (min-max) according to the normal distribution. Count and percentages were used to describe categorical variables; Continuous clinical variables were analyzed using Independent t-tests or the Mann-Whitney U test according to their distribution characteristics in group comparisons. Data analysis was performed using Statistical Package for the Social Sciences (SPSS) version 23.0 (IBM SPSS Statistics; New York, USA), and all statistical tests were two-tailed with the significance level set at $\alpha = .05$.

Results: Somatization symptom severity and social media addiction scores were positively correlated ($p=0.04$, $r=0.38$). As somatization scores increase, social media addiction scores increase too. However, no correlation was found between depression, anxiety, hostility, negative self, total brief symptom inventory scores and social media addiction scores ($p>0.05$). Somatization scores were positively correlated with DERS-16 scores ($p=0.001$, $r=0.60$). As emotional dysregulation increases, somatization symptom scores increase. In addition, depression ($p<0.001$, $r=0.77$), anxiety ($p<0.001$, $r=0.82$), hostility ($p<0.001$, $r=0.78$), negative self ($p<0.001$, $r=0.79$) and brief symptom inventory total scores ($p<0.001$, $r=0.82$) and DERS-16 scores were positively and strongly correlated. However, no correlation was found between DERS-16 scores and social media addiction scores ($p>0.05$).

Discussion: Our findings show a relation between social media addiction and somatization symptoms. The relationship between emotional dysregulation and somatization symptoms is also striking. However, there is no direct link between emotional dysregulation and social media addictionThe limitation of the study is the relatively small sample size. The data is collected from a single clinic is a limitation in generalizing the results. The technology using patterns in the psychiatric sample should also be compared with the community sample.

Keywords: social media, somatization, addiction, emotional dysregulation

REFERENCES

1-Hua Chen, Amir H. Pakpour, Hildie Leung, Marc N. Potenza, Jian-An Su, Chung-Ying Lin. Comparing generalized and specific problematic smartphone/internet use: Longitudinal relationships between smartphone application-based addiction and social media addiction and psychological distress

2- Betul Keles, Niall McCrae & Annmarie Grealish (2020) A systematic review: the influence of social media on depression, anxiety and psychological distress in adolescents, International Journal of Adolescence and Youth, 25:1

3-Cecilia Cheng, PhD and Angel Yee-lam Li, BA Internet Addiction Prevalence and Quality of (Real) Life: A Meta-Analysis of 31 Nations Across Seven World Regions Cyberpsychol Behav Soc Netw. 2014 Dec 1; 17(12): 755–760.

4-Karila, & Billieus, 2014 Comparing generalized and specific problematic smartphone/internet use: Longitudinal relationships between smartphone application-based addiction and social media addiction and psychological distress June 2020 Journal of Behavioral Addictions 9(

[Abstract:0067] [Schizophrenia and other psychotic disorders]

0067 - Neutrophil-to-Lymphocyte (NLR) Ratio in Psychosis

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INTRODUCTION: Schizophrenia is a chronic debilitating mental illness characterized by positive, negative, and cognitive symptoms. Although a growing number of evidences have been documented to better understand the pathophysiology of schizophrenia, current hypotheses are mostly dependent upon the neurotransmission of serotonin, dopamine, and glutamate which lack a comprehensive explanation. The pathophysiological mechanism is still not clearly established yet. Dysregulation in the immune system seems to be an alternative hypothesis in schizophrenia. According to data, proinflammatory cytokines are increased in both acute and chronic phases of the illness[1][2]. The inflammatory process might play an important role in the development of schizophrenia[3].

The neutrophil-to-lymphocyte ratio (NLR) is known to be a systemic inflammation marker correlated with increased levels of proinflammatory cytokines, NLR is also considered a measurable and easily accessible biomarker of the balance between the innate and adaptive immune system. An elevated level of NLR level is defined as an indicator of systemic inflammation, and it is stated that it can be used as an effective tool in navigating patient treatment. It would be more practical to look at NLR values for both affective and nonaffective psychosis. In addition to that, first episode psychosis is a great opportunity to differentiate between the acute and chronic effects of illness on the immune system. It was shown that patients with schizophrenia had significantly higher NLR values compared to the healthy controls[4]. In first-episode psychosis, NLR levels were also found to be higher compared to control[5]. In this study, we evaluated NLR levels for both affective and non-affective psychosis. We divided the patients into three groups such as first-

episode psychosis(FEP), schizophrenia(SCH), and bipolar disorder(BP). This enabled the determination of whether there was a change in the NLR level in different patient groups in the psychotic stage.

METHODS

Participants

This is a retrospective case-control study conducted on schizophrenia, first-episode psychosis, and bipolar disorder. Digital medical records were retrospectively analyzed who were hospitalized between 2016 to 2020. The total number of patients recruited for this study is 437. Patients were divided into 3 groups which are SCH (n:199), FEP(127), and BP(111) respectively. Patients were diagnosed by using a semi-structured clinical interview (SCID from the Diagnostic and Statistical Manual of Mental Disorders) based on DSM-V-TR criteria. Patients with psychotic features were included in this study. Patients with a previous history of head trauma, substance abuse, organic or metabolic disease, and immune suppressive problems and currently using immunosuppressive drugs were excluded from the study. The healthy control group (n:200) was selected by retrospectively examining the files of the people who had never been diagnosed with a psychiatric diagnosis and had not received any treatment, and who applied for a job application with the aim of obtaining a fully healthy report. The total number of participants included in this study is 637. The FEP group was selected from patients who had no previous psychiatric history and were admitted to the clinic after their first psychotic attack and started their treatment. The study was approved by the ethics committee of Gulhane Training and Research Hospital (2020/499).

Blood Sample

Blood samples were taken from the patients the next morning at 08:00 a.m. after their admission to the clinic was approved. Complete blood count (CBCs) results were retrospectively analyzed from the digital medical record system. CBCs parameters including NLR, PLR, and MLR were calculated for each patient and compared to healthy control. Results obtained from the CBCs were evaluated by using advanced analysis techniques

Statistical Analysis

The data obtained in the study were evaluated in the IBM SPSS (version 20.0) package program in a computer environment. The conformity of the data to the normal distribution was analyzed with the Shapiro-Wilk test. Mann-Whitney U/K Ruskal-Wallis tests were used in the analysis of continuous data that did not fit the normal distribution. Chi-square analysis was used to compare categorical variables. The statistical significance level was accepted as $p<0.05$

RESULTS: The study group consisted of a total of 637 participants, including 200 healthy controls (31.4%), 111 (17.4%) BP, 127 (19.9%) FEP, and 199 (31.2%) SCH. Among the participants, there was no difference in age between SCH and BP patients, while the mean age was found to be the lowest in the healthy control group, and lower in FEP patients than in SCH and BP patients ($p<0.05$ for each). While there was no difference in terms of gender between FEP and SCH patients in the study group, it was determined that the frequency of being male in healthy controls and female in BD patients was higher than in other groups. In this study, no difference was found between the patient groups in terms of substance use (Chi-square= 5.008; p= 0.082), platelet count was lower in SCH patients and no difference was found between the other groups in terms of platelet count. There was no statistical difference between the study groups in terms of lymphocyte, neutrophil, and monocyte counts and their ratios (NLR, MLR, PLR) ($p>0.05$ for each). Demographic and clinical features were presented respectively in Table- and Table 2.

DISCUSSION: There are many publications in the literature related to changes in NLR levels in psychosis. In this study, we did not find any difference in the NLR level, which is stated to be increased in psychotic disorders, and in other inflammation markers. It seems that there are differences between publications and the reported results are not consistent. It is thought that this may be due to the design of the study, comorbid pathologies observed in the patients the or any other confounding factors that has not been explored yet. Although there are findings that the NLR level changes in schizophrenia, the mechanism has not been clearly elucidated. The presence of first-episode psychosis patients in our study is important in terms of revealing the differences between the chronic and acute phases of the disease. In addition, the inclusion of affective psychotic patients in the study are valuable in terms of showing how there is a difference in inflammation in

different disease groups and different stages. Since inflammation will be affected by many variables, it is thought that prospective studies in which confounding factors are taken into account for clinical diagnostic purposes will yield more meaningful results. Our study is important in terms of evaluating different patient groups in the psychotic spectrum and showing that there is no significant difference between NLR and other blood parameters. Another distinguishing feature of our study is the high number of participants compared to the studies conducted so far. As a result, it is not possible to use the NLR level alone in diagnostic or treatment follow-up with the information obtained so far. A more specific marker of inflammation and a longitudinal prospective study design is needed to better understand the role of the immune system in schizophrenia spectrum disorder.

REFERENCES

1. Özdin S, Böke Ö. Neutrophil/lymphocyte, platelet/lymphocyte and monocyte/lymphocyte ratios in different stages of schizophrenia. Psychiatry Res. 2019;271:131-135.
2. Sandberg AA, Steen VM, Torsvik A. Is Elevated Neutrophil Count and Neutrophil-to-Lymphocyte Ratio a Cause or Consequence of Schizophrenia?—A Scoping Review. Frontiers in Psychiatry. 2021;12:728990.
3. Fond G, Lançon C, Auquier P, Boyer L. C-reactive protein as a peripheral biomarker in schizophrenia. An updated systematic review. Front Psychiatry. 2018;9:392.
4. Özdin S, Sarisoy G, Böke Ö. A comparison of the neutrophil-lymphocyte, platelet-lymphocyte and monocyte-lymphocyte ratios in schizophrenia and bipolar disorder patients–a retrospective file review. Nord J Psychiatry. 2017;71(7):509-512.
5. Onur D, Neslihan AK, Samet K. A comparative study of complete blood count inflammatory markers in substance-free acute psychotic disorder and substance-induced psychosis. Early Interv Psychiatry. 2021;15(6):1522-1530.

[Abstract:0077] [Neuroscience: Neuroimaging-Genetic- Biomarker]

0077 - Dopaminergic and glucocorticoid receptor gene polymorphisms and methylation patterns in patients with a synthetic cannabinoid-induced psychotic disorder: further support for association with suicide attempts

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OBJECTIVE: A relationship between cannabis use and schizophrenia has been reported for decades. The current development of high-efficacy synthetic cannabinoids (SCs) as a psychoactive drug has led to an increasing number of clinical reports of persistent psychotic effects in patients diagnosed with SC use disorders (SCUD). SCs, also referred to as “K2,” “spice,” or “synthetic marijuana,” differ from the partial agonist D9-tetrahydrocannabinol (D9-THC) and are generally CB1R and CB2R full agonists. Besides, some SCs might show a pharmacologically crucial affinity for psychosis-associated receptors, including dopamine, serotonin, and glutamate systems. Therefore, delusions and/or hallucinations are more likely with SCs than with cannabis misuse, and in comparison to cannabis, SC-related psychotic symptoms are related to more frequent agitation and behavioral dyscontrol. Acute psychotic effects can be seen even with a single exposure to SCs and include dissociation, depersonalization, illusions, auditory and visual hallucinations, paranoid delusions, disorganized behaviors, catatonia, aggression, and suicidal ideation or behavior (1). No earlier research has shown the polymorphisms and methylation status of MB-COMT promotor, DRD2, and NR3C1 genes on attempted suicide Turkish patients with SC-induced psychotic disorder (SCPD). Therefore, we hypothesized that polymorphisms and alteration of the methylation status of MB-COMT promotor, DRD2, and NR3C1 genes

might be related to the attempted suicide patients with SCPD. The present study aimed to evaluate the interaction of dopaminergic (DRD2 -141C Ins/Del, COMT Val158Met) and glucocorticoid receptor gene (NR3C1 BclI) polymorphisms and methylation patterns with attempted suicide in patients diagnosed with SCPD.

METHODS:

1) Patient Selection:

A sample of 109 patients diagnosed with SCPD consecutively admitted to the Bakirkoy Mazhar Osman Mental Health and Neurology Training and Research Hospital outpatient clinic and 100 age- and sex-matched healthy volunteers were included in the study. The interview was started by filling out data forms that included sociodemographic and clinical information. Ethics committee approval was obtained from the Clinical Research Ethics Committee of the Istanbul Faculty of Medicine for the study (2019/87).

2) DNA Analyses:

Methylation-specific polymerase chain reaction (MSP-PCR) was used to determine the methylation status of MB-COMT promotor, DRD2, and NR3C1 gene from DNA material. In addition, the polymerase chain reaction (PCR) and restriction fragment length polymorphism (RFLP) were used to determine DRD2 -141C Ins/Del, COMT Val158Met, and NR3C1 BclI gene polymorphisms.

Inclusion and Exclusion Criteria:

Subjects (18 to 65 years of age, of either gender, were literate, agreed on the participation in the study) diagnosed with SCPD according to DSM-5, and had no other systemic/neurological disease that may affect cognitive functions (dementia, epilepsy, Parkinson's disease, head trauma accompanied by loss of consciousness) included in the study. In addition, we excluded subjects who had mental retardation, neurodevelopmental disorders such as autism, and a diagnosis of axis-1 disorder other than SCPD as a result of the DSM-5.

3) Statistical Analyses:

Statistical analysis was performed using IBM SPSS version 21.0 (IBM Corp. released 2012; Armonk, NY, USA). Descriptive statistics included mean, standard deviation, frequency, and percentage. The Pearson chi-square test or Fisher's exact test was used for comparing of discrete variables. The odds ratio (OR) and the 95% confidence interval (CI) were also calculated. The Shapiro-Wilk test evaluated the suitability of continuous variables to normal distribution. Intergroup comparisons of continuous variables were performed by Mann Whitney U or Kruskal–Wallis testing. Genotype distributions in both the patients and the healthy controls were analyzed according to the Hardy-Weinberg Equilibrium (HWE). Statistical significance was accepted as $p < 0.05$ for the results of all analyses.

RESULTS: DRD2 -141C Ins/Del, COMT Val158Met, and NR3C1 BclI genotyping:

The patients diagnosed with SCPD were evaluated according to sociodemographic characteristics and clinical parameters, as shown in Table 1. When the percentages of MB-COMT promotor, DRD2, and NR3C1 gene methylation status in SCPD patients were compared with the control group, the percentage of DRD2 gene methylation of SCPD was found to be significantly lower than the control group (OR: 5.017; 95% Cl: 2.543–9.896; p=.000). When the COMT Val158Met and NR3C1 BclI genotype and the allele frequency distributions of SCPD patients were compared with the control group, there were a significant differences between groups. While the COMT Val/Val genotype frequency was significantly higher in the control group compared to the SCPD patient group (OR: 0.351; 95% Cl: 0.173-0.712; p=.003), the Val/Met genotype frequency was significantly higher in the SCPD group compared to control group (OR: 3.095; 95% Cl: 1.695-5.651; p=.000). Again the NR3C1 BclI CC genotype (OR: 1.940; 95% Cl: 1.067-3.525; p=.029) and C allele (OR: 1.071; 95% Cl: 1.067-2.943; p=.025) frequencies were significantly higher in the SCPD patient group compared to the control group (Table 2).

Comparison of methylation status and gene polymorphisms of the DRD2, MB-COMT, and NR3C1 in SCPD patients due to attempted suicide:

Comparing the DRD2 -141C Ins/Del, COMT Val158Met, and NR3C1 BclI genotype and the allele frequency distributions between the two groups due to the attempted suicide in the SCPD patient group demonstrated that the COMT Val158Met genotype distribution of SCPD patients was significantly different between the

groups of patients (Table 3). The percentage of patients with the Met/Met genotype was significantly higher in attempted suicide SCPD patients than the non-attempted SCPD patients (OR: 2.667; 95% Cl: 1.031–6.901; p=.039). The percentages of MB-COMT promotor, DRD2, and NR3C1 gene methylation status were not found to be significantly different between SCPD patients and the control group (p>.05) (data not shown). Again, when clinical parameters (age, age of onset, duration of disorder, the presence of alcohol usage, and former polysubstance abuse) were compared between groups in reference to the methylation status and gene polymorphisms of DRD2, MB-COMT, and NR3C1 of the patients with SCPD, there were not found to be significant differences between the groups (p>.05) (data not shown).

DISCUSSION: When we examined the association of dopaminergic and glucocorticoid receptor gene polymorphisms and methylation patterns in SCPD patients with a suicide attempt, our results demonstrated that only COMT Val158Met gene polymorphism might be associated with attempted suicide in Turkish patients diagnosed with SCPD. COMT is an important enzyme that plays a role in the inactivation of dopamine and noradrenaline. In the literature, some researches investigate the relationship between the 158 Val/Met COMT polymorphism and violence and/or suicidal behavior. In one study, no difference was found in the distribution of alleles between patients with schizophrenia and controls, while patients who attempted violent suicide had a higher rate of L (158 Met) allele homozygosity. In other studies related to the subject, the relationship of the L allele with aggressive behavior in schizophrenia patients has been proven again. A study comparing the COMT polymorphisms of the subjects who attempted suicide and the control group who did not have a lifetime psychiatric disorder found that the L allele was over-represented in those who attempted violent suicide. However, the genotype or allele frequencies did not differ statistically between the groups. In addition, when evaluated with self-report questionnaires, it was observed that LL carriers expressed their anger more extroverted, while HH carriers expressed their anger more introverted and reported more situational anger (2).

When the genotype distribution of the 158 Val/Met COMT polymorphism in Finnish and US patients with schizophrenia and schizoaffective disorder was examined, the low-activity allele (158 Met) was found to be higher in males with a history of the violent suicide attempt. Similar results were obtained in another Japanese sample, with a lower incidence of completed suicide in men with the highly active Val/Val genotype. The authors concluded that the Val/Val genotype might be a protective factor against suicide in males, meaning that the low-activity Met allele increases the risk of suicide (1). In a recent study, in patients with SCUD, COMT Val108Met gene polymorphism was associated with self-harming behavior, while COMT Val158Met gene polymorphism was related to a suicide attempt (3). In our study, the risk of suicide attempts in patients with the Met/Met genotype was significantly higher in parallel with other studies in the literature. Another epigenetic study found no relationship between MB-COMT gene methylation and suicide attempts in patients with SC or cannabinoid use disorder (4). Our recently published study also found no statistically significant relationship between COMT Val158Met gene polymorphism and suicide attempts in patients with ecstasy use disorder (5).

Our study's strength is that the first study showed the interaction of dopaminergic (DRD2 -141C Ins/Del, COMT Val158Met) and glucocorticoid receptor gene (NR3C1 BclI) polymorphisms and methylation patterns with attempted suicide in Turkish patients diagnosed with SCPD. Secondly, since all participants were from the same geographical area, our study's findings were more valuable. Nevertheless, despite the strengths of the current research, there are also several limitations. The first limitation was the small sample size, limiting the statistical power. Secondly, we can not rule out the effect of psychotropic drugs and confounding environmental factors (lifestyle, diet, etc.) on the epigenome. Therefore, future studies are needed to clarify the effects of psychotropic drugs on the epigenome.

REFERENCES

1. Wasserman D, Sokolowski M, Wasserman J, Rujesku D. Neurobiology and the genetics of suicide: New York: Oxford Univ. Press; 2009.

2. Rujescu D, Giegling I, Gietl A, Hartmann AM, Möller H-J. A functional single nucleotide polymorphism (V158M) in the COMT gene is associated with aggressive personality traits. Biological psychiatry. 2003;54(1):34-9.
3. Pehlivan S, Aytac HM, Kurnaz S, Pehlivan M, Cetinay Aydin P. Evaluation of COMT (rs4680), CNR2 (rs2501432), CNR2 (rs2229579), UCP2 (rs659366), and IL-17 (rs763780) gene variants in synthetic cannabinoid use disorder patients. Journal of addictive diseases. 2020;38(4):495-505.
4. Oyaci Y, Aytac HM, Pasin O, Cetinay Aydin P, Pehlivan S. Detection of altered methylation of MB-COMT promotor and DRD2 gene in cannabinoid or synthetic cannabinoid use disorder regarding gene variants and clinical parameters. Journal of Addictive Diseases. 2021;39(4):526-36.
5. Aytac HM, Oyaci Y, Aydin PC, Pehlivan M, Pehlivan S. COMTVal158Met polymorphism is associated with ecstasy (MDMA)-induced psychotic symptoms in the Turkish population. Neurosciences Journal. 2022;27(1):24-30.

TABLES:

Table 1. The clinical characteristics of cannabis-induced psychotic disorder patients.

			Mean±SD
Age			29.7±7.4
Age of onset (year)			17.0±3.8
Duration of disorder			12.7±6.4
		N	**%**
Sex	**Male**	109	100.0
	Female	0	0.0
Education	**Primary School**	45	41.3
Status	**Secondary School**	42	38.5
	High School	16	14.7
	University	6	5.5
Alcohol Usage	**No**	95	87.2
	Yes	14	12.8
Former polysubstance	**No**	63	57.8
abuse	**Yes**	46	42.2
Attempted suicide	**No**		89.7
	Yes		10.3

(Abbreviations: SD, standard deviation.)

Table 2. Comparison of frequencies of the DRD2 -141C Ins/Del, COMT Val158Met, and NR3C1 BclI polymorphisms and methylation status between synthetic cannabinoid-induced psychotic disorder patients and healthy controls.

	Genotype	**SC-induced Psychosis**		**Healthy Control**		**OR**	**95% CI**	**p***
		n [a]=	(%)	n=100	(%)			
DRD2	ins/ins	88	(80.7)	84	(84)	0.798*	0.390-1.633*	.537*
	ins/del	20	(18.3)	14	(14)	1.380*	0.656-2.906*	.395*
	del/del	1	(0.9)	2	(2)	0.454[&]	0.041-5.082[&]	.608[&]
	Allele							
	ins	196	(89.9)	182	(91.0)			
	del	22	(10.1)	18	(9.0)	0.881*	0.458-1.696*	.705*
	Methy. Status	n [a]=	(%)	n=100	(%)			
	Unmethylation	49	(45)	14	(14)			
	Partial methyl.	60	(55)	86	(86)	5.017*	2.543-9.896*	**.000***
		n[a] =	(%)	n=79	(%)			
COMT	val/val	16	(14.7)	26	(32.9)	0.351*	0.173-0.712*	**.003***
	val/met	70	(64.2)	29	(36.7)	3.095*	1.695-5.651*	**.000***
	met/met	23	(21.1)	24	(30.4)	0.613*	0.315-1.191*	.147*
	Allele							
	val	102	(46.8)	81	(51.3)			
	met	116	(53.2)	77	(48.7)	0.836*	0.555-1.260*	.391*
	Methy. Status	n [a]=	(%)	n=100	(%)			
	Unmethylation	35	(32.1)	43	(43)			
	Partial methyl.	74	(67.9)	57	(57)	0.627*	0.357-1.102*	.104*
		n[a] =	(%)	n=85	(%)			
NR3C1	CC	78	(71.6)	48	(56.5)	1.940*	1.067-3.525*	**.029***
	CG	28	(25.7)	32	(37.6)	0.573*	0.310-1.058*	.074*
	GG	3	(2.8)	5	(5.9)	0.453[&]	0.105-1.951[&]	.277[&]
	Allele							
	C	184	(84.4)	128	(75.3)			
	G	34	(15.6)	42	(24.7)	1.071*	1.067-2.943*	**.025***
	Methy. Status	n [a]=	(%)	n=100	(%)			
	Unmethylation	7	(6.4)	9	(9)			
	Partial methyl.	102	(93.6)	91	(91)	0.694*	0.248-1.939*	.484*

Abbreviations: SC, Synthetic Cannabinoid; Methy., methylation; [a]n=109, *; Pearson chi-square, [&]; Fisher's Exact Test.

Table 3. Comparison of frequencies of the DRD2 -141C Ins/Del, COMT Val158Met, and NR3C1 BclI polymorphisms and methylation status in synthetic cannabinoid-induced psychotic disorder patients due to attempted suicide.

SC-induced Psychosis	Genotype	Attempted Suicide Yes		No		OR	CI	
		n [a]=	(%)	n=76	(%)			
DRD2	ins/ins	26	(78.8)	62	(81.6)	0.839*	0.304-2.317*	.734*
	ins/del	7	(21.2)	13	(17.1)	1.305*	0.468-3.641*	.611*
	del/del	0	(0.0)	1	(1.3)	1.440[&]	1.271-1.632[&]	1.000[&]
	Allele							
	ins	59	(89.4)	137	(90.1)			
	del	7	(10.6)	15	(9.9)	0.923*	0.358-2.381*	.868*
	Methy. Status	n [a]=	(%)	n=76	(%)			
	Unmethylation	16	(48.5)	33	(43.4)			
	Partial methyl.	17	(51.5)	43	(56.6)	0.815*	0.359-1.851*	.625*
		n[a] =	(%)	n=76	(%)			
COMT	val/val	4	(12.1)	12	(15.8)	0.736[&]	0.219-2.476[&]	.772[&]
	val/met	18	(54.5)	52	(68.4)	0.554*	0.239-1.281*	.165*
	met/met	11	(33.3)	12	(15.8)	2.667*	1.031-6.901*	**.039***
	Allele							
	val	26	(39.4)	76	(50.0)			
	met	40	(60.6)	76	(50.0)	0.650*	0.361-1.169*	.149*
	Methy. Status	n [a]=	(%)	n=76	(%)			
	Unmethylation	9	(27.3)	26	(34.2)			
	Partial methyl.	24	(72.7)	50	(65.8)	1.387*	0.563 -3.413*	.476*
		n [a]=	(%)	n=76	(%)			
NR3C1	CC	24	(72.7)	54	(71.1)	1.086*	0.436-2.706*	.859*
	CG	9	(27.3)	19	(25.0)	1.125*	0.446-2.838*	.803*
	GG	0	(0.0)	3	(3.9)	1.452[&]	1.278-1.650[&]	.247[&]
	Allele							
	C	57	(86.4)	127	(83.6)			
	G	9	(13.6)	25	(16.4)	1.247*	0.547-2.841*	.599*
	Methy. Status	n [a]=	(%)	n=76	(%)			
	Unmethylation	2	(6.1)	5	(6.6)			
	Partial methyl.	31	(93.9)	71	(93.4)	1.092[&]	0.201 -5.935[&]	1.000[&]

Abbreviations: SC, Synthetic Cannabinoid; Methy., methylation; [a]n=33, *; Pearson chi-square, [&]; Fisher's Exact Test.

[Abstract:0086] [Mood disorders]

0086 - The effect of childhood traumatic experiences on sexual function in patients with premenstrual dysphoric disorder and premenstrual syndrome

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INTRODUCTION: Although premenstrual symptoms are experienced by almost every woman of childbearing age in the world, premenstrual syndrome and premenstrual dysphoric disorder are considered within the scope of the definition of premenstrual syndrome and premenstrual dysphoric disorder according to the severity and characteristics of these symptoms that affect the quality of life and functionality of the individual. It is possible to evaluate the psychopathophysiology of premenstrual disorders in a very broad biopsychosocial framework and to examine the etiological causes in detail in neurobiological, genetic, psychological and sociocultural fields. Within the framework of these reasons, some studies have drawn attention to the presence of childhood traumatic experiences in patients with premenstrual disorder.(1) There are studies reporting sexual dysfunction in patients with premenstrual disorder. Similarly, the relationship between childhood trauma and sexual dysfunction has been examined in many studies.(2) However, there are no studies evaluating the relationship between these parameters in patients with premenstrual disorder. The aim of this study was to examine the relationship between the presence of childhood trauma and sexual dysfunction in patients with premenstrual syndrome and premenstrual dysphoric disorder.
METHOD: This study included 100 consecutive women aged 18-45 years, with regular menstruation and menstrual cycles of 25-35 days, who were diagnosed with PMS or PMDD according to DSM-5 diagnostic criteria, who applied to the Gynecology and Obstetrics outpatient clinic of Recep Tayyip Erdogan University Training and Research Hospital between March 1, 2020 and December 31, 2020 with premenstrual complaints and who had not received any psychiatric treatment for the last 6 months. Patients with mental retardation, dementia, alcohol and substance addiction, post-traumatic stress disorder, menstrual irregularity, hormone or oral contraceptive therapy, anemia, endometriosis, hyperprolactinemia, pregnancy, lactation, urogenital surgery, menopause were excluded from the study. Sociodemographic and clinical data form, Premenstrual Syndrome Rating Scale (PMSS), Childhood Trauma Questionnaire (CTQ-28), Arizona Sexual Experiences Scale (ASEX) were applied to the patients. Data were analyzed using SPSS-20.0.
RESULTS: In our study, the rate of participants reporting sexual dysfunction was 20% (n:20). Pearson correlation analysis was performed between the scale scores used in the study. Statistical analyses between the Arizona Sexual Experiences Scale (ASEX) used to assess sexual dysfunction and CTQ-28 and PMSS revealed a significant correlation between ASEX and CTQ-28 emotional abuse subscale and ASEX and PMSS depressive thinking subscale scores (p=0.029, p=0.002). In the evaluation between the presence of childhood traumatic experiences and sexual dysfunction, it was observed that 29.8% (n:17) of the trauma group reported sexual dysfunction, whereas this rate was 7% (n:3) in the other group and a statistically significant difference was found (p=0.005). When the relationship between sexual dysfunction and premenstrual syndrome severity in those with childhood traumatic experiences was evaluated by predictive linear regression analysis, it was found that there was a significant relationship between premenstrual syndrome level and sexual dysfunction in the group with trauma, and ASEX score increased as PMSS score increased (p=0,003, R=0,387). However, the same relationship was not found in the group without childhood trauma (p=0,169) (Table 1.). Whether sexual dysfunction is a mediating variable in the effect of childhood trauma and its sub-dimensions (emotional abuse, physical abuse, emotional neglect, physical neglect, sexual abuse) on the development of premenstrual disorder was evaluated by mediation model regression analysis. The results of the analysis showed that the indirect effect of childhood trauma, emotional abuse and sexual abuse on premenstrual disorders was smaller

than the direct effect and therefore played a partial mediating role (p=0.0265, p=0.0002, p=0.0317) (Tablo 2, 3, 4).

DISCUSSION: It is known that one out of every three people, regardless of whether they are male or female, experience at least one sexual dysfunction at some point in their lives. Studies have shown that the rate of sexual dysfunction in women varies between 20-73%. (3) In our study, the rate of participants reporting sexual dysfunction was found to be 20% and is similar to the literature. Studies have reported that patients with premenstrual disorder are more likely to have sexual dysfunction. Nowosielski et al. reported that the risk of sexual dissatisfaction in women with premenstrual disorder was twice as high compared to healthy women, that they reported more sexual distress compared to healthy women, and that the presence of PMS was negatively correlated with sexual satisfaction.(4) In our study, a statistically significant relationship was found between the Arizona Sexual Experiences Scale, which was used to evaluate sexual dysfunction, and the PMSS depressive thinking subscale score. Our findings are consistent with the literature.

Most of the studies on childhood traumatic experiences and sexual function have dealt with the issue in terms of sexual abuse. In a study conducted by Seehus et al. on the role of family environment and multiple forms of childhood abuse in shaping sexual function and satisfaction with 417 women aged 18-25 years, it was found that family dynamics and different types of childhood abuse directly and indirectly affect adult sexual function and satisfaction. (2) Childhood sexual abuse has been defined as one of the most prominent risk factors for the development of sexual dysfunction in adulthood, including problems with sexual desire, arousal, orgasm and sexual pain. The most commonly reported sexual dysfunctions are desire and arousal problems. Women with a history of abuse report more fear, anger and disgust during sexual arousal with a partner than women who have not been abused. (5)

In our study, when the relationship between the presence of childhood traumatic experiences and sexual dysfunction was evaluated, sexual dysfunction was found to be 29.8% in the trauma group and 7% in the other group and a significant difference was found between them. When the relationship between sexual dysfunction and premenstrual syndrome severity in those with childhood traumatic experiences was evaluated by predictive linear regression analysis, it was found that there was a significant relationship between premenstrual syndrome level and sexual dysfunction in the group with trauma, and ASEX score increased as PMSS score increased. However, the same relationship was not found in the group without childhood trauma. In addition, a significant relationship was found between the Arizona Sexual Experiences Scale, which was used to evaluate sexual dysfunction, and the CTQ-28 emotional abuse sub-dimension. In our study, whether sexual dysfunction is a mediating variable in the effect of childhood trauma and its sub-dimensions (emotional abuse, physical abuse, emotional neglect, physical neglect, sexual abuse) on the development of premenstrual disorder was evaluated by mediation model regression analysis. As a result of the analysis, significant relationships were found in the CTQ-28 total score and emotional abuse and sexual abuse sub-dimensions (p=0.0265, p=0.0002, p=0.0317). However, when examined in terms of the mediating role of sexual dysfunction, it was seen that the indirect effect on premenstrual disorders in terms of childhood trauma, emotional abuse and sexual abuse was smaller than the direct effect, so it played a partial mediating role. Studies on psychology and behavior have long focused on understanding the relationships between two variables. The effect of the independent variable on the dependent variable, the relationship between them, the explanatory power of their variables, or the independent variables predicting the dependent variable are the starting point of many studies. However, as a result of methodological advances in the field of psychology and behavior, the mechanism by which the relationship between dependent and independent variables is realized or the conditions under which the relationship between dependent and independent variables changes have gained importance. Recently, a significant portion of the studies conducted in our country and abroad have been aimed at determining mediational and/or regulatory effects. (6) When the literature was examined, no other study was found on the mediating role of sexual dysfunction on childhood trauma and premenstrual disorders using mediational regression analysis. In this respect, we think that our study may be a guide for future studies.

CONCLUSION: There is a relationship between the presence of childhood trauma and sexual dysfunction in patients with premenstrual syndrome and premenstrual dysphoric disorder. The presence of concurrent

childhood traumatic experiences in women with premenstrual disorder may change the course of the disease, treatment and therapy approaches. Therefore, it is important to question childhood traumatic experiences together with additional comorbid conditions such as sexual dysfunction in the initial presentation and evaluation of women with premenstrual complaints.

Keywords: Premenstrual Syndromes; Premenstrual Dysphoric Disorder; childhood maltreatment; childhood trauma; sexual disfunction

REFERENCES

1. Perkonigg A, Yonkers KA, Pfister H, et al: Risk factors for premenstrual dysphoric disorder in a community sample of young women: the role of traumatic events and posttraumatic stress disorder. The Journal of clinical psychiatry 2004; 65:1314-1322

2. Seehuus M, Clifton J,Rellini AH: The Role of Family Environment and Multiple Forms of Childhood Abuse in the Shaping of Sexual Function and Satisfaction in Women. Archives of sexual behavior 2015; 44:1595-1608

3. TUĞUT N: Cinsel İşlev Bozukluğu ve Güncel Yaklaşımlar. Turkiye Klinikleri J Obstet Womens Health Dis Nurs-Special Topics 2016; 2(1):70-75

4. Nowosielski K, Drosdzol A, Skrzypulec V, et al: Sexual satisfaction in females with premenstrual symptoms. The journal of sexual medicine 2010; 7:3589-3597

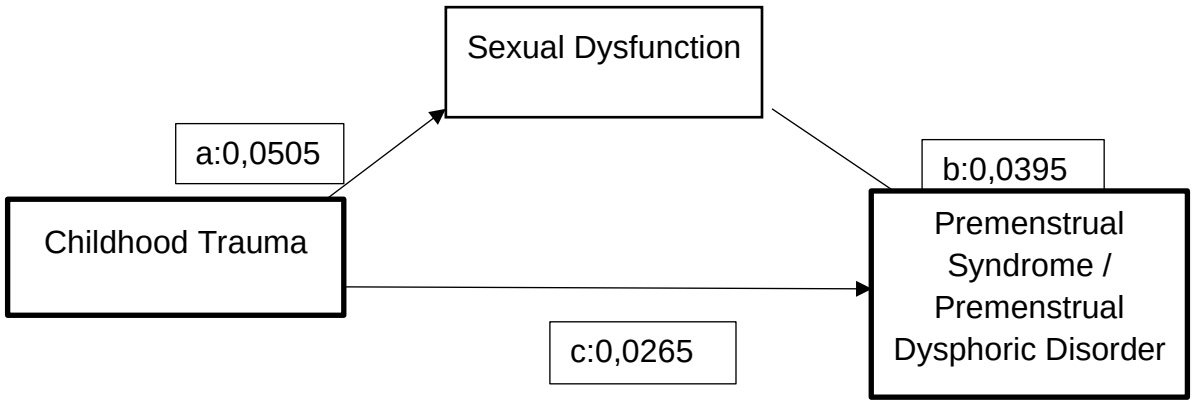
5. E. W: Women's sexuality after childhood incest, New York, W.W. Norton and Co, 1992

6. Sait Gürbüz MEB: Aracılık Modellerinin Analizinde Yeni Yaklaşım: Baron ve Kenny'nin Yöntemi Hâlâ Geçerli mi? Türk Psikoloji Dergisi 2021 37: 1-14

Table 1. Predictive Linear Regression Analysis of PMSS Scores of Participants with and without Childhood Trauma by ASEX

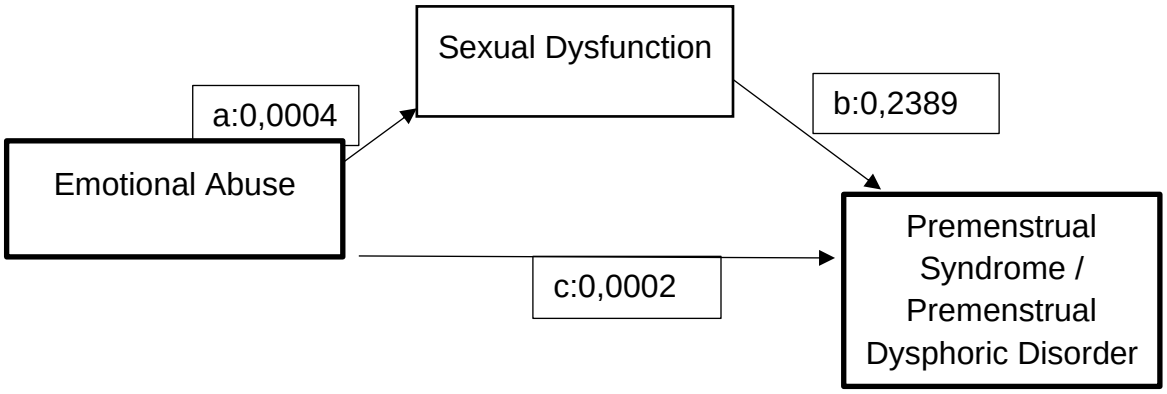
Childhood Trauma (+)	**Dependent Variable:**	ASEX (a)						
	Independent Variable	**R**	**R^2**	**Adjusted R^2**	**F**	**B**		**p**
	PMSS (b)	0,387[a]	0,150	0,134	9,669	0,065	3,110	0,003[b]
Childhood Trauma (-)	**Dependent Variable:**	ASEX (a)						
	Independent Variable	**R**	**R^2**	**Adjusted R^2**	**F**	**B**	**t**	**p**
	PMSS (b)	0,214[a]	0,046	0,022	1,961	-0,021	-1,400	0,169[b]

Table 2. Childhood Trauma - Sexual Dysfunction - (PMS-PMDD)
Mediation Model Regression Analysis Diagram



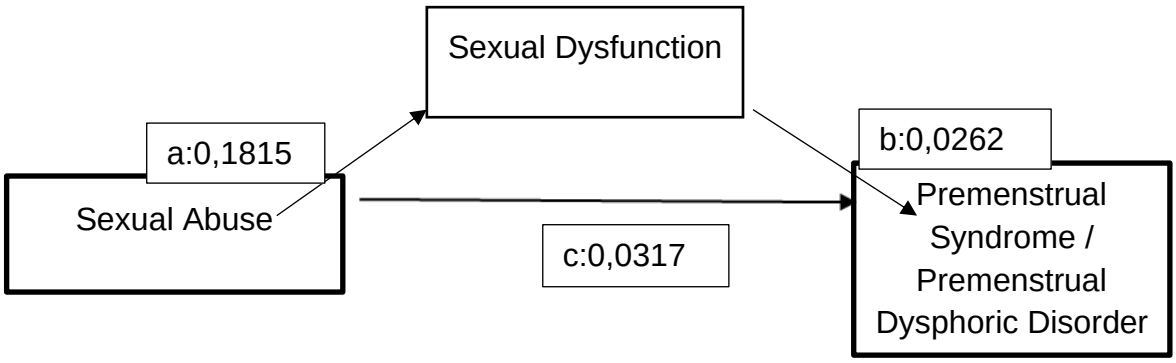
Indirect effect of Childhood Trauma on Premenstrual Syndrome / Premenstrual Dysphoric Disorder (a and b) = 0.1583
Direct effect of Childhood Trauma on Premenstrual Syndrome / Premenstrual Dysphoric Disorder (c)= 0.8712
Total effect of Childhood Trauma on Premenstrual Syndrome / Premenstrual Dysphoric Disorder (a and b + c)= 1.0296

Table 3. Emotional Abuse - Sexual Dysfunction - (PMS-PMDD)
Mediation Model Regression Analysis Diagram



Indirect effect of Emotional Abuse on Premenstrual Syndrome / Premenstrual Dysphoric Disorder (a and b) = 0.4998
Direct effect of Emotional Abuse on Premenstrual Syndrome / Premenstrual Dysphoric Disorder (c)= 4.8171
Total effect of Emotional Abuse on Premenstrual Syndrome / Premenstrual Dysphoric Disorder (a and b + c)= 5.3169

Table 4. Sexual Abuse - Sexual Dysfunction - (PMS-PMDD)
Mediation Model Regression Analysis Diagram



Indirect effect of Sexual Abuse on Premenstrual Syndrome / Premenstrual Dysphoric Disorder (a and b) = 0.7049
Direct effect of Sexual Abuse on Premenstrual Syndrome / Premenstrual Dysphoric Disorder (c)= 5.0514
Total effect of Sexual Abuse on Premenstrual Syndrome / Premenstrual Dysphoric Disorder (a and b + c)= 5.7563

[Abstract:0097] [Schizophrenia and other psychotic disorders]

0097 - Prediction of treatment response to negative symptoms using structural mr in patients with first episode psychosis

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ABSTRACT
INTRODUCTION: Psychotic disorders are defined as a cluster of psychiatric disorders characterized by delusions, hallucinations, and disorganized behavior that lead to impaired reality testing [1]. Although psychotic symptoms are characteristic of schizophrenia and other psychotic disorders, they can also be seen in mood disorders, neurological diseases, and other medical conditions [2].
Psychotic symptoms; characterized by delusions, hallucinations, disorganized speech, disorganized behavior (including catatonia), and negative symptoms6. Negative symptoms constitute a significant portion of the morbidity associated with schizophrenia. Other negative symptoms include alogy, anhedonia, and asociality [3]. Although negative symptoms have long been recognized as a clinically significant component of schizophrenia, targeted symptomatic treatment has largely been inadequate [4].
The literature focuses on the predictors of possible outcomes in schizophrenia and the factors affecting the course. The factors identified are not always consistent across studies, but premorbid functioning, age at onset, duration of untreated psychosis (TPS, Duration of untreated psychosis, DUP) and severity of emerging symptoms were among the most reliable factors [5].
In neuroimaging studies, structural and functional changes in the frontal and temporal lobes have been observed, especially in schizophrenia patients with a general point of vie
[6,7]. In large-scale meta-analyses, a smaller hippocampus volume, smaller amygdala, thalamus, nucleus accumbens, and intracranial volumes, as well as larger pallidum and lateral ventricular volumes, were reported as brain structural abnormalities compared to controls in schizophrenia [8]
Research on the neurobiological origin of psychiatric diseases has always been the field of interest of psychiatry. The development of statistical parametric mapping and voxel-based analysis methods in the mid-1990s and the application of machine learning approaches to neuroimaging data in the early 2000s enabled the

individualization of data for groups [9]. Over the past three decades, traditional univariate mass imaging approaches have revealed neuroanatomical abnormalities in individuals with psychosis [10]. Because these abnormalities were detected using group-level inferences, it was not possible to use this information to make diagnostic and treatment decisions for individual patients. Because these abnormalities were detected using group-level inferences, it was not possible to use this information to make diagnostic and treatment decisions for individual patients [11].

The aim of our study is to examine the factors that predict the treatment response to negative symptoms of first episode psychosis in children and adolescents and to evaluate the associated brain regions with a machine learning approach.

METHOD: Participants:Our study included 45 patients diagnosed with first episode psychosis and 38 healthy controls aged 12-18 years, whose MR images were obtained via OpenNeuro MRI Dataset. In the study, it is planned to use MRI images taken to rule out organic etiology in routine practice for patients with first episode psychosis, and additional MRI is not planned for the purpose of the study. In the study, it is planned to use MRI images taken to rule out organic etiology in routine practice for patients with first episode psychosis, and additional MRI is not planned for the purpose of the study. The control group will consist of 38 healthy adolescents aged 12-18 years, whose MR images were obtained via the OpenNeuro MRI Dataset.

Subsequently MR images have been obtained by using 1.5 Tesla MR devices and images obtained with 3D T1 weighted MP-RAGE sequences have been used for region of interest analysis. Volumes of brain subsections have been measured with Siemens Healthineers İntroduces Artificiai İntelligence Based Assistants For Magnetic Resonance İmaging.

Instruments

Sociodemographic information was taken from children and their parents who were included in the study using a sociodemographic data form prepared by the researchers. The Kiddie Schedulefor Affective Disorders and Schizophrenia (K-SADS), Positive and Negative Syndrome Scale (PANSS), Scale for Assesment of Positive Symptoms (SAPS), Scale for Assesment of Negative Symptoms (SANS), Calgary Depression Scale for Schizophrenia (CDRS), Brief Negative Symptom Scale (BNSS), The Children's Global AssessmentScale (CGAS) was applied to the cases.

Statistical Analysis

Statistical analyzes of the data were indicated by categorical variables, frequency values and number of cases. Continuous variables are presented with mean and standard deviation data. The-square test was used in the comparison of categorical variables. When comparing volume data of brain sections between healthy control and case groups, ANCOVA analysis of variance controlled for age and sex was used. Spearman correlation analysis was applied for continuous variables that did not fit the normal distribution. In the analyzes performed, $p<0.05$ was accepted as the level of significance.

Neuroimaing Analysis

In machine learning analysis, the most significant features among the brain regions were selected by using the feature selection method (Feature Selection Univariate) and the F test. Random Forest, Naive Bayes, Support Vector Machine, Logistic Regression models were applied as machine learning model, and since the most meaningful results were obtained with the Logistic Regression Model, this model was continued. The selected model was trained with a leave one out cross validation and then tested.

Results: Our study were included 45 cases and 38 healthy controls. Brain volume ($p=0.008$) and total white matter volume ($p<0.001$) were found to be significantly lower in our case group when compared to healthy controls. There was no significant difference in total gray matter and cortical gray matter volumes between first episode psychosis patients and healthy controls. When subcortical volume values were compared with healthy controls, globus pallidus, caudate nucleus and putamen volumes were found to be significantly higher ($p<0.001$). In addition, when the ventricular volumes were compared with the healthy controls, the volumes of the third ventricle ($p=0.03$) and total ventricle ($p<0.001$) were found to be significantly higher. There was no significant difference between right and left lateral ventricle volumes were compared with the healthy controls. Hippocampal volumes were found to be significantly lower than healthy controls ($p<0.001$).

Conclusion: Brain structural changes were detected in patients with first episode psychosis compared to healthy controls. When the structural MR images and the applied scale scores were evaluated with the machine learning approach, it was shown that the severity of the disease could be estimated with structural MR images before the treatment (AUC=0.8). In addition, BNSS and SANS scale scores at the 3rd month after the treatment were tried to be predicted, and the BNSS and SANS scale scores at the 3rd month were estimated with an accuracy rate of 62% by applying logistic regression from machine learning algorithms to the determined brain regions.

REFERENCES

[1] Arciniegas DB Psychosis. [cited 2022 Jan 17]; Available from: www.ContinuumJournal.comGaebel W, Zielasek J. Focus on psychosis [Internet]. 2015. Available from: www.dialogues-cns.org
[2] McClellan J, Stock S. Practice Parameter for the Assessment and Treatment of Children and Adolescents With Schizophrenia. Journal of the American Academy of Child & Adolescent Psychiatry [Internet]. 2013 Sep 1 [cited 2022 Jan 21];52(9):976–90.
[3] American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders [Internet]. Fifth Edition. American Psychiatric Association; 2013 [a.yer 22 Mart 2020].
[4] Azorin J-M, Belzeaux R, Adida M. Negative Symptoms in Schizophrenia: Where We have been and Where We are Heading[Internet]. [cited 2022 Jan 21].
[5] Kamens S, Davidson L, Hyun E, Jones N, Morawski J, Kurtz M, vd. The Duration of Untreated Psychosis: A Phenomenological Study. Psychosis. 2018;10(4):307-18
[6] Vita A, de Peri L, Deste G, Sacchetti E. Progressive loss of cortical gray matter in schizophrenia: a meta-analysis and meta-regression of longitudinal MRI studies. Translational Psychiatry [Internet]. 2012 [cited 2022 Jan 30];2(11):e190.
[7] Sci-Hub | Neurocognition and neuroimaging of persistent negative symptoms of schizophrenia | 10.1586/ern.11.173 [Internet]. [cited 2022 Jan 30
[8] Keshavan MS, Collin G, Guimond S, Kelly S, Prasad KM, Lizano P. Neuroimaging in schizophrenia [Internet]. [cited 2022 Jan 30].
[9] Davatzikos C. Machine learning in neuroimaging: Progress and challenges
[10] Chan RCK, Di X, Mcalonan GM, Gong Q-Y. Brain Anatomical Abnormalities in High- Risk Individuals, First-Episode, and Chronic Schizophrenia: An Activation Likelihood Estimation Meta-analysis of Illness Progression.
[11] Davatzikos C, Shen D, Gur RC, et al. . Whole-brain morphometric study of schizophrenia revealing a spatially complex set of focal abnormalities. Arch Gen Psychiatry.2005;62(11):1218–1227.

[Abstract:0100] [Autism Spectrum Disorders]

0100 - Investigation of serum zonulin, occludin, claudin-5, junction adhesion molecule and tricellulin levels in children with autism spectrum disorder

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Investigation of serum zonulin, occludin, claudin-5, Junction Adhesion Molecule and Tricellulin levels in children with autism spectrum disorder

INTRODUCTION: Autism spectrum disorder (ASD) is a neurodevelopmental disorder characterized by deficiencies in social communication and interaction and the presence of repetitive behaviors, limited interests or activities that negatively affect social, occupational or other areas in the early stages of development (1).

The prevalence of ASD is gradually increasing, and it has been reported that approximately 1 out of 44 children has ASD (2). Recently, many biomarkers have been researched to determine the etiology in ASD. In this context, intestinal blood-brain barrier (BBB) permeability has been of interest.

Zonulin is a member of a family of structurally and functionally related proteins that reversibly regulate intestinal permeability by modulating intercellular Tight Junctions (TJ) (3). Zonulin appears to be the primary modulator of regulating permeability at both the gut-blood and blood-brain barriers and is used as a clinical indicator of gut permeability.

Claudin-5 is the predominant tight junction protein in brain endothelial cells and specifically limits the extracellular permeability of molecules larger than 400 Da across the blood-brain barrier (BBB).

JAM-A is predominantly expressed in the brain and is present in tight junctions specific to the cerebral vascular system. We hypothesized that JAM-A, an endothelial tight junction component, might play a role in the etiopathogenesis of ASD.

Occludin is an integral phosphoprotein that plays an important role in the TJ structure. It contributes to TJ stabilization and optimal barrier function (4).

Tricellulin is responsible for keeping cells together and for the passage of macromolecules (5). Tricellulin plays a role in the cellular barrier, and its suppression causes the barrier to weaken (6). It has been determined that recessive mutations in the tricellulin gene cause non-syndromic deafnessn(7).

In the light of this information, abnormalities in TJs located in the gut-brain barrier should be examined in relation to ASD. The present research aimed to explore whether the concentrations of serum Zonulin, Occludin, JAM-A, Tricellulin and Claudin-5 vary between ASD patients and healthy controls. The present research also intended to explore whether there is an association between Zonulin, Occludin, JAM-A, Tricellulin and Claudin-5 concentrations and ASD severity.

MATERIALS AND METHODS

Participants

The ASD group consisted of 40 children aged 2-12 years, who applied to the Child and Adolescent Psychiatry outpatient clinic of Suleyman Demirel University (SDU) Faculty of Medicine, were newly diagnosed with ASD or were followed up with the diagnosis of ASD in our clinic. ASD diagnosis was confirmed using a diagnostic psychiatric interview based on the Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-5) (American Psychiatric Association 2013). Children with gastrointestinal (GI) disease (eg Crohn's disease, ulcerative colitis) or chronic disease (eg diabetes mellitus, hypertension, epilepsy, cerebral palsy) infections or obesity were excluded to control for confounding variables. The control group consisted of 40 age- and gender-matched healthy children who applied to SDU Medical Faculty outpatient clinics and volunteered with their parents. Those with normal laboratory tests (hemogram, sedimentation, C-reactive protein), no medication, no chronic disease (diabetes, hypertension, epilepsy, cerebral palsy), no infectious disease, GIS disease or obesity, K-SADS-PL-T semi-structured psychiatric interview Children without any psychiatric disease were included in the study according to the form. Written consent was obtained from the parents of all children included in the study.

Diagnostic and Symptomatic Assessment

In both groups, the sociodemographic data form, Childhood Autism Rating Scale (CARS), Autism Behavior Checklist (AuBC) were administered by clinicians to determine the severity of autistic symptoms. The Aberrant Behavior Checklist (ABC) is populated by parents. In the control group, children aged 6 years and over were interviewed by the clinician based on the Schedule for Afective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version-Turkish Version (K-SADS-PL-T) and DSM-5 diagnostic criteria, and children under 6 years of age were interviewed based only on DSM-5 diagnostic criteria. Height and weight were measured in both groups.

Blood Samples

Fasting venous blood samples were taken from both groups between 08.00–10.00 a.m. Blood samples were centrifuged at 3000 rpm for 10 min, serum was obtained, and the samples were stored at −80 °C until the day of the study. Serum JAM-A, Occludin, Tricellulin, Zonulin, Claudin levels were measured by enzyme-linked

immunosorbent assay (ELISA) method. Results are given in ng/ml for tricellulin, zonulin, claudin and ng/l for JAM-A, Occludin.

Statistical analysis

The statistical analysis was conducted using SPSS 22. The Shapiro–Wilk test was used to determine whether the distribution of the variables was normal. Relationships between dichotomous variables were assessed with the χ^2 test. The psychological test scores and biochemical parameters of the patient and control group were compared using the Student's t test or the Mann–Whitney U test according to distribution properties. Also, Spearman's correlation test was performed to evaluate the correlations between biochemical parameters and sociodemographic (age, sex, and BMI percentile) and clinical variables (CARS total score, AuBC sensorial stimulus, AuBC relationship, AuBC use of body and objects, AuBC language, AuBC personal-social development, and ABC subscale scores). The level of significance was accepted as $p < 0.05$ at a 95% confidence interval.

RESULTS: A total of 80 children, 40 (34 boys and 6 girls) with ASD and 40 (34 boys and 6 girls) healthy controls, were included in this study. The mean age was 71.05 ± 32.20 months for the ASD group and 69.40 ± 30.49 months for the control group. There was no difference between the groups in the distribution of mean age (t= 0.235; p= 0.815) and gender ($x^2 = 0$, p = 1). The differences between the weight percentile (t = 0.576; p = 0.566), height percentile (t = 0.790; p = 0.432) and BMI percentiles (t = -0.699; p = 0.487) of the subjects and controls were not significant.

Table 1. Demographic characteristics of ASD cases and controls

	ASD (n= 40)	CONTROL (n=40)	t	p
Sex (female/ male)	6/34	6/34	0	1
Age (months)	71.05 ± 32.20	69.40 ± 30.49	0.235	0.815
Weight percentile	62.87 ± 29.40	59.29 ± 26. 11	0.576	0.566
Height percentile	49.75 ± 33.46	43.71 ± 34.95	0.790	0.432
BMI percentile	62.28 ± 35.85	67.45 ± 30.00	0.699	0.487

In the whole sample, mean serum Zonulin levels were 40.15 ± 52.46 ng/ml in the ASD group, 29.22 ± 30.20 ng/ml in the control group (t=1.141, p=0.257), mean serum Occludin levels were 0.29 ± 0.22 ng/ml in the ASD group, 0.24 ± 0.048 ng in the control group /ml (t=1.196, p=0.238), mean serum JAM-A levels were 1387.97 ± 1291.91 ng/l in the ASD group, 1140.74 ± 1155.02 ng/l in the control group (t= 0.902, p= 0.370), mean serum Tricellulin levels were 37.12 in the ASD group ± 29.2 mg/ml, 26.72 ± 22.32 mg/ml in the control group (t=1.789, p= 0.077), mean serum Claudin-5 levels were in the ASD group 1.80 ± 0.05 mg/ml, 1.83 ± 0.11 mg/ml in the control group (t= -1.871 , p=0.067). There was no significant correlation between serum Zonulin, Occludin, JAM-A, Tricellulin, Claudin-5 levels between the groups.

Table 2. Serum Zonulin, occludin, claudin, JAM-A, Tricellulin levels of ASD and control group children

	ASD (n=40)	Control (n=40)	t	p
Zonulin ng/ml	40.15 ± 52.46	29.22 ± 30.20	1.141	0.257
Occludin ng/ml	0.29 ± 0.22	0.24 ± 0. 048	1.196	0.238
Claudin mg/ml	1.80 ± 0.05	1.83 ± 0.11	-1.871	0.067
JAM-A ng/l	1387.97±1291.91	1140.74 ± 1155.02	0.902	0.370
Tricellulin mg/ml	37.12 ± 29.2	26.72 ± 22.32	1.789	0.077

Spearman correlation analysis was performed to determine whether there was a correlation between CARS, AuBC, BMI percentiles, age and serum levels of Zonulin, Occludin, Claudin, Tricellulin and JAM-A in the ASD group. There was a positive correlation between serum zonulin levels and age in the ASD group (r=0.35, p=0.023). There was no correlation between serum Zonulin, Occludin, Claudin, Tricellulin, JAM-A levels and sociodemographic and clinical scale scores (BMI percentile, CARS total scores, and AuBC subscale scores).

In addition, there was no significant relationship between age and serum Occludin, Claudin, Tricellulin, JAM-A.

DISCUSSION: This study examined whether serum Zonulin, Occludin, Claudin, Tricellulin, JAM-A levels are associated with individuals diagnosed with ASD in childhood. The main finding of our study was that there was no significant difference in serum Zonulin, Occludin, Claudin, Tricellulin, and JAM-A levels between the study and control groups.

Zonulin is a safe parameter that indicates intestinal permeability. In our study, there was no significant difference between serum zonulin levels between the ASD group and the control group, no correlation was found between BMI percentiles and autism severity, and a positive correlation was found between age and serum zonulin concentration.

Fiorentino et al. (8) ın a postmortem study conducted with individuals diagnosed with ASD and healthy controls, they found that Claudin-5 levels were higher in the cortex and cerebellum of patients diagnosed with ASD (8). The authors suggested that this increase in serum claudin-5 levels may be a compensatory mechanism for the deterioration in BBB. In our study, no significant correlation was found between serum claudin-5 levels between individuals diagnosed with ASD and control groups. There was no relationship between serum claudin-5 level and age, BMI percentile, autism severity.

In our study, no significant difference was found between the groups in serum occludin levels. There was no correlation between serum occludin levels and BMI percentiles, age, CARS scores. Future studies are needed to explore this issue by evaluating the potential role of Occludin in the etiology of ASD.

In our study, no significant difference was found between the groups in serum tricellulin levels. No correlation was found between serum tricellulin levels and BMI percentiles, age, and CARS scores.

In our study, no significant difference was found between the groups in serum JAM-A levels. There was no correlation between serum JAM-A levels and BMI percentiles, age, and CARS scores.

In addition to the small sample size, the cross-sectional nature of the study is an important limitation. Since the majority of the participants in our study were men, the results obtained from our study cannot be generalized to female subjects. The low number of female participants in our study is another limitation. Despite these limitations, our study is the first in the literature to examine serum claudin-5, JAM-A, and tricellulin levels in individuals with ASD. It is also the first study in the literature in which serum claudin-5, JAM-A, tricellulin, occludin, and zonulin serum levels were examined simultaneously.

Keywords: Autism spectrum disorder, Zonulin, Ocludin, Claudin, JAM-A, Tricellulin

REFERENCE

1. DSM 5 Diagnostic and statistical manual of mental disorders | Arlington; American Psychiatric Association; 5 ed.; 2013. 947 p. | bivipsil. Accessed March 4, 2022. https://pesquisa.bvsalud.org/portal/resource/pt/psa-52826

2. Maenner MJ, Shaw KA, Bakian A v., et al. Prevalence and Characteristics of Autism Spectrum Disorder Among Children Aged 8 Years - Autism and Developmental Disabilities Monitoring Network, 11 Sites, United States, 2018. MMWR Surveill Summ. 2021;70(11):1-16. doi:10.15585/mmwr.ss7011a1

3. Fasano A. Intestinal zonulin: open sesame! Gut. 2001;49(2):159-162. doi:10.1136/GUT.49.2.159

4. Cummins PM. Occludin: one protein, many forms. Mol Cell Biol. 2011;32(2):242-250. doi:10.1128/MCB.06029-11

5. Mariano C, Sasaki H, Brites D, Brito MA. A look at tricellulin and its role in tight junction formation and maintenance. Eur J Cell Biol. 2011;90(10):787-796. doi:10.1016/J.EJCB.2011.06.005

6. Ikenouchi J, Furuse M, Furuse K, Sasaki H, Tsukita S, Tsukita S. Tricellulin constitutes a novel barrier at tricellular contacts of epithelial cells. Journal of Cell Biology. 2005;171(6):939-945. doi:10.1083/JCB.200510043

7. Riazuddin S, Ahmed ZM, Fanning AS, et al. Tricellulin Is a Tight-Junction Protein Necessary for Hearing. Am J Hum Genet. 2006;79(6):1040. doi:10.1086/510022

8. Fiorentino M, Sapone A, Senger S, et al. Blood-brain barrier and intestinal epithelial barrier alterations in autism spectrum disorders. Mol Autism. 2016;7(1). doi:10.1186/S13229-016-0110-Z

[Abstract:0118] [Anxiety disorders]

0118 - An examination of the anxiety sensitivity characteristics of medical college students based on their separation anxiety disorder diagnosis

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An examination of the anxiety sensitivity characteristics of medical college students based on their separation anxiety disorder diagnosis
BACKGROUND: Most of the anxiety disorders had been linked with different types of anxiety sensitivity characteristics in the literature. On the other hand, medical students are known to be susceptible to both anxiety disorders and depression due to several factors in the literature. According to our knowledge, there is no study in the literature that examined the relationships between anxiety sensitivity and Separation Anxiety Disorder (SEPAD) concurrently in a young adult population.
OBJECTIVE: The present study aims to investigate the prevalence of SEPAD in a medical student population and the relationships between SEPAD and anxiety sensitivity characteristics in this relevant sample.
METHODS: The sample of this study consisted of 369 young adults who are students at a medical school in Turkey. The Structured Clinical Interview for Separation Anxiety Symptoms (SCI-SAS) was applied for all participants by researchers. Participants were asked to fill in the socio-demographic form, Separation Anxiety Symptoms Inventory, Adult Separation Anxiety Questionnaire, and Anxiety Sensitivity Index-3 (ASI-3). The study has been approved by the Institutional Review Board of the university.
RESULTS: The rate of those with significant childhood SEPAD is 14.9%, the rate of those with adult SEPAD is 20.1% in the present study. Total and all three sub-scores of ASI-3 were significantly higher in both groups who met childhood or adult SEPAD criteria than those who did not meet the childhood or adult SEPAD criteria.
CONCLUSIONS: SEPAD may be diagnosed commonly in a medical student sample. Moreover, anxiety sensitivity may have a key role in the progress of SEPAD. The assessment of anxiety sensitivity characteristics of individuals with SEPAD may have important therapeutical implications for them.

Keywords: anxiety sensitivity, medical school, medical students, separation anxiety, separation anxiety disorder

[Abstract:0125] [Others]

0125 - Family factor and experiences of domestic violence in the existence processes of transgender individuals

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TRANSSEXUALİTY AND DOMESTİC VİOLENCE
BACKROUND AND OBJECTIVE: Transsexuality is when a person perceives himself as the opposite sex, is extremely uncomfortable with biological sex characteristics, and wants to have primary and secondary sex characteristics of the opposite sex. Transgender individuals seek treatment to change their primary and/or secondary gender characteristics.
The World Health Organization has divided violent behaviors into four different subtypes: physical, sexual, psychological violence and deprivation. Studies focusing on the experiences of transgender individuals show that they experience many psychological difficulties such as not accepting their gender identity, worrying about the social consequences of gender identity, fear of rejection, internalized transphobia, in addition to sexual dysphoria, and that they have different types of violence defined in different platforms such as family, school environment, and public spaces. show that they are exposed to varying degrees. The form and severity of these negative attitudes and behaviors that transgender people encounter due to gender expressions that do not comply with the normative values of the society, like every individual with a sexual minority status, vary according to the acceptances of the society in which they live.
Research on the subject has suggested that families refuse to have trans children to avoid stigma and loss of social status. It has been commented that in most cultures, the social status of the family is seen as more important than the well-being of the transgender individual, and that the "honorable family image" is associated with dignity, pride, economic opportunities. The cases of domestic violence experienced by transgender individuals are also thought to have a strong connection with the concepts of stigma and honor.
In this study, it is aimed to understand the family factor in the existence processes of transgender individuals and to focus on their experiences of domestic violence.
METHODS: This research was designed with the phenomenology method, which is one of the five basic qualitative research methods. A face-to-face interview was conducted with 19 FtM and 1 MtF individuals using a semi-structured interview form, and audio recordings were made. Then, the audio recordings were documented and the obtained transcripts were subjected to content analysis. The 269 codes obtained as a result of the analysis were grouped under two themes.
Institutional ethical consent was obtained (Ethics committee application number: 2021000355-1)
In our study, the proposed methods were used to evaluate the validity and reliability in qualitative research. In qualitative research, the criterion of credibility is used instead of internal validity in quantitative research.
In order to meet this condition, the researcher received counseling at every stage from the preparation of the study questions to the interpretation of the findings. Participants were asked whether the results directly reflected their own thoughts, and participant confirmation was provided.
In addition, in order to make the participants feel more comfortable and to have more sincere answers, the participants were interviewed in the polyclinics where they were followed during the gender transition process. Thus, "long-term interaction" was tried to be provided.
The concept of transferability, which is used instead of external validity in quantitative research, means that the results of the study cannot be directly generalized to similar environments, but that it gives results that those who read the study can transfer and apply to studies that will be carried out in similar environments. This condition is provided by purposive sampling and detailed description methods.

The homogeneous sampling method, which is one of the purposive sampling methods, was used in our study, and while the findings were explained, direct quotations from different participants were frequently included for almost every theme.
Consistency and confirmability are concepts used instead of reliability in quantitative research. To meet this condition, raw data, generated codes and themes were sent to a faculty member. It was asked to evaluate both the consistency and objectivity and whether the results of the study could be reached from the raw data.

RESULTS

Theme and Sub-themes	**f**
Family Through the Perspective of a Transgender Person	172
Family Factor in Transgender Individual's Existence Process	62
The Family's Perspective on the Concept of Transsexuality	11
Reasons for the Family's Transphobic Attitude	19
Having a Transgender Child	59
Family's Attempts to "Correct" Transsexuality	21
Transgender Individuals' Experiences of Domestic Violence	97
Experiences of Psychological Violence	84
Experiences of Economic Violence	8
Experiences of Physical Violence	5

In the theme of Family Through the Eyes of the Trans Person, the sub-themes of the family factor in the existence process of the trans person, the family's view of the concept of transsexuality, the reasons for the transphobic attitude of the family, the transgender person in the process of existence, a transgender child and the family's attempts to "correct" transsexuality were discussed.The participants talked about what they expected from their families during the difficult process they went through
I don't use drugs, I'm not addicted to anything, that's not a bad thing for me. I wish they would look like that too, they didn't… (P13)
I would like to talk to my family. So that they can cure my problem and hold my hand...white (p20)
Most participants said that although their families initially reacted negatively to gender differences or sexual role behaviors, they got used to this situation over time
It took a long time for my mother to accept it. It actually proceeds like a grieving process. First they refuse. Then they slowly get used to it (P3)
Some participants stated that it is easier for their families to accept the transition from female to male gender:
My father was saying that if you were a boy but you wanted to be a girl, I would have blown your nose. For example, I think my brother would kill him if he was a trans woman…(P1)
The participants talked about how important the support from their families is in terms of tackling the difficulties in the gender transition process.
My father said, act as you want, use any name you want, it's okay with me. I felt good, there was a big mountain behind me and no one could interfere with me. (p4)
participants stated that their families thought that transsexuality emerged due to wannabe. others stated that their families had associated transsexuality with illness or deviance:
My mom thought I was like this because I watched more series than Netflix (p5)
They see my masculinity as a disease. So what about my congenital problem? Find a cure for it too if it's a sin…(p19)
Participants cited gender roles, ignorance and religiosity as the reason for their families' transphobic attitudes:
Like I said, I'm not the person in their head. They have a normal girl on their minds. He should get married and have children. That's how they think… (p7)

According to the participants, their families denied having trans children for a long time. Because of this situation, they are worried about both their children and their family situation:
We have a name and surname. My father says it doesn't suit us, that's why they don't take me to public events (p16)
Participants frequently stated that their families resorted to pressure and religious methods in order to correct their sexual identity.
My mother used to say that if you grow that hair long, you will think it's beautiful, you'll think it's like a woman (p8)
Psychological, physical and economic violence experiences were discussed in the theme of domestic violence experiences of transgender individuals.
Participants stated that their families distanced themselves from them because they were transgender, their families exerted pressure and violence, and they refused to meet their needs:
My mother has given up on me, she is attached to my other brother, my brother wants something today, that day it is done, my brother cries, my mother hugs him. I didn't do anything to deprive them of.. (p9)
My father told me I was the devil's spawn (p10)
My uncle and cousins threatened to kill me (P11)
My brother was saying I am disgusted with you, you are acting like this to get attention. (p3)
I had to work throughout my student life because my father did not send money. (p13)
CONCLUSION: Close family members are a very important part and close witness of the existence of transgender individuals. Despite this close witness, families cannot come to the stage of acceptance and support, or they find it very difficult to come. According to our study, the biggest reason for this situation is stereotyped social norms and expectations, that is, the heteronormative social order. Just as transsexuality is perceived as a threat to heteronormativity, leading to transphobia and legitimizing violence, having a transgender child is perceived as a threat to family status and brings violence with it. Therefore, transgender individuals have experienced psychological, economic and physical violence within the family in various dimensions. It is observed that these violent behaviors are triggered by the feelings of hatred aroused by the gender presentation aimed at changing the gender difference, protecting the family status or not directly conforming to the social acceptances.
Our study provides valuable information to evaluate the attitudes of families towards their children's gender identity differences and to understand the domestic violence experiences of transgender individuals. The findings obtained can form the basis for more detailed studies on this subject.

REFERENCES

Rogers, M. (2017). Transphobic 'Honour'-Based Abuse: A Conceptual Tool. Sociology, 51(2), 225–240. https://doi.org/10.1177/0038038515622907
Brandon J, Hafez S, Cohesion CfS. Crimes of the Community: Honour-based Violence in the UK: Centre for Social Cohesion; 2008.
Kenagy GP. Transgender health: findings from two needs assessment studies in Philadelphia. Health Soc Work. 2005;30(1):19-26.

[Abstract:0127] [Obsessive-compulsive disorders (OCD)]

0127 - The relationship between sexual satisfaction and sexual myths in patients with obsessive compulsive disorder

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INVESTIGATION OF THE RELATIONSHIP OF SEXUAL SATISFACTION AND SEXUAL MYTHS IN PATIENTS DIAGNOSED WITH OBSESSIVE COMPULCIAL DISORDER

OBJECTIVE: It was aimed to evaluate the sexual satisfaction and belief in sexual myths of Obsessive Compulsive (OCD) patient and control groups. OCD is considered to be one of the most important problems in the whole society, in the family and social life, and in one of the areas of life.

Sexuality is one of the important components of quality of life and mental well-being. The most accepted definition of sexual satisfaction belongs to Lawrence and Byers. According to this definition, sexual satisfaction is an emotional response based on an individual's subjective evaluation and includes positive and negative experiences of sexual intercourse. Sexual satisfaction was found to be associated with mental and physical well-being.

Sex myths are often exaggerated, false, unscientific beliefs about sex life that a person accepts as true. It is shown among the causes that can lead to sexual dysfunctions and a decrease in sexual satisfaction.

Studies on the relationship between OCD and sexual life have shown that OCD can significantly affect close relationships and sexual health. It has been stated that obsessive compulsive symptoms are associated with worse sexual functions and sexual satisfaction levels. Compared with healthy controls (30%, 50%) of OCD patients were found to have sexual dysfunction.

METHODS: Patients who applied to the Ondokuz Mayıs University Psychiatry outpatient clinic and received inpatient treatment in the Psychiatry Service were included in this study. The study, which was started in June 2021, was terminated in April 2022 when the number of patients and control groups determined by power analysis were reached. Informed signed consent was obtained from patients who met the inclusion criteria when they agreed to participate in the study.

Our study is a cross-sectional study consisting of 40 OCD patients, 40 AD patients and 40 healthy controls. Sociodemographic and Clinical Data Form, Dimensional Obsession Compulsion Scale (BOCS), Golombok-Rust Sexual Satisfaction Scale (GRISS), Sexual Myths Scale (CME), Hamilton Anxiety Rating Scale (HADS) were used as measurement tools in the study. The control groups were selected considering that they showed similar distribution with the participants in the OCD group in terms of sociodemographic variables and the treatments they used.

The research data were evaluated by uploading to the computer environment. Descriptive statistics were presented as mean (±) standard deviation, median (Q1-Q3), frequency distribution, and percentage. The conformity of the variables to the normal distribution was examined using visual (histogram and probability graphs) and analytical methods (Kolmogorov-Smirnov/Shapiro-Wilk Tests). Mann-Whitney U Test, Krukal-Wallis and Chi-square tests were used for group comparisons that did not fit the normal distribution. The relationship between the variables was examined using the Spearman Correlation Test. Univariate and multivariate linear regression analyzes were used for modelling, and retrospective elimination model was used for multivariate analyses.

RESULTS: There was no statistically significant difference between the groups in terms of age, gender, educational status, marital status, socioeconomic status, and having children. It has been determined that there is a statistically significant difference between the groups in terms of working status, and this difference occurs when the OCD group participates in working life at lower rates than the control group.

When the clinical data of the groups were compared, it was determined that there was no statistically significant difference in terms of the drugs they used, inpatient treatment and sexual problems. It was observed that there was a statistically significant difference between the groups in terms of receiving sexual education, and the control group received significantly higher sexual education than the OCD and AD groups in the analysis. When the OCD and AD groups were compared in terms of disease duration, it was determined that there was a difference between the groups and the disease duration of the OCD group was statistically higher. BOCS was examined in the OCD group and it was seen that the total scores of the group ranged between a minimum of 19 and a maximum of 63, with a median value of 35.

It was observed that there was a significant difference between the groups in terms of sexual myth total scores. In the test, it was observed that the mean sexual myth score of the OCD group was significantly higher than anxiety and healthy controls.

It was observed that there was a significant difference between the groups in the total scores of the Golombok-Rust Sexual Satisfaction Scale, and the total score of the OCD group was higher than that of the anxiety and control groups.
When the GRISS subscale scores of women were compared between the groups, it was observed that the OCD group scored significantly higher than the control group in terms of satisfaction and touch, and the OCD group scored statistically significantly higher than the control and anxiety groups in terms of avoidance and anorgasmia. When the GRISS subscale scores of men were compared between the groups, it was observed that the OCD group scored significantly higher than the control group in terms of frequency and touch, and the OCD group scored statistically significantly higher than the control and anxiety groups in terms of avoidance.
When the relationship between the Sexual Myths Scale and the Golombok-Rust Sexual Satisfaction Scale was examined in women in the OCD group, it was determined that there was a statistically significant positive correlation between sexual myths and total score, communication and avoidance. When the relationship between the Sexual Myths Scale and the Golombok-Rust Sexual Satisfaction Scale was examined in men in the OCD group, it was found that there was a significant positive correlation between sexual myths and avoidance.
When the relationship between BOCS and GRISS scales was examined in women in the OCD group, it was observed that there was a positive correlation between avoidance and contagion obsessions, symmetry-perfectionism and communication. When the relationship between BOCS and GRISS scales was examined in men in the OCD group, no significant relationship was found between the scales.
When the relationship between sexual myths and dimensional obsession compulsion scale in women in the OCD group was examined, a positive correlation was observed between BOCS total score and contagion subscale and sexual myths total score. When the relationship between sexual myths and dimensional obsession-compulsion scales in men in the OCD group was examined, no relationship was observed between BOCS and sexual myths.
In the analysis performed to predict sexual satisfaction using sociodemographic and clinical data defined in the OCD group, univariate analyzes were first performed. As a result of univariate analyzes, it was observed that age, duration of illness, being at high school or higher education level and having sexual education significantly affected sexual satisfaction. The best model was obtained in the 6th step in the analysis made with the retrospective elimination method with all variables, and only the disease duration variable remained in this model.
In the analysis to predict sexual myths using sociodemographic and clinical data defined in the OCD group, univariate analyzes were first performed. Age, disease duration, marital status, education level, number of children and sexual education variables were found to be significant in univariate analyzes. In the analysis made with the retrospective elimination method with all variables, the best model was found in the 5th step, and it was observed that the education level and age variables remained in the model.
DISCUSSION: Our research provides valuable information about the sexual life of OCD patients. In the light of the research data, it has been shown that the sexual satisfaction levels of OCD patients are lower than the control groups, and their belief in sexual myths is higher. The findings have the potential to provide a basis for the psychotherapeutic approach in this regard.
OCD is a chronic mental health problem that is accepted as one of the most serious causes of deterioration in quality of life and disability. Similarly, when all psychiatric diseases are evaluated, it is seen as one of the most important causes of deterioration in family and social relations. Research on mental health emphasizes the need to reveal patients' strengths, such as life satisfaction and well-being. In terms of OCD, only the symptom-oriented treatment approach may cause the evaluations of patients' quality of life and well-being to be overlooked. With the change of this paradigm, it is predicted that the quality of life of the patients will be positively affected and the long-term treatment responses will be better. Improvements in the sex life of OCD patients are likely to offer a better quality of life despite symptomatology. Better sexual functions and a higher sexual satisfaction can be expected to provide a stronger psychological functioning despite OCD.

It is known that OCD patients may experience many problems related to sexual life and their sexual satisfaction levels are lower. Despite this, sexual life is seen as a subject that remains in the background in OCD patients. The typical treatment approach of OCD focuses on symptom reduction, there is no psychotherapeutic protocol for sexual dysfunctions or sexual satisfaction of the individual. It is clear that interventions for sexual life in OCD patients should be one of our treatment goals.

Tables:

1. Comparison of sexual myth total scores between groups

	OCD (n:40)	**AB (n:40)**	**Control (n:40)**	**Statistics**	**p**	**Post-hoc**
Sexual Myth Total Score	69,5±19,3	57,1±16,3	53,6±18,8	F:8,436	0,001	OC>AB>Control

Note: F: One-Way ANOVA test. Post-hoc Tukey test was used.

2. Comparison of the total scores of the Golombok-Rust scale of sexual satisfaction

	OCD (n:40)	**AB (n:40)**	**Control (n:40)**	**Statistics**	**p**	**Post-hoc**
GRISS Total Score	38 (Q1:26-Q3:55)	26 (Q1:20-Q3:37)	19 (Q1:14-Q3:34)	KW: 20,356	0,001*	OC>AB>Control

Note: KW: Kruskal-wallis test. Post hoc One-way ANOVA KW test was used. *p<0.050

REFERENCES

Pozza A, Veale D, Marazziti D, Delgadillo J, Albert U, Grassi G, et al. Sexual dysfunction and satisfaction in obsessive compulsive disorder: protocol for a systematic review and meta-analysis. Systematic reviews. 2020;9(1):1-13.

Lawrance K-a, Byers ES, Cohen JN. Interpersonal exchange model of sexual satisfaction questionnaire. Sexuality-related measures: A compendium. 1998;2:525-30.

Pozza A, Marazziti D, Mucci F, Grassi G, Prestia D, Dèttore D. Sexual arousal in obsessive-compulsive disorder with and without contamination/washing symptoms: A moderating role of disgust sensitivity. The Journal of Nervous and Mental Disease. 2020;208(9):694-700.

Kendurkar A, Kaur B. Major depressive disorder, obsessive-compulsive disorder, and generalized anxiety disorder: do the sexual dysfunctions differ? Primary care companion to the Journal of clinical psychiatry. 2008;10(4):299.

[Abstract:0146] [Neuroscience: Neuroimaging-Genetic Biomarkers]

0146 - Comparison of structural magnetic resonance imaging of the whole brain with cortical thickness, voxel-based morphometry and network analysis in sexually abused female adolescents

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INTRODUCTION: Dramatic changes occur in both adolescent brain and behavior. In adolescence the reorganization of human brain gains pace by neuronal pruning and synaptogenesis which makes the brain open to the effects of both positive (e.g. education, exercise and social interaction)[1,2] and negative (e.g. physical or sexual abuse and neglect) environmental factors [3]. Adolescents have a high frequency of risky behavior that undermines the importance ofsafety and thus, many adolescents are exposed to maltreatment [4]. Effects of adolescence adverse events(AAE) are well established in the adult brain by neuroimaging studies [5–7] . Psychiatric patients have AAE history frequently and it is repeatedly shown that there are differences in brain structure and function between patients with AAE and patients without AAE or healthy controls. These structural and functional alterations suggest that the effects of stressful life events can induce structural alterations that endure through adulthood. Most significant changes are observed in the prefrontal cortex, limbic system, and cortical regions related to social adjustment and emotion control [8]. However, studies with adolescents investigating the immediate effects of AAE on the adolescent brain are scarce [9–11]. The brain maturation in the adolescence is a very dynamic process and different brain regions have different developmental phases which makes them vulnerable to maltreatment at different times. The hippocampus presents a good example for the timing of the interaction of environmental factors and brain development as it is most susceptible to the effects of maltreatment between 3 and 5 years of age and during peri-pubertal ages of 11 and 13 years [12]. Therefore, not only the presence of negative environmental factors but also the age of the subject is important for the differences observed in adolescents with a history of AAE. In this study, we focused on the short-term effects of sexual abuse on adolescent brain structures. Based on the previous studies investing AAE on adults, we hypothesized that prefrontal cortex and limbic areas (especially amygdala and stress sensitive hippocampus) are vulnerable to the effects of the sexual abuse during adolescence. We also determined the somatosensorial and visual associated areas as a priori regions as smaller gray matter (GM) volumes of these regions are reported in PTSD patients with sexual abuse history [13]. To investigate the gray matter differences, we utilized voxel-based morphometry and cortical thickness measurements as two complementary approaches. Voxel based morphometry is a useful tool to compare GM volumes across groups and uses each voxel. However, cortical thickness analysis is more sensitive to the cortical architecture as the

measurement of the radial distance between the outer and inner borders that spans the cortical layer presents a more suitable instrument for the columnar pattern [14].

2. MATERIAL AND METHODS

2.1. Subjects

Department of Child and Adolescent Psychiatry, Ege University School of Medicine is a reference center for the psychiatric evaluation of traumatized children who are sent by the local Child and Adolescent Court. All children who had sexual abuse incident referred to our department by the court order between 2013 and 2017 are evaluated for the eligibility to our study. The study was approved by the local ethical review board of Ege University School of Medicine (document number: 12-1.1/63). The workflow of the study starts with the application of the subjects with the court order. An experienced child and adolescent psychiatrist from our research team meets the subject and her legal representative or family and informs them about the study. The informed consent clearly explains that the psychiatric evaluation for jurisdictional reasons and the current study are two independent processes; and declining to participate in the study has no impact on the jurisdictional evaluation processes. After obtaining informed consent from the subjects and their legal representatives or families, the same psychiatrist evaluated the subjects and applied the psychometric tests except for the IQ tests. Developmental and medical history of the subjects are obtained from their families and medical records. The psychiatric evaluation process included the Turkish version of The Kiddie Schedule for Affective Disorders and Schizophrenia Present and Lifetime (K-SADS-PL) [15], Beck Depression Inventory (BDI) [16], the State-Trait Anxiety Inventory (STAI) [17], Childhood Trauma Questionnaire (CTQ) [18]. A psychologist applied the Wechsler Intelligence Scale for Children (WISC-R) [19] for the subjects between the ages of 9-16 and the Wechsler Adult Intelligence Scale (WAIS-R) [20] for the subjects after the age of 16. The Magnetic Resonance Imaging (MRI) scans were obtained in the same week and the same psychiatrist escorted the subjects (both abused and control) until all procedures end. We contacted 134 childhood abuse cases and 104 healthy control subjects for the study. As we have limited our interest to the effects of sexual abuse during adolescence, we included only the subjects with a history of sexual abuse during preadolescence and adolescence. One hundred and fourteen sexually abused subjects and 38 healthy control subjects met the inclusion and exclusion criteria. From the sexual abuse group 57 subjects and 33 healthy control subjects accepted to participate in the study. As sexually abused subjects are frequently victims of multiple kinds of trauma adolescents with multiple traumas (e.g., neglect) were not excluded. In total ninety adolescent female subjects between 13 to 18 years old (mean age: 16.5± 0.2) with no developmental delay are included in the study. There were 57 subjects in the sexually abused group and 33 in the healthy control group. Healthy control group was composed of female adolescents who responded to the local advertisements in schools. We included healthy subjects with similar age and education levels to the sexually abused group. Exclusion criteria for both study groups were as follows: having an Intelligence Quotient (IQ) score of 70 or below, a chronic medical illness like asthma or diabetes mellitus, a history of head injury with loss of consciousness longer than three minutes, any neurological illness, a pervasive developmental disorder, any personal or family history of psychotic disorders or bipolar disorder, a history of perinatal complications. Since previous studies reported that antidepressant medications may affect hippocampal volumes; we excluded subjects that used antidepressants within four weeks prior to the study.

2.2. MRI Acquisition

MRI examinations were performed on a 3 Tesla MRI scanner (Siemens, Magnetom Verio, Erlangen, Germany) with 12-channel head coil. Turbo spin-echo T2-weighted, FLAIR and MPRAGE sequences were acquired in all subjects. To exclude any brain abnormalities, an experienced neuroradiologist evaluated TSE T2-weighted and FLAIR images. MPRAGE (Magnetization Prepared Rapid Gradient Echo), which is a 3D T1-weighted sequence (1 mm slice thickness) covering entire brain, was transferred to a personal computer for further structural analyses. A neuroradiologist conducted a clinical evaluation using FLAIR and TSE scans. we used MPRAGE scans for the region of interest analysis. To conduct further analysis, we transferred all imaging data to a PC workstation.

2.3. Cortical Thickness Analysis

We used FreeSurfer Software (ver.6.0 stable) (http://surfer.nmr.mgh.) for cortical thickness analysis[21]. FreeSurfer's processing includes motion correction, removal of non-brain tissue using a hybrid watershed/surface deformation procedure, automated Talairach transformation, and segmentation of the subcortical GM, white matter (WM), cerebrospinal fluid (CSF), and volumetric structures (including the ventricles, caudate, putamen, amygdala and hippocampus). For the segmentation of GM volumes we used recommended mainstream pipeline of FreeSurfer software. Statistics and the final images derived from these segmentations are also a part of FreeSurfer pipeline outputs for regions of interest [21].

2.4. Amygdala and Hippocampus Volume Measurements

This method is an estimation of the probability for each voxel belonging to a certain structure which is based on a priori knowledge of spatial relationships obtained with a training set. It uses an extended (spatial nonstationary) Markov Random Field model for voxel intensities and spatial locations to locate and parcellate subcortical structures. This approach allows the probabilities to vary over space and be anisotropic. An article by Fischl et al [22] describes the stages of processing.

2.5. Voxel-based Morphometry

We manually reoriented the images to place their native-space origin at the anterior commissure using SPM12 (www.fil.ac.uk/spm/) running under Matlab R2016a (The Mathworks, Inc., Natick, MA, USA). The default settings that are described in detail in the manual of the Computational Anatomy Toolbox (CAT12) were used for the next steps of the VBM analysis (http://dbm.neuro.uni-jena.de/cat12/CAT12-Manual.pdf). In order to improve the registration quality of the images we preferred the Diffeomorphic Anatomical Registration through an Exponentiated Lie (DARTEL) algebra algorithm [23]. Preprocessing procedures of the MRI data were as follows. First, we segmented the original individual T1-weighted images into GM, WM and CSF. To identify problems with the images by assessing basic image properties, noise and geometric distortions we used the CAT12 toolbox that provides ratings of image data quality (IQR), after segmentation. All data appeared to have a good-to-excellent quality, so all images of 90 participants were used for further analysis. Second, to create a study-specific template by DARTEL we used the segmented images of all the subjects. Third, we warped the individual segmented images to the study-specific template and we spatially normalized them to Montreal Neurological Institute (MNI) space. Finally, we smoothed modulated the GM images with a 8-mm full width at half maximum (FWHM) isotropic Gaussian kernel. As a result; we obtained the smoothed and modulated GM images for each subject. To test the effects of sexual abuse on specific brain structures a priori regions were determined regarding the findings of previous studies [8,9,12,24] and the hippocampus, parahipocampal gyrus, anterior cingulate cortex, amygdala, insula, orbitofrontal cortex, superior frontal gyrus, middle frontal gyrus, inferior frontal gyrus, somatosensorial cortex, primary visual cortex, fusiform gyrus, precuneus, supramarginal gyrus, angular gyrus and superior temporal gyrus regions were identified using the Wake Forest University PickAtlas Toolbox, Version 2.0.[25] that provides a method for generating region of interest (ROI) masks based on the Talairach Daemon database [26].

2.6. Network Analysis

In order to asses network properties of both groups, Graph Theory Analysis performed on all subjects using cortical thickness values and structural covariance networks approach. A graph is defined as a set of nodes linked by edges, which is represented as ROIs correlated by cortical thickness values in this study. Desikan-Killiany Atlas was used to parcellate cortex into 68 cortical ROIs and mean thickness values were calculated for each region using these ROIs. Interregional correlations between all ROI pairs were calculated and used to construct correlation matrices. We used lowest density value for graph creation in order to obtain smallest fully inter-connected networks for both groups. All network analysis were performed using igraph package [27] for R statistical software package [28].

2.7. Statistical Analysis

All sociodemographic and clinical variables were tested for a normal distribution by using Shapiro Wilk test and Levene’s test for equality of variances. Comparisons between abused and control groups according to the distribution of data were carried out by using Mann-Whitney U or t-test for sociodemographic and clinical variables. We used age and IQ scores as confounding factors during the comparisons among the groups if otherwise stated. Total intracranial volume was also added as a covariate in the one-way analysis of variance

(ANOVA) at the hippocampus and amygdala volume comparisons and VBM analyses. We used General Linear Model for the cortical thickness comparison between the abused and control groups. The Monte Carlo absolute correction values and $p< 0.05$ corrected

RESULTS

3.1 Sociodemographic and Clinical Variables

There was no significant difference between groups, regarding age and education levels. However, IQ scores and socioeconomic status (SES) scores of subjects in the abused group were lower than the control subjects. As one would expect, mean values for BDI, STAI and total CTQ scores of the abused group were higher than the control group. Even though subjects in the abused group had higher scores in all CTQ subscales compared to controls, only the mean value of sexual abuse scores were above the cut-off scores for the sexually abused subjects. For all subjects, the incident of abuse happened when they were 9-17 years old, with 5.3% (n=3) between 9-10 years old, 14% (N=8) between 11-12 years old, and 35.1% (N=20) between 13-14 years old, 38.6% (N=22) between 15-16 years old, and 7% (N=4) when they were 17 years old. Average time elapsed between the incident of abuse and initiation of psychiatric evaluation was 20.1±14.8 months. At the time of evaluation, 21 subjects out of 57 abused individuals (44.3%) had at least one diagnosis, 17 had depression (29.8%), 9 had comorbid depression and PTSD (15.8%). One subject was diagnosed with depression and ADHD, while three (5.3%) had subthreshold depressive symptoms. Although 14 subjects reported using an antidepressant in the past, none of the participants were on any antidepressant drug during the last four weeks into the onset of the study. Three individuals in the abused group (5.3%) reported occasional smoking, 5 preferred not to reply the question on substance abuse, while none in the control group reported a history of any drug abuse

Table1. Demographical and clinical variables of the sexually abused group and the healthy control group.

Variables	Sexually Abused Group (N=57) Mean ± SD	Control Group (N=33) Mean ± SD	Comparison
Age (years)	16.35 ± 1.11	17.6 ± 1.83	U=1043 p > 0.05
Education (years)	9.83 ± 1.47	10.67 ± 1.5	U=1044 p > 0.05
SES	28.6 ± 6.1	28.6 ± 6.1	T=8 df=88 p < 0.001
CTQ Emotional Abuse	10.7±5.6	5.5±1.2	U=250 p<0.001
CTQ Physical Abuse	7.9±4.9	5±0	U=511 p<0.001
CTQ Physical Neglect	8.2±3.4	5.6±1.6	U=459 p<0.001
CTQ Emotional Neglect	12±6.5	7.8±4.2	U=572 p<0.001
CTQ Sexual Abuse	14.8±7.3	5±2	U=184 p<0.001
CTQ Total	53.7±21.5	29±5.1	U=168 p<0.001
BDI Scores	21.2. ±17.3	4.75 ± 4.57	U=414 p < 0.001
STAI 1 Scores	46.3. ±14.8	31.6±7.7	U=414 p<0.001
STAI 2 Scores	49.9±13.6	38.7±6.5	U=404 p<0.001
IQ Scores	82.1 ± 16.3	100.3 ± 10.1	T=5.7 df=88 p < 0.001

Table 1: BDI: Beck Depression Inventory CTQ: Childhood Trauma Questionnaire IQ: Intelligence Quotient SES: Socio-Economic Situation STAI: State-Trait Anxiety Inventory

3.2. The Cortical Thickness Analysis

Pars triangularis (T=3.5 , p<0.01, cluster size=694 mm2, x=51 y=-30 z=6) and the superior temporal cortex(T=2.92, p<0.01, cluster size=595 mm2, x=56 y=-5 z=-9) in the right hemisphere and supramarginal cortex (T=2.74, p<0.01, cluster size=588 mm2 , x=-53 y=-52 z=18) in the left hemisphere had smaller cortical thickness in the abused group when compared to those of controls

3.2.1. The Effect of Sexual Abuse Scores on the Cortical Thickness of the Sexually Abused Group

There was no correlation the effect of CTQ sexual abuse scores IQ and age, no relationship with any corrected cortical region either in the left or right hemisphere, as a result of the correlation analysis.

3.2.2. The Effect of Total Trauma Scores on the Cortical Thickness of the Sexually Abused Group

There was no correlation the effect of CTQ total trauma scores IQ and age, no relationship with any corrected cortical region either in the left or right hemisphere, as a result of the correlation analysis.

3.3. VBM Analysis

VBM analyses revealed that abused group had smaller gray matter volumes of right fusiform gyrus and left thalamus compared to those of controls (Table 2, Figure 2). It was previously reported some areas might be specifically associated with sexually abuse in females. When these areas were determined as a priori regions for ROI analysis and the p value threshold was set to uncorrected 0.001, we observed smaller gay matter volumes in the visual cortices bilaterally but not in the primary somatosensorial areas (Table 2, Figure 2).

Table 2. Gray matter differences between the groups in voxel-based morphometry analysis.

Region	x	y	z	Cluster size (mm3)	P value	t-value	Side	Brodmann Area
Abused<Control								
Fusiform Gyrus	42	-41	-14	823	0.027*	5.06	R	BA 37
Thalamus	-2	-11	11	4833	0.046*	4.89	L	BA 50
Secondary visual association cortex	18	-90	14	607.5	<0.001**	4.44	R	BA 18
Visual association cortex	-9	-90	14	287	<0.001**	4.00	L	BA 18

*The threshold was set at p<0.05 (FWE-corr); *: FWE corrected, **: uncorrected*
L: left, R: right; BA, Brodmann area
x, y, z, coordinates of primary peak locations in the MNI space;
T statistical value of peak voxel showing gray matter difference among the abused and control group

Figure - 2

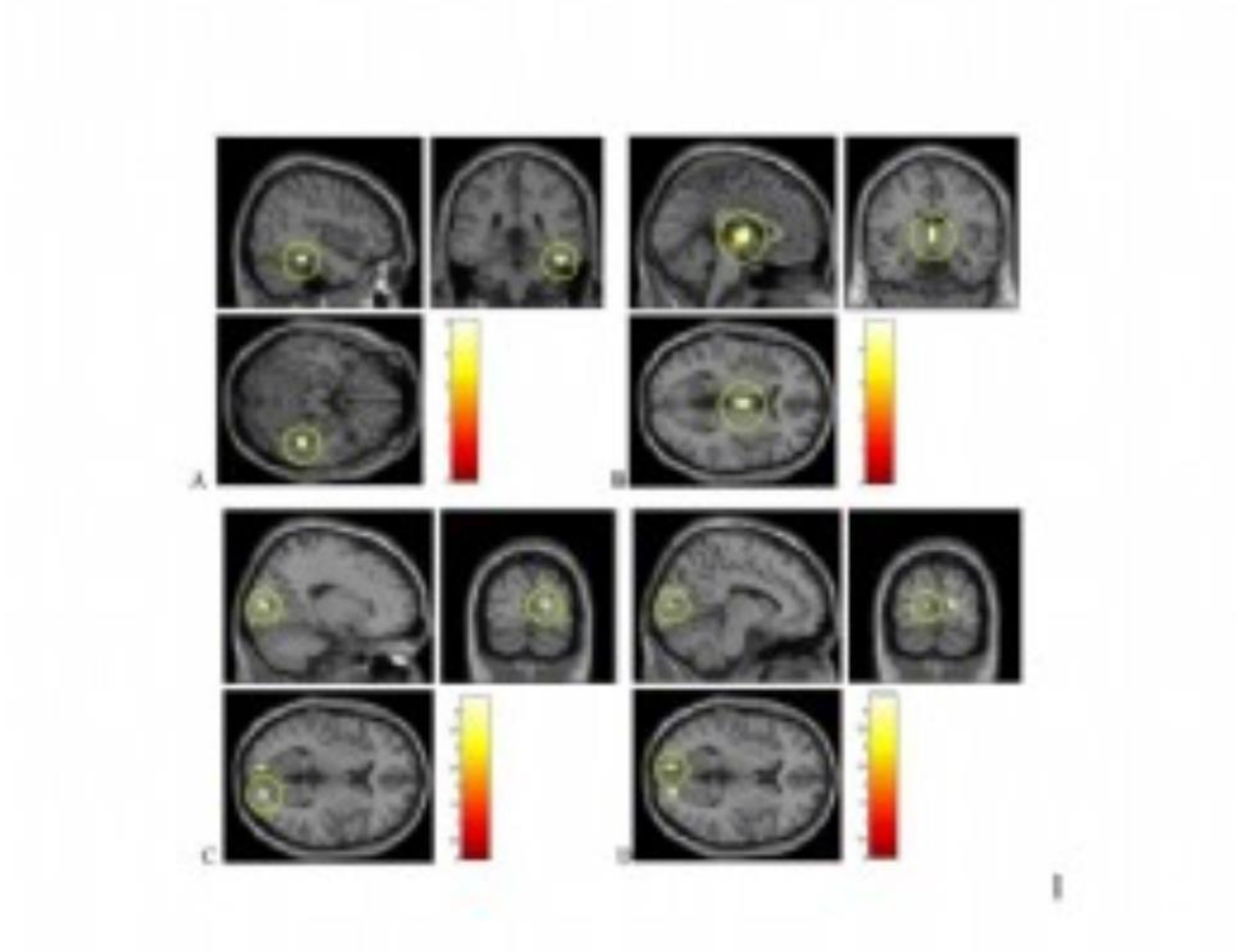

Figure 2. Decreased grey matter volume was detected in the right fusiform gyrus (A), left thalamus (B), right visual association cortex (C) and left visual association cortex (D) for the sexually abused group.

3.4. The comparison of hippocampus and amygdala volumes

Sexually abused subjects had larger right and left hippocampal volumes than those in the control subjects (Table 3). Right amygdala volumes of the abused group had significantly greater volumes than the control subjects while the left amygdala volumes were larger on a trend level significance. We did not find any correlation of hippocampal or amygdala volumes and CTQ for sexual abuse or total CTQ scores.

Table 3. Amygdala and hippocampus volumes of the sexually abused group and the healthy control group.

Volume	Sexually Abused Group (N=57) Mean ± SD	Healthy Control Group (N=33) Mean ± SD	F-value	p-value
R Hippocampus	4208.29±379.90	4117.72±330.65	5.68	p <.05
L Hippocampus	4033.47±364.86	3923.56±336.66	8.45	p <.05
R Amygdala	1746.93±189.72	1692.44±149.3	6.54	p <.05
L Amygdala	1602.39±178.29	1549.89±152.29	3.62	p=0.60

L: Left R: Right

3.5. Network Analysis

We found significant measures of center of gravity in the right superior frontal gyrus ($p<0.001$ uncorrected and $p<0.04$ FDR corrected) in the sexually abused group. We also found significant center of gravity measures in left middle frontal gyrus ($p<0.001$ and $p=0.144$ FDR corrected) in the sexually abused group Moreover, we also found significant center of gravity measures in left superior frontal gyrus ($p<0.001$ and $p<0.01$ FDR corrected) in the sexually abused group. There was no significant difference between the groups regarding network properties at the level of graph, including clustering coefficient, modularity, and reliability (Table 4,

Table 4. Statistical results for network measures of significant nodes

Structure	Network Measure	p value	p value (FDR corrected)
Right Superior Frontal Gyrus	Betweenness Centrality	p<0.001	0.041*
Left Superior Frontal Gyrus	Betweenness Centrality	<0.001	0.01*
Left Middle Frontal Gyrus	Betweenness Centrality	p<0.001	0.144

FDR corrected statistically meaningful p values (p<0.05)

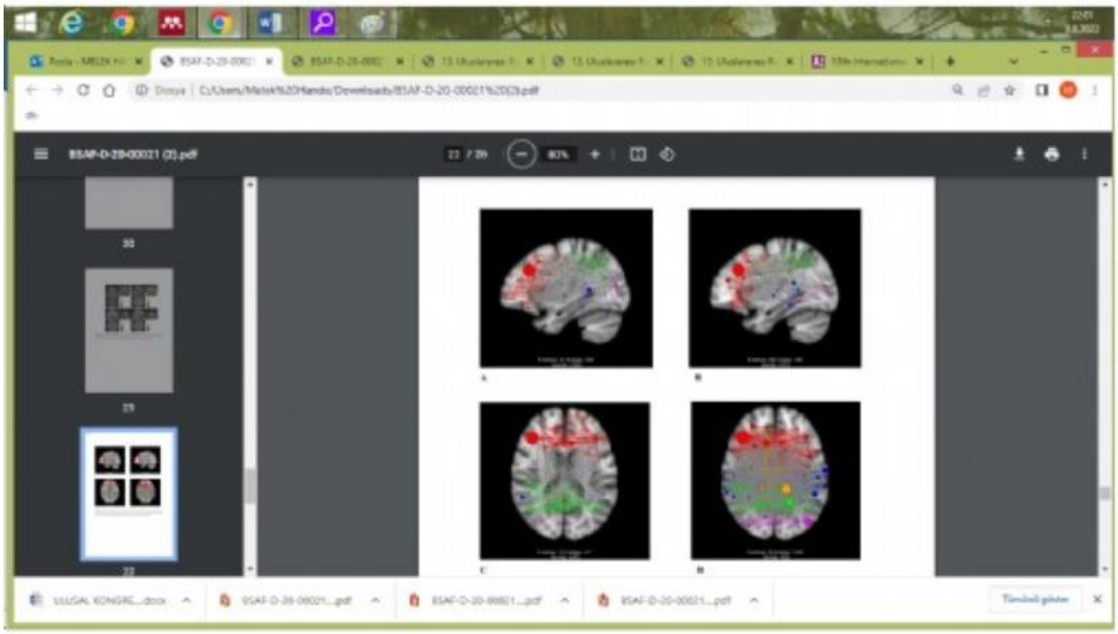

Figure 3: Graph vertex level differences associated with sexual abuse. A Superior frontal gyrus axial plan in the sexually abused group, B Superior frontal gyrus axial plan in the control group, C Superior frontal gyrus sagittal plan in the sexually abused group, D Superior frontal gyrus sagittal plan in the control group

4. DISCUSSION: In this study, we investigated the effects of sexual abuse, which is one of the most significant environmental adverse events in life -time, on the female adolescent brain structure and functionality. When we compared brain structures of 57 subjects with a history of sexual abuse with 33 control subjects we found several differences. In the abused group right pars triangularis of the frontal cortex, superior temporal cortex and left supramarginal cortex had thinner cortical thickness than the control group. When the effects of sexual abuse or total abuse scores are removed from the model the differences in the cortical thickness disappeared. VBM analysis revealed that right fusiform gyrus, left thalamus and bilateral secondary visual cortex volumes were smaller in the abused group when compared with control group. Based on previous studies we determined a priori regions and conducted ROI analysis, which showed that bilateral hippocampus and right amygdala volumes were larger in the abused group when compared with the control group. However, we did not find any correlation of CTQ scores with any of the volume measurements. Betweenness centrality measurements demonstrated alterations of bilateral superior frontal gyri in the abused group. We found smaller cortical thickness volumes in right pars triangularis and right superior temporal cortex which have important roles in non-verbal communication based on emotional cues. Van Schie and colleagues found that during mentalization sexually abused adolescents had increased activity in the left inferior frontal cortex coupled with increased right superior temporal gyrus activity [31]. Likewise, Gold and colleagues found that adolescents with abuse history had thinner inferior frontal cortex and right superior temporal cortex[32]. Along the same lines, Busso and colleagues also found that abused adolescents had smaller cortical thickness in the right inferior frontal gyrus [33]. We also found that sexually abused girls had smaller cortical thickness in the left supramarginal gyrus. There are several studies that found script-driven imagery of sexual abuse led to abnormal responses in inferior parietal lobule including supramarginal gyrus in functional brain imaging [34,35]. Cortical thickness reduction involving inferior frontal gyrus, superior temporal cortex and inferior parietal lobule may have a role in the difficulties that sexually abused individuals experience in mentalizing and giving appropriate emotional responses to social cues. There are few studies focusing on the effect of significant adverse events on the adolescent brain when many of the cortical networks are re-organized at cellular and functional level and the relation of observed differences with the properties of the maltreatment is unclear. Edmiston and colleagues found that regional gray matter volumes of maltreated children are related to CTQ scores though there was a gender effect on the results [9]. On the other hand, Kelly and colleagues

found smaller cortical thickness in children exposed to maltreatment they did not find any correlation of these measurements with the elements of maltreatment (i.e. severity, age of onset and duration) [10]. However, the time gap between the occurrence of the abuse and obtaining the brain images precluded to specify if the observed structural alterations are the outcome of the direct effects of the abuse or result of deviation of the normal neurodevelopmental trajectory of the adolescent brain because of adverse events (short vs long-term effects). In a longitudinal study, Whittle et al found that brain structures may not be directly affected by the presence or severity of the AAE but psychopathology may mediate the effects of these traumatic events on brain structures [11]. In this cross-sectional study we did not find any correlations between the CTQ scores and volumetric measurements, and it is possible that the long-term consequences of the mediator effects of psychopathology on brain structures may be detected by follow-up. We found that the short-term effects of sexual abuse on the adolescence brain are not limited to the emotion regulation areas like frontal lobe and stress sensitive areas like hippocampus and amygdala, but also in the highlevel visual perception and integration areas. Adult studies showed that primary and association areas of the visual system are sensitive to effects of the sexual abuse and the decrease in GM volume is correlated with the duration of exposure before age 12 with gradual impairment in visual memory [13].Other related regions like fusiform and middle occipital gyrus, which play a role in face recognition and processing, also had GM reduction in patients with PTSD that sexually abused before 18 years old [13]. Our findings of reduced GM volume in the visual association areas and fusiform cortex extend the previous findings and suggest that the sensitivity of visual association and face processing areas to the effects of the sexual abuse continues during adolescence. We also observed reduced cortical thickness in supramarginal gyrus which interacts with the visual system and contribute to the control of movements driven by visual spatial information and motor planning by integrating the information coming from other parts of the brain including inferior parietal lobule, inferior frontal gyrus and premotor cortex. It should be noted that supramarginal gyrus is a part of mirror neuron system and help to understand the gestures of the others [36].Some patients report difficulty in remembering events or the environment suggesting further memory problems [37]. Dissociation and dissociation related symptoms are common in abused subjects and it was showed that dissociation and memory functions are closely associated [38]. Our finding of the cortical alterations in frontal cortex, hippocampus and amygdala might be related to defective encoding of the trauma context and moreover associated with dissociative symptoms[39].Memory problems and dissociative symptoms described in other studies might be related to hippocampal volume changes. It is also known that abused subjects have difficulty in maintaining their social relations particularly due to lack empathy which might be related to an inability to the recognition of emotions of others [40].Avoidance behavior to traumatic cues is also common. The impaired social cue reception and facial emotion discrimination might be related to supramarginal cortex, inferior temporal cortex and amygdala volume alterations. In the present study we found larger volumes of bilateral hippocampus and right amygdala in the sexually abused group when compared with control subjects. Amygdala and hippocampus are two adjacent structures, which play a critical role in stress reactivity, context-dependent learning and conditioning especially in threatening situations. Based on the accumulated information of hippocampal sensitivity to stress and bulk of evidence pointing smaller hippocampal volumes in adults with AAE history, we expected to find smaller hippocampal and amygdala volumes in the abused group. Contrary to the findings of previous adult studies [5] and our expectations AAE subjects in our study had larger HCV and amygdala volumes compared to those the controls. Nevertheless, there are also reports of larger hippocampus and amygdala volumes in adults exposed to AAE [41–43]. Moreover, most of the pediatric studies with maltreatment history did not show anatomical differences in stress-sensitive structures including hippocampus, and some studies even found an increased volume of grey matter in HCVs of maltreated young people[44–46]. The inconsistency between child and adolescent studies including ours with adult studies, might be related to the immediate and delayed effects of early life stress. In fact, rodent studies showed that early life stress did not lead to a significant reduction of hippocampal synaptic density up to early adulthood [47]. This idea was supported by the longitudinal study of Whittle and colleagues, that abused adolescents had greater hippocampal volumes at baseline than healthy controls, but during the follow-up, the hippocampus grew more slowly if the subject had any psychopathology [11]. Hippocampus and amygdala volumes follow an inverted Ushaped through healthy childhood and while the hippocampus reaches

peak volume at the age of 17.3, the amygdala has the largest volume at the age of 19.7 [48]. These peak volume ages are later than our subjects. There is also a possibility that structural findings of adult studies regarding medial temporal lobe structures may be related to disproportioned growth of hippocampus and amygdala during this sensitive period. We speculate that our observation of the increased hippocampus volumes in the abused group was related to ongoing neuroplastic changes associated with the processing the traumatic event that took place, which causes a temporary increase of hippocampal growth as suggested by the previous studies showing neuroplasticity related hippocampal volume growth due to memory or navigation-related activities [49,50]. Amygdala, which is responsible for threat detection and rapid response, has been studied extensively in abused subjects. While structural studies produced mixed results, functional studies reported a hyperactive amygdala in abused subjects [51]. It is reported that exposure to early life stress leads to volume increase by supporting new spine and dendritic formation in amygdala, and stress-induced amygdala growth continues long after the stressor stops in animal models, contrary to hippocampal shrinkage [52–54]. A longitudinal study with children suggested that early exposure to maltreatment might increase the volume of amygdala initially but later subsequent exposures to stress lead to a reduction in the amygdala volume [42]. Although early exposure to malnutrition initially increases the volume of amygdala in childhood, it may result in a reduction in amygdala volume in late adolescence or adulthood by sensitizing amygdala to advanced stress[55]. Indeed, other studies which found smaller amygdala were conducted with older participants who had more significant psychopathology and multiple exposures [56]. The greater amygdala volume observed in the abused subjects in our study implies the neuroplastic changes caused by maltreatment in this structure, as shown in preclinical studies. As the current literature suggests, amygdala volumes in our subjects may change by age and multiple stress inducing activity. During adolescence, especially between 14-16 years of age, the prefontal cortex is profoundly reorganized at single neuron and network levels [57]. Indeed, we observed reduced cortical thickness in the pars triangularis in the abused group, suggesting that abuse-related factors negatively impact on the frontal cortex. Furthermore, our network analyses revealed that, sexual abuse during adolescence induces network alterations especially in the frontal cortex. Areas of the superior frontal gyrus showing altered network architecture in our sexually abused subjects have been implicated in a variety of higher order cognitive processes such as working memory [58,59]. Regions that are important in attention, person perception, mentalizing and social cognition have less centrality in the sexually abused group when compared with control group [60]. Sexual abuse is known as one of the major risk factors for future psychiatric symptoms like impulsivity, emotional instability and social disabilities which are related to dysfunctional frontal cortex. Emerging evidence suggest that sexual abuse alters trajectories of brain development to affect sensory systems, network architecture and circuits involved in the reward anticipation , threat detection and emotional regulation [61]. Thus, our findings of altered betweenness centrality measure in the frontal cortex might be related to changed network architecture in the sexually abused adolescence. The presentation of only female adolescence data is one of the limitations of our study and the observed alterations might not reflect the male abused victims. The different maturation trajectory and hormonal status of male and female brains might lead to different structural alterations to similar stress factors among the genders [11,62,63]. Our study group was heterogeneous in many aspects which might decrease the power of the findings. First, it was mixed in terms of the specific diagnoses and patterns of comorbidity, and we did not enough number to examine the effects of a single disorder. Second, even all our subjects had abuse history through the adolescence, brain maturation shows differences in specific areas even in this limited time period. For instance, frontal cortex reaches its peak thickness at age of twelve but temporal lobe at sixteen[64]. Thus, the time of trauma might be an important factor for the neuroplasticity of the response of specific regions to trauma. The cross-sectional design of our study precluded our ability to make deductions on the relationship between the effects of sexual abuse and the differences in cortical thickness and medial temporal lobe structures. Another possibility should be considered regarding our findings. Since medial temporal lobe structures with prefrontal cortex are important in theory of mind functions (i.e. to represent the mental state of others in one's mind) it is plausible that girls with volume or network connectivity differences may also be more susceptible to experience AAE [65].

5. CONCLUSION: In summary, we found differences in cortical thickness, gray matter volume and network architecture in adolescent girls exposed to sexual abuse. We observed significantly reduced cortical thickness in the sexually abused group in three regions: right superior temporal cortex, right pars triangularis cortex and left supramarginal cortex. In addition, VBM analyses revealed significantly smaller volume in the right fusiform gyrus and left thalamus. In medial temporal lobe structures, we observed increased volume in right and left hippocampal and right amygdala. Finally, we found significant network alterations in superior frontal gyrus bilaterally in sexually abused group.

Our observations lend support for the hypothesis that AAE during adolescence may alter brain structure and connectivity as demonstrated by the gray matter changes of cortical regions. The alterations in visual perception and processing regions in sexually abused adolescence may imply an adaptation process to stress, suggesting weakening in sensory systems and paths transmitting repeated aversive experiences [66]. Further studies may have the potential to elucidate the biological basis of the detrimental behavioral effects of sexual trauma, that will lead to improved strategies for the prevention and intervention of trauma related brain alterations. The differences in cortical thickness, gray matter volume and network architecture may represent neurobiological deviations in brain regions managing autobiographical, emotional, cognitive and regulatory processes which may consequently lead to increased risk for psychopathology. Clearly longitudinal studies up to adolescence are needed to scrutinize the role of altered brain structure and network architecture as the biopsychological consequences of sexual abuse.

SUMMARY: The effects of adolescent adverse events (AAE) on brain structures in adult brain is well established. However, there are few reports on the immediate effects of SA on adolescent brain. To investigate the effects of AAE on dynamic brain structures of adolescents. We included fifty-seven female adolescents with a history of AAE during adolescence and thirty-three healthy female adolescents. We compared structural brain images of the groups in terms of cortical thickness, and whole brain VBM and network analysis. We found that hippocampus and amygdala volumes are greater in the abused adolescents and areas in prefrontal, temporal and parietal cortices thicknesses are reduced with AAE as well as visual association and face processing areas. There is also evidence that structural network involving superior frontal gyrus is compromised with AAE. These findings emphasize the importance of having sexual abuse in adolescence, which may cause changes in brain structure.

REFERENCES

[1] De Bellis MD, Spratt EG, Hooper SR. Neurodevelopmental biology associated with childhood sexual abuse. J Child Sex Abus 2011;20:548–87. doi:10.1080/10538712.2011.607753.

[2] Pechtel P, Pizzagalli DA. Effects of early life stress on cognitive and affective function: an integrated review of human literature. Psychopharmacology (Berl) 2011;214:55–70. doi:10.1007/s00213-010- 2009-2.

[3] Romeo RD. The impact of stress on the structure of the adolescent brain: Implications for adolescent mental health. Brain Res 2017;1654:185–91.

[4] Raj A, Silverman JG, Amaro H. The relationship between sexual abuse and sexual risk among high school students: Findings from the 1997 Massachusetts Youth Risk Behavior Survey. Matern Child Health J 2000;4:125–34.

[5] Paquola C, Bennett MR, Lagopoulos J. Understanding heterogeneity in grey matter research of adults with childhood maltreatment—A meta-analysis and review. Neurosci Biobehav Rev 2016;69:299–312. doi:10.1016/j.neubiorev.2016.08.011.

[6] Calem M, Bromis K, McGuire P, Morgan C, Kempton MJ. Meta-analysis of associations between childhood adversity and hippocampus and amygdala volume in non-clinical and general population samples. NeuroImage Clin 2017. doi:10.1016/j.nicl.2017.02.016.

[7] Stark EA, Parsons CE, Van Hartevelt TJ, Charquero-Ballester M, McManners H, Ehlers A, et al. Posttraumatic stress influences the brain even in the absence of symptoms: A systematic, quantitative metaanalysis of neuroimaging studies. Neurosci Biobehav Rev 2015. doi:10.1016/j.neubiorev.2015.07.007.

[8] Teicher MH, Samson JA, Anderson CM, Ohashi K. The effects of childhood maltreatment on brain structure, function and connectivity. Nat Rev Neurosci 2016;17:652–66.

[9] Edmiston EE, Wang F, Mazure CM, Guiney J, Sinha R, Mayes LC, et al. Corticostriatal-limbic gray matter morphology in adolescents with self-reported exposure to childhood maltreatment. Arch Pediatr Adolesc Med 2011. doi:10.1001/archpediatrics.2011.565.
[10] Kelly PA, Viding E, Wallace GL, Schaer M, De Brito SA, Robustelli B, et al. Cortical thickness, surface area, and gyrification abnormalities in children exposed to maltreatment: Neural markers of vulnerability? Biol Psychiatry 2013. doi:10.1016/j.biopsych.2013.06.020.
[11] Whittle S, Dennison M, Vijayakumar N, Simmons JG, Yücel M, Lubman DI, et al. Childhood maltreatment and psychopathology affect brain development during adolescence. J Am Acad Child Adolesc Psychiatry 2013;52. doi:10.1016/j.jaac.2013.06.007.
[12] Andersen SL, Tomada A, Vincow ES, Valente E, Polcari A, Teicher MH. Preliminary evidence for sensitive periods in the effect of childhood sexual abuse on regional brain development. TL - 20. J Neuropsychiatry Clin Neurosci 2008;20 VN-r:292–301. doi:10.1176/appi.neuropsych.20.3.292.
[13] Tomoda A, Navalta CP, Polcari A, Sadato N, Teicher MH. Childhood Sexual Abuse Is Associated with Reduced Gray Matter Volume in Visual Cortex of Young Women. Biol Psychiatry 2009. doi:10.1016/j.biopsych.2009.04.021.
[14] Pakkenberg B, Gundersen HJG. Neocortical neuron number in humans: effect of sex and age. J Comp Neurol 1997;384:312–20.
[15] Gokler, B. & Unal, Fatih & Pehlivanturk, B. & Kultur, Ebru & Akdemir, Devrim & Taner, Y.. (2004). Reliability and Validity of Schedule for Affective Disorders and Schizophrenia for School Age ChildrenPresent and Lifetime Version-Turkish Version (K-SADS-PL-T). Turk J Child Adolesc Ment Health. 11. 109-116.
[16] Hizli IN. A study on the validity of the Beck Depression Inventory. Turkish journal of psychology 1998;6:118–23.
[17] Öner N, LeCompte WA. Durumluk-sürekli kaygı envanteri el kitabı. Boğaziçi Üniversitesi Yayınları; 1985.
[18] Sar V, Ozturk E, Ikikardes E. Validity and reliability of the Turkish version of Childhood Trauma Questionnaire. Turkiye Klin Tip Bilim Derg 2012;32:1054–63.
[19] Savaşır I, Şahin N. Wechsler çocuklar için zeka ölçeği (WISC-R) el kitabı. Türk Psikologlar Derneği Yayınları, Ankara 1995.
[20] SEZGİN N, BAŞTUĞ G, KARAAĞAÇ SY, YILMAZ B. Wechsler Yetişkinler için Zeka Ölçeği gözden geçirilmiş formu (WAIS-R) Türkiye standardizasyonu: Ön çalışma. Ankara Üniversitesi Dil ve TarihCoğrafya Fakültesi Derg 2017;54.
[21] Fischl B. FreeSurfer. Neuroimage 2012;62:774–81.
[22] Fischl B, Salat DH, Busa E, Albert M, Dieterich M, Haselgrove C, et al. Whole brain segmentation: automated labeling of neuroanatomical structures in the human brain. Neuron 2002;33:341–55.
[23] Ashburner J. A fast diffeomorphic image registration algorithm. Neuroimage 2007;38:95–113.
[24] Teicher MH, Anderson CM, Polcari A. Childhood maltreatment is associated with reduced volume in the hippocampal subfields CA3, dentate gyrus, and subiculum. Proc Natl Acad Sci U S A 2012;109:E563- 72. doi:10.1073/pnas.1115396109.
[25] Maldjian JA, Laurienti PJ, Kraft RA, Burdette JH. An automated method for neuroanatomic and cytoarchitectonic atlas-based interrogation of fMRI data sets. Neuroimage 2003;19:1233–9. doi:10.1016/S1053-8119(03)00169-1.
[26] Lancaster JL, Woldorff MG, Parsons LM, Liotti M, Freitas CS, Rainey L, et al. Automated Talairach atlas labels for functional brain mapping. Hum Brain Mapp 2000;10:120–31.
[27] Csardi, Gabor & Nepusz, Tamas. (2005). The Igraph Software Package for Complex Network Research. InterJournal. Complex Systems. 1695.
[28] Team RDC. R: A language and environment for statistical computing. R Found Stat Comput Vienna, Austria 2008.
[29] Ashburner J, Csernansky JG, Davatzikos C, Fox NC, Frisoni GB, Thompson PM. Computer-assisted imaging to assess brain structure in healthy and diseased brains. Lancet Neurol 2003;2:79–88. 15

[30] Lyoo IK, Sung Y H, Dager SH, Friedman SD, Lee J-Y, Kim SJ, et al. Regional cerebral cortical thinning in bipolar disorder. Bipolar Disord 2006;8:65–74.
[31] Schie CC Van, Harmelen A Van, Hauber K, Crone EA, Elzinga BM, Schie CC Van, et al. The neural correlates of childhood maltreatment and the ability to understand mental states of others. Eur J Psychotraumatol. 2017 Feb 9;8(1):1272788.
[32] Gold AL, Sheridan MA, Peverill M, Busso DS, Lambert HK, Alves S, et al. Childhood abuse and reduced cortical thickness in brain regions involved in emotional processing. J Child Psychol Psychiatry Allied Discip 2016;57. doi:10.1111/jcpp.12630.
[33] Busso DS, McLaughlin KA, Brueck S, Peverill M, Gold AL, Sheridan MA. Child Abuse, Neural Structure, and Adolescent Psychopathology: A Longitudinal Study. J Am Acad Child Adolesc Psychiatry 2017;56:321-328.e1. doi:10.1016/j.jaac.2017.01.013.
[34] Bremner JD, Narayan M, Staib LH, Southwick SM, McGlashan T, Charney DS. Neural correlates of memories of childhood sexual abuse in women with and without posttraumatic stress disorder. Am J Psychiatry 1999 Nov;156(11):1787-95. ,
[35] Lanius RA, Williamson PC, Bluhm RL, Densmore M, Boksman K, Neufeld RWJ, et al. Functional connectivity of dissociative responses in posttraumatic stress disorder: A functional magnetic resonance imaging investigation. Biol Psychiatry 2005. doi:10.1016/j.biopsych.2005.01.011.
[36] Teixeira S, Machado S, Velasques B, Sanfim A, Minc D, Peressutti C, et al. Integrative parietal cortex processes: neurological and psychiatric aspects. J Neurol Sci 2014;338:12–22.
[37] Ogle CM, Block SD, Goodman GS, Timmer S. NIH Public Access 2013;25:321–32. doi:10.1017/S0954579412001083.Autobiographical.
[38] Chu JA, Frey LM, Psy D, Ganzel BL, Ed M, Matthews JA, et al. Memories of Childhood Abuse: Dissociation, Amnesia, and Corroboration 1999:749–55.
[39] Flor H, Nees F. Learning , memory and brain plasticity in posttraumatic stress disorder : Context matters 2014;32:95–102. doi:10.3233/RNN-139013.
[40] Leist T, Dadds MR. Adolescents' ability to read different emotional faces relates to their history of maltreatment and type of psychopathology. Clin Child Psychol Psychiatry 2009;14:237–50.
[41] Baldaçara L, Zugman A, Araújo C, Cogo-moreira H, Luiz A, Lacerda T, et al. Reduction of anterior cingulate in adults with urban violence- related PTSD. J Affect Disord 2014;168:13–20. doi:10.1016/j.jad.2014.06.036.
[42] Pechtel P, Lyons-Ruth K, Anderson CM, Teicher MH. Sensitive periods of amygdala development: The role of maltreatment in preadolescence. Neuroimage 2014;97:236–44. doi:10.1016/j.neuroimage.2014.04.025.
[43] Kuhn M, Scharfenort R, Schümann D, Schiele MA, Münsterkötter AL, Deckert J, et al. Mismatch or allostatic load? Timing of life adversity differentially shapes gray matter volume and anxious temperament. Soc Cogn Affect Neurosci 2016;11:537–47. doi:10.1093/scan/nsv137.
[44] Lupien SJ, Parent S, Evans AC, Tremblay RE, Zelazo PD, Corbo V, et al. Larger amygdala but no change in hippocampal volume in 10-year-old children exposed to maternal depressive symptomatology since birth. Proc Natl Acad Sci 2011;108:14324–9.
[45] Woon FL, Hedges DW. Hippocampal and amygdala volumes in children and adults with childhood maltreatment-related posttraumatic stress disorder: A meta-analysis. Hippocampus 2008;18:729–36. [46] Tupler LA, De Bellis MD. Segmented hippocampal volume in children and adolescents with posttraumatic stress disorder. Biol Psychiatry 2006;59:523–9. doi:10.1016/j.biopsych.2005.08.007. [47] Andersen SL, Teicher MH. Delayed effects of early stress on hippocampal development. Neuropsychopharmacology 2004;29:1988–93. doi:10.1038/sj.npp.1300528.
[48] Wierenga L, Langen M, Ambrosino S, van Dijk S, Oranje B, Durston S. Typical development of basal ganglia, hippocampus, amygdala and cerebellum from age 7 to 24. Neuroimage 2014. doi:10.1016/j.neuroimage.2014.03.072.
[49] Draganski B, Gaser C, Kempermann G, Kuhn HG, Bu C. Temporal and Spatial Dynamics of Brain Structure Changes during Extensive Learning 2006;26:6314–7. doi:10.1523/JNEUROSCI.4628- 05.2006.

[50] Maguire EA, Woollett K, Spiers HJ. London taxi drivers and bus drivers: A structural MRI and neuropsychological analysis. Hippocampus 2006;16:1091–101. doi:10.1002/hipo.20233.
[51] Hein TC, Monk CS. Research Review: Neural response to threat in children, adolescents, and adults after child maltreatment–a quantitative meta-analysis. J Child Psychol Psychiatry 2017;58:222–30.
[52] Mitra R, Jadhav S, McEwen BS, Vyas A, Chattarji S. Stress duration modulates the spatiotemporal patterns of spine formation in the basolateral amygdala. Proc Natl Acad Sci U S A 2005;102:9371–6. doi:10.1073/pnas.0504011102.
[53] Vyas A, Jadhav S, Chattarji S. Prolonged behavioral stress enhances synaptic connectivity in the basolateral amygdala. Neuroscience 2006;143:387–93. doi:10.1016/j.neuroscience.2006.08.003.
[54] Vyas A, Pillai AG, Chattarji S. Recovery after chronic stress fails to reverse amygdaloid neuronal hypertrophy and enhanced anxiety-like behavior. Neuroscience 2004;128:667–73. doi:10.1016/j.neuroscience.2004.07.013.
[55] Kuo JR, Kaloupek DG, Woodward SH. Amygdala volume in combat-exposed veterans with and without posttraumatic stress disorder: a cross-sectional study. TL - 69. Arch Gen Psychiatry 2012;69 VNr:1080–6. doi:10.1001/archgenpsychiatry.2012.73.
[56] Teicher MH, Anderson CM, Ohashi K, Polcari A. Childhood maltreatment: altered network centrality of cingulate, precuneus, temporal pole and insula. Biol Psychiatry 2014;76:297–305.
[57] Andersen SL, Teicher MH. Stress, sensitive periods and maturational events in adolescent depression. Trends Neurosci 2008;31:183–91. doi:10.1016/j.tins.2008.01.004.
[58] Boisgueheneuc F Du, Levy R, Volle E, Seassau M, Duffau H, Kinkingnehun S, et al. Functions of the left superior frontal gyrus in humans: A lesion study. Brain 2006. doi:10.1093/brain/awl244.
[59] Haxby J V., Petit L, Ungerleider LG, Courtney SM. Distinguishing the functional roles of multiple regions in distributed neural systems for visual working memory. Neuroimage 2000. doi:10.1006/nimg.2000.0592.
[60] Amodio DM, Frith CD. Meeting of minds: the medial frontal cortex and social cognition. Nat Rev Neurosci 2006;7:268–77. doi:10.1038/nrn1884.
[61] Teicher MH, Samson JA. Annual Research Review: Enduring neurobiological effects of childhood abuse and neglect. J Child Psychol Psychiatry Allied Discip 2016;57:241–66. doi:10.1111/jcpp.12507. [62] Krogsrud SK, Tamnes CK, Fjell AM, Amlien I, Grydeland H, Sulutvedt U, et al. Development of hippocampal subfield volumes from 4 to 22 years. Hum Brain Mapp 2014;35:5646–57. doi:10.1002/hbm.22576.
[63] Ruigrok ANV, Salimi-Khorshidi G, Lai MC, Baron-Cohen S, Lombardo M V., Tait RJ, et al. A metaanalysis of sex differences in human brain structure. Neurosci Biobehav Rev 2014;39:34–50. doi:10.1016/j.neubiorev.2013.12.004.
[64] Giedd JN. The Teen Brain: Insights from Neuroimaging. J Adolesc Heal 2008;42:335–43. doi:10.1016/j.jadohealth.2008.01.007.
[65] Siegal M, Varley R. Neural systems involved in “theory of mind.” Nat Rev Neurosci 2002. doi:10.1038/nrn844. [66] Teicher MH, Tomoda A, Andersen SE. Neurobiological consequences of early stress and childhood maltreatment: Are results from human and animal studies comparable? Ann. N. Y. Acad. Sci., vol. 1071, 2006, p. 313–23. doi:10.1196/annals.1364.024.

[Abstract:0157] [Schizophrenia and other psychotic disorders]

0157 - The relationship beetwen schizoprenia and schizoaffective disorder and light eye color

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INTRODUCTION: Schizophrenia and schizoaffective disorder are chronic mental illnesses that usually occur during adolescence and cause significant disability. Along with genetic and environmental factors, dopamine is the most emphasized assumption in its etiology. Dopamine is a neurotransmitter synthesized from the tyrosine amino acid. Another molecule synthesized from the same premise as dopamine is melanin, which is responsible for human pigmentation. The first step for melanin and dopamine synthesis is the oxidation of tyrosine by tyrosine hydroxylase enzyme. The color and amount of melanin pigment in the iris cells determine the eye color. There are two kinds of melanin pigments in an human being: eumelanin as the dark melanin pigment and pheomelanin as the dark melanin pigment. While eumelanins are the subgroup of black-brown melanin pigments formed by the 5,6-dihydroxyindole intermediate substances, pheomelanins are the subgroup of the yellow-red melanin pigments formed by the oxidation of cysteine-L-DOPA precursors [1] (Figure 1). The regulator of the mechanism controlling the transformation of pheomelanin synthesis from the eumelanin is melanocortin-1 receptor (Mc1r). While eumelanin synthesis occurs by the activation of Mc1r, dopaquinone molecule is transformed to pheomelanin when Mc1r is not active [2]. In addition, dopaquinone also transforms into DOPA by the tyrosinase enzyme. Mutations of Mc1r are reported to be strongly related with red hair and light color skin [3]. Current data suggest that schizophrenia is related with melanin type/levels.
In this study, it was aimed to investigate the relationship of eye color with schizophrenia and schizoaffective disorder, which the impairment in the dopamine system is accepted in their etiology, and also aimed to enlighten to use the eye colour, which is a physical character, as a predictor in schizophrenia and schizoaffective disorder
METHODS: This is an epidemiologic and a multidisciplinary study performed by the Psychiatry and Biostatistics Departments.
As regarded the prevalance of schizophrenia and schizoaffective disorder is 1% and standart deviation (SD) is = 0.01, it is calculated that at least 380 patients, who met the inclusion criteria, should be included into the study. Four thousand patients aging between 18 and 65, who were diagnosed as schizophrenia and schizoaffective disorder according to DSM-V Criteria, were included into the study.
As the eye colour distribution of our country is known, in order to determine the risk status of eye colour on the disease, healthy control group is included into the study with the advice of Biostatistics Department. Four thousand and two patients, aging between 18 and 65, were included as the control group of the study.
Exclusion criteria of the study is as follows: for the patient group; mental retardation, any physical disease or trauma history that can effect eye colour, for the control group; mental retardation, any physical disease or trauma history that can effect eye colour, any neuropsychiatric disease for life, history of psychotic disorder in the family history.
Evaluation of eye colour:
Despite current classification scales are different, eye colours are classified in three categories such as blue, mixed and brown in the most relevant epidemiologic and genetic study [4].

In this study, eye color was determined by 2 clinician as blue, green, hazel, brown and black. The study was presented to the Pamukkale University Ethics Comittee, and approval (date November 6, 2021 and number 60116787-020/78483) was obtained.

RESULTS: The study included 274 schizophrenia patients, 126 schizoaffective disorders and 402 healthy individuals between the ages of 18-65. Mean age of the subjects was 41±12,86 years in the schizophrenia group, 42,5±11,40 years in the schizoaffective disorders group and 44±12,75 years in the healthy group. Of the schizophrenia patients, 146(53,3%) were male and 128(46,7%) were female. Of the schizoaffective disorders, 78(61,9%) were male and 48(38,1%) were female. Of the healthy group, 197(49%) were male and 205(51%) were female.

Although eye colour was evaluted in 5 categories as blue, green, hazel, brown and black in our study, eye colour of the 3 subjects were not definitely decided (dark brown or black) commonly by the clinicians who evalaute eye colours, so nobody has black eye colour in our study.

Distribution of the brown colour through the groups was as follows; 71,9% (n=197) in schizophrenia, 63,3% (n=80) in schizoaffective disorder, 68,7% (n=276) in healthy subjects and brown eye colour was lower in the schizoaffective disorder group, however it is not statistically significant. Although it is not statistically significant, hazel eye colour was higher (22,2% (n=28) in the schizoaffective disorder group according to the other groups; 15% (n=41) in the schizophrenia group and 19,9% (n=80) in the healthy subjects. Distribution of the green colour through the groups was as follows; 7,3% (n=20) in schizophrenia, 8,7% (n=11) in schizoaffective disorder, 7,5% (n=30) in healthy subjects. Blue eye colour was markedly higher, although it is not statistically significant, compared with the healthy subjects in both schizophrenia and schizoaffective disorder groups (5,8%, 5,6%, p=0,462 respectively) (Table 1).

When independent variables; blue, green, hazel and brown eye colours are analyzed on the dependent variables; schizophrenia and schizoaffective disorder, although it is not statistically significant, development of schizophrenia and schizoaffective disorder risk is 1,472 times higher in the subjects having blue colour according to the other eye colours and Wald value was found higher (p=0,246, wald:1,343) according to the other eye colours (Table 2).

Risk of having schizophrenia in the subjects having blue eye colour is 1,5 times higher (%95 CI=0,734-3,064) according to the subjects not having blue eye colour, this risk is 1,402 times higher (%95 CI=0,561-3,505) for schizoaffective disorder, but Wald value was found markedly higher in schizophrenia compared with schizoaffective disorder (Table 3, Table 4).

Disease beginning year (29,5±11,39) in the blue eye coloured schizophrenia was found further in the non-blue eye coloured schizophrenia (25±11,20), and disease beginning year was found similar among the patients having blue and other eye colours in the schizoaffective disorder group. The difference between the groups was not statistically significant (respectively p=0,201-0,907).

Hospitalization was lower in the blue eye coloured schizophrenia compared with the other eye colours and the difference between the two groups was statistically significant (respectively 62,5%-83,3%) (p=0,046).

Referans ve perseküsyon sanrıları, mavi göz rengine sahip şizofreni (sırasıyla %1,3, %93,8) ve şizoafektif bozukluk (sırasıyla tanılı hastalarda Others göz rengine sahip hastalara göre daha sıktı.

Reference and percecutory delusions were found higher in the blue eye colured schizophrenia (respectively 81,3%-93,8%) and schizoaffective disorder (respectively 85,7%, 85,7%) patients according to the patients having other eye colours.

CONCLUSIONS: The results of our study are that the risk of developing schizophrenia in people with blue eye color may be 1.5 times higher than those without blue eye color. In the schizophrenia patients with blue eye color, the age of onset of the disease is advanced, inpatient treatment is less and paranoid features are more common. The results made us think that blue eye color may be a good prognostic marker for schizophrenia, despite the risk of developing schizophrenia in people with blue eye color may be 1.5 times higher.

The lack of a clear relationship between blue eye color and schizoaffective disorder; made us think that it may be caused by the affective part of the disease, so the light eye color may not be related to the affective symptom or disorder.

Consequently, blue eye colour can be a risk factor for schizophrenia, and also can be a good progostic factor. Further studies are needed to confirm our findings and to clarify the etiological mechanisms behind them.
Keywords: Schizophrenia, schizoaffective disorder, eye color, blue, melanine

REFERENCES:
1. d'Ischia M, Wakamatsu K, Napolitano A, Briganti S, Garcia-Borron J-C, Kovacs D, et al. Melanins and melanogenesis: methods, standards, protocols. Pigment Cell Melanoma Res. 2013;26(5):616–33
2. Daal A van. The genetic basis of human pigmentation, Forensic Science International: Genetics Supplement Series. 2008;1(1):541–3
3. Schaffer J V., Bolognia JL. The melanocortin-1 receptor: Red hair and beyond. Archives of Dermatology 2001;137:1477–85
4. Richard A. Sturm ML. Genetics of human iris colour and patterns. Pigment Cell & Melanoma Research 2009;22:5-10

[Abstract:0196] [Attention deficit hyperactivity disorder (ADHD)]

0196 - Reflection of ADHD into adulthood, symptoms in the past and future

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ABSTRACT
Objection: Attention deficit hyperactivity disorder (ADHD) is a chronic disease involving early childhood, adolescence and adulthood. While impulsivity, lack of self-control and struggle with authority may be seen in childhood; emotional fluctuations, illegal transactions and alcohol-substance use are prominent in adulthood. We aim to examine the potential functionality/symptom severity and predictors of short-term outcomes in adolescents diagnosed with ADHD.
Method: Our study group consists of 49 young adults, who were diagnosed as ADHD between 2013-2017 with an age-distribution of 15-18 years. The files of young adults were examined for the severity of ADHD and comorbidity at the time of diagnosis. Sociodemographic Information Form, SNAP-IV and Adult ADHD Self-Report Screening Scale for DSM-V was used.
Results: A positive correlation was found between SES scores and age. While females with ADHD had more comorbid diagnoses and depressive disorder, received fewer traffic penalty, and had lower rates of getting loans from the bank, males showed more criminal problems.
Conclusion: Continuation of ADHD symptoms into adult life brings with some debilitating consequences such as aggrevation of academic and professional functionality, mental and physical impairments, and illegal behaviors with differences regard to gender. Understanding the possible outcomes of ADHD might help to reduce the long term disabilities with specific interventions tailored to at-risk populations as a protective health care service.
Özet
Giriş: Dikkat eksikliği hiperaktivite bozukluğu (DEHB), erken çocukluk, ergenlik ve yetişkinlik dönemini kapsayan kronik bir hastalıktır. Çocukluk döneminde dürtüsellik, özdenetim eksikliği ve otorite ile mücadele görülebilirken; duygusal dalgalanmalar, yasa dışı işlemler ve alkol-madde kullanımı yetişkinlikte öne çıkmaktadır. Çalışmamızda DEHB tanılı ergenlerdeki geleceğe dönük işlevsellik/semptom şiddeti ve kısa dönem bulguların yordayıcılarını incelemeyi amaçlıyoruz.
Yöntem: Çalışma grubumuz 2013-2017 yılları arasında DEHB tanısı almış 15-18 yaş aralığında 49 genç erişkinden oluşmaktadır. Genç erişkinlerin hasta dosyaları tanı anındaki DEHB şiddeti ve komorbidite açısından incelendi. Sosyodemografik Bilgi Formu ve DSM-V için Yetişkin DEHB Öz-Bildirim Tarama Ölçeği kullanıldı.

Bulgular: Sosyo-ekonomik statü puanları ile yaş arasında pozitif bir ilişki bulundu. DEHB'li kadınlarda daha fazla eştanı ve depresif bozukluk, daha az trafik cezası ve bankadan kredi alma oranları daha düşükken, erkekler daha fazla davranım sorunu göstermekteydi.
Sonuç: DEHB belirtilerinin erişkin yaşamda devam etmesi bireylerin akademik ve mesleki işlevselliklerini azaltmakta, ruh ve beden sağlıklarını olumsuz etkilemekte ve madde kullanımı, antisosyal ve yasa dışı davranışlar açısından riski artırmaktadır.
Anahtar Kelimeler: dikkat eksikliği hiperaktivite bozukluğu, genç erişkin, dürtüsellik, prognoz, komorbidite
Introduction: Attention deficit hyperactivity disorder (ADHD) is among the most common neurodevelopmental disorders that begins in childhood and is characterized by inattention, hyperactivity, and impulsivity (1). It is recognized as a chronic disease involving early childhood, adolescence and adulthood (2). According to World Health Organization the worldwide prevalence of adults with ADHD (aged 18–44 years) reported as ~2.8% (range, 0.6–7.3%) (3). Although ADHD is more common in boys than girls, it has been determined that the male cluster is much more intense in clinical-based studies compared to population-based studies (4). 70% of ADHD symptoms appearing in childhood persist until adolescence and 66% until adulthood (5-6).

The clinical manifestations of ADHD show age- and period-specific differences. These differences, which are also taken into account in DSM-V, affect the clinical reflections of daily life. Hyperactivity, which is evident in childhood, leaves its place to attention deficit in adolescence (7). Unwillingness to study, difficulty in planning, forgetfulness and time management problem are findings associated with ADHD in adolescence and early adulthood (8). In addition, although the expressive behaviors of these children decrease with age, emotional fluctuations accompanied by persistent restlessness. Studies have shown that 25-45% of children with ADHD have serious emotional problems (9). Behaviors such as temper tantrums, irritability, making quick decisions without thinking, impulsive activities end with negative consequences, and losing control may cause long-term negative consequences (10). Although it is not part of the basic diagnostic criteria, emotional problems negatively affect the lives of individuals with ADHD by both increasing the severity of ADHD symptoms and causing comorbid diseases (11-14). It has been reported that two main features of ADHD that cause problems in emotion regulation are impulsivity and insufficient self-control (14). While an individual with ADHD shows hypersensitivity to emotional stimuli, he/she has difficulty with managing intense emotions and overcoming them (14). While this situation can manifest itself with impulsivity, lack of self-control and struggle with authority in childhood, it might be seen with emotional fluctuations, illegal transactions and alcohol-substance use in adulthood (15). Individuals, who have problems in monitoring and regulating their own behavior, act impulsively, react without considering the consequences, omit whether people are surprised, angry, or hurt. (16). In addition, these individuals who have a tendency to high-risk behaviors as a potential contributor, may face many negative consequences in the long term, such as accidents as a result of careless driving and delinquency (16, 17).

There is a limited number of studies investigating the transition period of ADHD from childhood throughout life, and there is a need for guidance on how to ensure this transition effectively (18). Our aim in conducting this study is to evaluate the severity of ADHD symptoms and symptomatology after five years of children followed up with the diagnosis of ADHD in our outpatient clinic.

The aim of our study is to examine the functionality and symptom severity of children followed up in our outpatient clinic with the diagnosis of ADHD in adolescence and early adulthood. In this study, it is suggested that the frequency of ADHD diagnosis decreases with age, whereas deviant behaviors such as cigarette-alcohol-substance use, traffic fines, accidents, loan debts that affect daily functioning are common.

Method: This study was designed as a longitudinal study.

Sample

This longitudinal follow-up study was carried out between 1.06.2021-1.10.2021 in Istanbul Marmara University Pendik Training and Research Hospital (MUTRH) Child and Adolescent Psychiatry Clinic. To create the sample of the study, the files of patients form the medical record system of the hospital were abstracted. Data of the patients applied to the outpatient clinic between 2013-2017 years and were between the ages of 15-18 at the time of diagnosis were investigated. Mental retardation, pervasive developmental

disorder, substance abuse, chronic or severe medical conditions, neurologic diseases such as seizure, and presence of psychosis were determined as exclusion criterias of the study. Among those patients, 203 files were found to be diagnosed with ADHD according to DSM-V criteria. 113 patients were called by phone, informed about the study and invited to participate. Sociodemographic Information Form, Adult ADHD Self-Report Screening Scale (ASRS-5) for DSM-V, and study consent forms were delivered online to 66 patients who verbally approved to participate in the study. 12 patients with inappropriately filled forms, 4 patients with mental retardation (in Wechsler Intelligence Scale for Children (WISC-R): those with an intelligence quotient below 70), and 1 patient with a diagnosis of epilepsy were excluded from the study. The remaining 49 adolescents, 18 women and 31 men, have composed our study sample (median: 22.33 years old).
Local Ethics Committee approved the study (protocol number 2021/874).

Assessment Tools

1. Sociodemographic Questionnaire

The sociodemographic characteristics were obtained by using the sociodemographic information form/questionnaire developed by the researcher. In the questionnaire, age, gender, educational status, occupation, the number of people living at home, and the monthly income per person in the family were questioned. In addition to the questions examining alcohol and substance use, comorbid diagnoses, psychiatric medication, and current psychiatric follow-up were evaluated. In the questionnaire, by using a Likert-type scale, yes/no questions were used to evaluate the negative situations that the participants might encounter in adulthood, such as criminal records, traffic fines, history of involving in accidents, frequency of getting into fights, and credit debt. In addition, parents' educational status, occupation, marital status, psychiatric history, and if any, whether their siblings were diagnosed with ADHD were evaluated.
Finally, the socioeconomic status scores of the participants were calculated by evaluating parameters such as their educational status, occupation, and monthly income. An independent scoring system was created for each sub-title, and the socioeconomic status score is calculated by adding the participant's educational status score, occupational group score, monthly income score of his own, monthly income score per capita in the family, mother's educational status score, mother's occupational group score, father's education level score, father's occupational group score.

2. Adult ADHD Self-Report Screening Scale for DSM-V (ASRS-5)

Adult ADHD Self-Report Scale (ASRS-5) for DSM-V is an updated version of the Adult ADHD Self-Report Scale (ASRS v1.1). The validity study of the scale was performed by Ustun et al. (19) in 2017 and Turkish validity and reliability was carried out by Genç et al (20). ASRS-V is a likert-type scale consisting of six questions. The “0-24 continuous score” obtained by scoring each item in the range of 0-4 and with a threshold of 11 in total score, indicating a diagnosis of adult ADHD.

3. SNAP-IV (Swanson, Nolan, and Pelham Rating Scale–Fourth version)

The SNAP-IV is a 26 item likert-type scale including 3 subscales; inattention (nine items), hyperactivity/impulsivity (nine items), and oppositional (eight items). Higher scores represent more problem symptoms, and it is used in population-based studies to identify possible ADHD diagnosis in children (21).

Results: A total of 49 adolescents, 18 females (22.6±0.6 years old), 31 males (22.4±0.6 years), participated in our study. Sociodemographic variables of the participants are summarized in Table 1.

	Female (n=18) n (%)	Male (n=31) n (%)	Statistical analyses
Educational Level			
Secondary School	0 (0)	3 (9.7)	
High School	9 (50)	12 (38.7)	X^2=2.086, p=0.352
University	9 (50)	16 (51.6)	

Maternal Educational Level			
Illiterate	2 (11.2)	1 (3.2)	
Primary School	6 (33.3)	13 (41.9)	X^2=4.949, p=0.293
Secondary School	1 (5.6)	5 (16.1)	
High School	6 (33.3)	11 (35.5)	
University	3 (16.7)	1 (3.2)	
Paternal Educational Level			
Primary School	6 (33.6)	12 (38.7)	
Secondary School	3 (16.7)	5 (16.1)	X2=0.266, p=0.966
High School	7 (38.9)	10 (32.3)	
University	2 (11.1)	4 (12.9)	
Parents Living Together	17 (94.4)	27 (87.1)	X2=1.245, p=0.537
Maternal Psychopathology	4 (22.2)	2 (6.5)	X2= 2,636, p=0.104
Paternal Psychopathology	2 (11.1)	2 (6.5)	X2= 0.330, p=0.566
Unemployment	5 (27.8)	12 (38.7)	X2= 0.601, p=0.438
	Mean±SD	Mean±SD	
Age	22.60±0.64	22.43±0.63	t=0.943, p=0.351
Maternal Age	47.94±6.26	47.29±5.14	t=0.396, p=0.694
Paternal Age	51.22±5.69	52.13±5.40	t=-0.555, p=0.588
Average of household	3.56±1.38	3.45±1.28	t=0.265, p=0.792
Income per Person (Monthly/TL)	1984.16±1268.08	3740.68±4476.25	t=-1.621, p=0,112
Personal Income (Monthly/TL)	2302.78±1627.15	4207.45±5349.88	t=-1.466, p=0.073
SES	6.00±1.30	5.92±1.41	t=-0,199, p=0.843

There was no significant correlation between SES and SNAP teacher-AD score (r=0.014, p=0.944), SNAP teacher-H/I score (r=-0.034, p=0.867), SNAP parent-AD score (r=-0.159, p=0.309), and SNAP parent-H/I

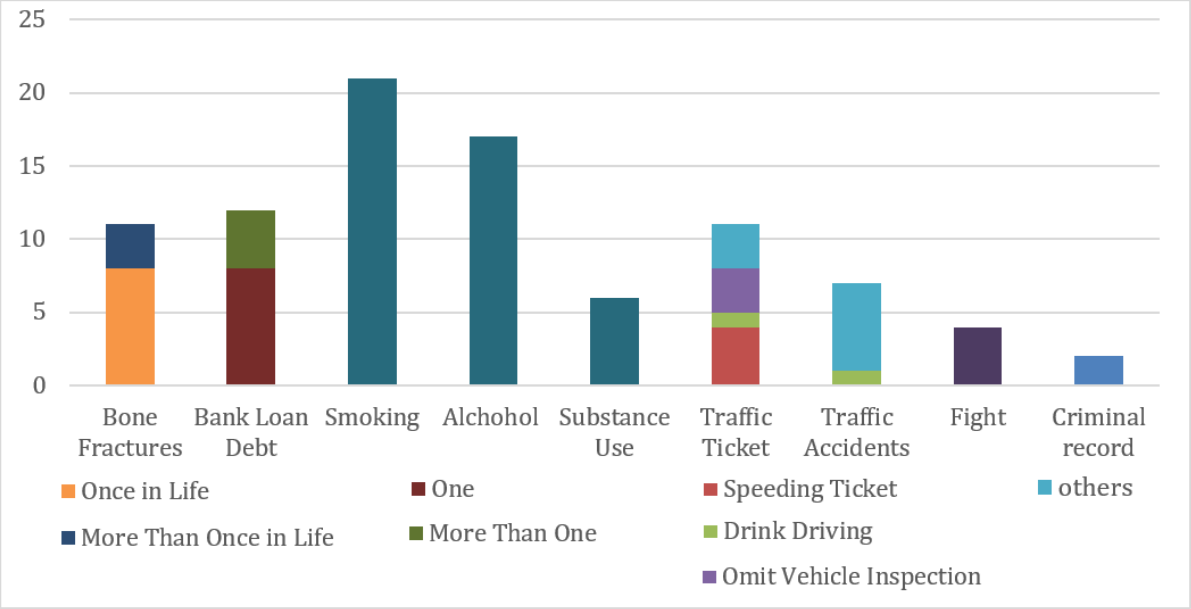
score (r=-0.018, p=0.911). Also, there was a negative correlation between educational level and teacher form H/I (r=-0,535, p=0.005).
No significant difference was found between the genders in terms of SNAP and ASRS-5 scores (Table 2).
Table 2. SNAP and ASRS-5 scores between the gender after removing the effect of socioeconomic level.

	Female (n=18) Mean±SD	Male (n=31) Mean±SD	X^2/Z	*P*	Odds ratio (95% CI) Adjusted[a]
SNAP total	30.78±9.98	29.84±11.51	-0.457	0.648	
SNAP TF-AD score	10.87±4.79	15.31±7.08	-1.614	0.119	
SNAP TF-H/I score	8.37±8.89	14.50±9.54	-1.540	0.137	
SNAP parent-AD score	15.81±6.25	13.81±5.22	1.126	0.267	
SNAP parent H/I score	17.12±5.36	15.92±6.40	0.627	0.534	
ASRS-5 total	9.44±5.17	8.12±4.44	-0.624	0.533	
	N (%)	N (%)			
ASRS-5 total cut off (+)	7 (38.9)	10 (32.3)	0.221	0.638	
Question 1	4 (22.2)	4 (12.9)	0.724	0.395	
Question 2	4(22.2)	4(12.9)	0.724	0.395	
Question 3	6(33.3)	3(9.7)	4.250	0.039*	0.20 (0.04-1.00)*
Question 4	5(27.8)	8(25.8)	0.023	0.880	
Question 5	6(33.3)	13(41.9)	0.355	0.551	
Question 6	5(27.8)	6(19.4)	0.464	0.496	

a Fisher's Exact Test, * p≤0.05, TF: Teacher form, AD: Attention Deficit, H/I: Hyperactivity/ Impulsivity
Psychopathology was present in 6 of the mothers, 3 of whom had mood disorder and 4 of them had anxiety disorder. Psychopathology was present in 4 of the fathers, one of whom had mood disorder and psychotic disorder comorbidly, 2 had anxiety disorder and one had OCD. None of parents have diagnosis of ADHD. Psychopathology was present in 9 of the siblings, 2 of whom had anxiety disorder, 1 had OCD, 2 had neurodevelopmental disorders, 4 had ADHD.
At least one comorbid diagnosis was found in 18% of the young people who participated in the study. Major depression in 14.3%, conduct disorder in 8.2%, oppositional defiant disorder in 6.1%, panic attack in 6.1%, social phobia in 4.1%, substance abuse in 2%, 2% of 49 participants. Generalized anxiety disorder was found in 2%, bipolar disorder in 2%, obsessive compulsive disorder in 2%, enuresis in 2%, encopresis in 2% and post-traumatic stress disorder (PTSD) in 2%. 69.4% of them were taking medication during our child psychiatry follow-up. 16.3% of the young people were still on psychiatric medication. Differences in comorbidity between the genders are summarized in Table 3.
34.7% of the participants in our study were unemployed and the occupational status of the employed participants was as follows: 24.5% low skilled workers, 8.2% unskilled workers, 6.1% small employers, 6.1% casual temporary workers, 6.1% medium skilled workers, 4.1% unpaid family workers, 4.1% marginal jobs,

2% self-employed professionals, 2% mid-level civil servant, 2% self- employed small trader. Low-skilled workers was the most common occupational status for both genders (27.8 for female, and 22.6 for male). Possible current outcomes of ADHD in adult life are summarized in Figure 1.

Figure 1. Possible current outcomes of ADHD in adult life



%75.5 of the participants had problems in daily functioning. 6 different items are evaluated to determine the daily functioning of participants: having a criminal record, having a traffic accident, having their driver's license confiscated, having bank debt, getting involved in fights, and substance use. In line with these items, the rate of daily functioning was higher in women than in men (Table3). There was no significant difference between the groups according to daily functioning in terms of SNAP teacher form-AD score, SNAP teacher form-H/I score, SNAP parent-AD score and SNAP parent-H/I score (p>0.05). It was found that women had more comorbid diagnoses and depressive disorder, received fewer traffic penalties, and had lower rates of getting loans from the bank, even after the covariation of socioeconomic level (Table 3).

Table 3. Comorbidity rates and daily functioning between the genders after removing the effect of socioeconomic level.

	Female (n=18) N (%)	Male (n=31) N (%)	X^2/Z	*P*	Odds ratio (95% CI) Adjusted[a]
Comorbidity	10 (55.6)	8 (25.8)	4.337	0.037*	0.28 (0.08-0.95)*
Depression	5 (27.8)	2 (6.5)	4.230	0.040*	0.17 (0.03-1.03)*
Anxiety Disorders	3 (16.7)	2 (6.5)	1.297[a]	0.342	
Externalization Dis.	2 (11.1)	3 (9.7)	0.026[a]	0.873	

History of Medication	14 (77.8)	20 (64.5)	0.943	0.332	
Current Medication	5 (27.8)	3 (9.7)	2.731	0.098	
History of Methylphenidate	8 (57.1)	17 (58.6)	0.008	0.927	
Daily Functioning	8 (44.4)	17 (54.8)	0.492	0.483	
Criminal Offense	0 (0)	2 (6.5)	1.211[a]	0.526	
Have an accident	2 (11.1)	4 (12.9)	0.034[a]	0.854	
Suspension of driving licence	0 (0)	1 (3.2)	0.593	0.441	
Credit debt	3 (16.7)	9 (29)	0.942[a]	0.494	
Involve in a fight	2 (11.1)	2 (6.5)	0.330	0.618	
Substance use	1 (5.6)	5 (16.1)	1.185	0.393	
Bone fracture	2 (11.1)	10 (32.3)	2.754[a]	0.168	
Smoking	10 (55.6)	15 (48.4)	0.234	0.628	
Alcohol	6 (33.3)	11 (35.5)	0.023	0.879	
Able to get loan from the bank	8 (44.4)	22 (71)	3.375	0.066	
Traffic ticket	0 (0)	11 (35.5)	8.236[a]	.004[**]	NS

[a] Fisher's Exact Test, * $p \leq 0.05$

Discussion: In this study we aimed to find out the outcomes of ADHD in early adulthood. The most prominent result of this study is male participants have more conduct problems and criminal offenses than females. Within this context, daily functioning seemed to be higher in females.

Persistence of ADHD Symptoms

In many longitudinal follow-up studies, it has been observed that a significant rate of ADHD diagnosis and symptoms persist into adulthood. While the diagnosis of ADHD is permanent at a rate of 5.7% to 77%, it was persistent between the rates of 60% and 86% in symptomatology (22). 66% of hyperactive children still

showed at least one of the ADHD symptoms in adult life, and the ongoing symptoms were of higher severity (23). In our study, almost one-third of the participants were diagnosed with possible ADHD. It was determined that women showed persistence at higher rates than men, even if not at a significant level, and had more significant difficulty in unwinding and relaxing compared to the men. This result might show that the emotional dimensions of the symptoms become more significant in the transition to adult life in ADHD women. It should be kept in mind that only the dimensions emphasized in childhood, such as attention, hyperactivity and impulsiveness in ADHD, can change form in adult life such as restlesness and explosiveness and cause impairments in daily functioning.

Academic Functioning: Many studies show that ADHD adversely affects academic life of patients including high school and college success (24-27), and adverse effects of ADHD, especially on academic performance, are improved most consistently with the combination of psychopharmacologic and behavioral interventions (28-30). While considering the treatment schedule, comorbid psychiatric diagnoses should also be taken into account (30). In Turkey the ratio of at least high school graduates in the general population aged 25 years and over was calculated as 45,6% in 2021(TurkStat, National Education Statistics Database, 2008-2021) (31). In our study, one of the outcome was that 42.9% of the participants were high school graduates while 51% were university graduates. Moreover, as the H/I scores in teacher report form increases, educational level deteriorates. Although, our participants seem be more educated compared to statistically the average of Turkey, our results show that it might be influenced by the main parameters of ADHD such as hyperactivity. All of our participants were being followed up by a child psychiatrist, majority of them were having pharmacological treatment, and almost all of the parents were enlightened with a detailed psychoeducation. Moreover our study population has less comorbid rates than expected (32). The high rate of treatment maintenance and less comorbid diagnoses may have caused the participants' education level to be higher than previous reports. By clarifing comorbid diagnoses and participation to early and convenient intervention methods may ameliorate ADHD-related academic problems.

Occupational/Economic Functioning: Studies have reported that patients with ADHD have lower occupational and financial supplies and have difficulties in salary management (33-35). In our study group, 27,8% of women and 38,7% of men were unemployed. Minimum and maximum unemployment rates in Turkey during our data collection period are 15.8%-20.3% for male and 26.1%- 32.1% for female (TURKSTAT, Labour Force Statistics) (36). The unemployment rate for men was higher than reported, while it was similar for women. Considering that women participating in our study are more functional in daily life compared to men, and men diagnosed with ADHD have more impairements in business life than the average, it can be hypotheized that ADHD adversely affects men more than women. Moreover low-skilled workers was the most common occupational status for both genders. This result is not suprising considering that our study was conducted in a tertiary general hospital with low/middle SES, and almost half of the participants were high school graduates.

Antisocial Behaviors and Criminality: In literature there are evidences that childhood hyperactivity might result in higher rates of emergency room visits, susceptibility to accidents, and being sued more often (37-40). It is notified that across various cultures children diagnosed with ADHD exhibit severe antisocial and disruptive behaviors, commit physical attacks and violations of the law those require police interventions more than expected (41-43). Furhermore, having a diagnosis of ADHD in childhood is a potent predictor of tobacco, alcohol and illicit substance use in adulthood (44). Among our participants, although not statistically significant, boys display more problematic behaviours such as substance use, smoking, alcohol drinking, traffic penalty, seizure of driving license, getting involved in fights and have more bone fractures than girls. Regardless of gender, traffic tickets such as speeding, drink driving, and incautious traffic accidents are seen in almost 1/5 of our participants, while 6 participant tried or used substance regularly. Moreover, nearly 15% of our participants had comorbid disruptive behaviour disorders such as conduct disorder and oppositional defiant disorder that may predispose to antisocial personality disorder in the future. Consistent with the literature, these results support that attention deficiency and impulsivity can lead to criminality in common life by impairing executive functions. Considering that our study was conducted on an online platform and

that items such as substance use were illegal, our results might have underestimation bias. More comprehensive face-to-face studies in larger population samples are needed to generalize our results.

Pharmacotherapy and ADHD severity: Parental psychopathology, severity of ADHD, and comorbid diagnoses in chidhood are supposed to be the most prominent factors of ADHD severity in adulthood (45). ADHD severity and functional impairments in adulthood have also been shown to be associated with family-related sociodemographic factors such as per capita income in the family and parental educational level (45). Studies have revealed some conflicting findings for the reciprocal relation between stimulant therapy and daily functioning, including that using drug treatment in childhood was not a predictor of ADHD diagnosis in adult life (46-47). The majority of our participants were receiving drug treatment, especially methylphenidate, at the time of follow-up. A substantial number of participants were currently on medication, but none of the participants were using methylphenidate. Considering one-third of the participants had ADHD symptoms above the cut-off point, the lack of methylphenidate use is striking. While the majority of participants received medication for ADHD in adolescence, it is supposed that the diagnosis of ADHD have gone unrecognised in adult psychiatric clinics and has remained untreated in adult life.

Psychopathology: ADHD is usually accompanied with various psychopathologies mostly including disruptive behavior disorders, depression, and anxiety in adolescents (32). Our study was conducted in mid adolescence age, and many diagnoses were not included due to exclusion criteria. Thereby, our comorbid psychopathologies might be found to be relatively low regarding the literature. Women with ADHD are more prone to have any comorbid psychopathologies such as depressive disorder and anxiety which are linked to mood disorders than man in adulthood (48). In contrast, lifetime rates of substance use disorders and problems with alcohol, as well as antisocial personality disorder and conduct disorder are higher in men with ADHD (48). In our study, overall comorbidity and depressive disorder were higher in female participants than in men during the follow-up period. In addition, men exhibit antisocial behaviors that may be associated with criminality more than women in adult life. Recently, the complaint of feeling of inner restlessness (ASRS question 3) which may be defined as a depressive symptom, was more severe in women. Our finding that comorbid mood disorders mostly seen in ADHD diagnosed women reveal themselves with subjective impairments, including inner restlessness, is consistent with the literature. Given these findings, it can be concluded that these mood symptoms may leave women with ADHD with more distorted cognitions and more vulnerability to the impairing effects of their ADHD compared to men with ADHD (48).

Limitations: Our study should be evaluated considering its limitations and strengths. Out of 203, 90 file had missing data. Since the study was performed online, and some statements in sociodemographic form include confidential information, there might be disclosure bias regarding substance use, and other criminal issues. Furthermore, our sample size was relatively small and there was a limited number of participation to our study, which might be due to our longitudinal and online study design, and the longer the time passes most of the participants were dropped out of hospital follow-up. As far as we know, our study is the first longitudinal reseach analyzing daily functioning of young adults with ADHD in our country. With a longer and comprehensive design, the significance of future studies can be ameliorated.

Conclusion: In our study, symptom severity, comorbidity and long-term outcomes of ADHD were investigated in a group of mid-adolescents in Turkey. As a result of our study, we determined that ADHD did not have prominent longitudinal reflections on employment, education or income level, however, it greatly affects daily functioning. In addition, while a higher rate of comorbidity was found in women, with internalizing symptoms such as depression, externalized behaviors that may be related to criminality and daily functioning such as substance use, bone fracture and traffic ticket were more commonly seen in men. The last but not least, the majority of our study group consisted of young people under regular follow-up and treatment, which might be related with a relatively high SES compared to relevant studies in the literature, and highlights the importance of appropriate and effective treatment in the management of ADHD. Hence, it is important for healthcare providers to be more alert, and considerate about the reflections of ADHD in adult life.

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Keywords: attention deficit and hyperactivity disorder, young adult, impulsivity, prognosis, comorbidity

REFERENCES

1. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders (5th ed). Washington, DC; American Psychiatric Association: 2013.
2. Karacetin, G., Arman, A. R., Fis, N. P., Demirci, E., Ozmen, S., Hesapcioglu, S. T., ... & Tekden, M. (2018) Prevalence of Childhood Affective disorders in Turkey: An epidemiological study. J Affect Disord. 2018 Oct 1;238:513-521. doi: 10.1016/j.jad.2018.05.014. Epub 2018 May 30. PMID: 29936389.
3. Fayyad J, Sampson NA, Hwang I, et al. The descriptive epidemiology of DSM-IV Adult ADHD in the World Health Organization World Mental Health Surveys. Atten Defic Hyperact Disord 2017; 9: 47-65.
4. Skounti, Maria, Anastas Philalithis, and Emmanouil Galanakis. "Variations in prevalence of attention deficit hyperactivity disorder worldwide." European journal of pediatrics 2007; 166.2: 117-123.
5. Langley K, Fowler T, Ford T, et al. Adolescent clinical outcomes for young people with attention-deficit hyperactivity disorder. Br J Psychiatry 2010; 196(3): 235–240.
6. Faraone SV, Asherson P, Banaschewski T, Biederman J, Buitelaar JK, Ramos-Quiroga JA, et al. Attention-deficit/hyperactivity disorder. Nat Rev Dis Primers. 2015;1:15020.
7. Ayaz AB, Ayaz M, Yazgan Y. Dikkat eksikliği hiperaktivite bozukluğunda sosyal cevaplılıkta görülen değişiklikler [Alterations in social reciprocity in attention-deficit hyperactivity disorder]. Turk Psikiyatri Derg. 2013 Summer;24(2):101-10. Turkish. PMID: 23754263.
8. Altın, M., Altın, G. E., & Semerci, B. (2016). An online survey of Turkish psychiatrists' attitudes about and experiences of adult attention deficit hyperactivity disorder in clinical practice. Neuropsychiatric disease and treatment, 12, 2455–2461.
9. Sobanski E., Banaschewski T., Asherson P., Buitelaar J., Chen W., Franke B., et al. . (2010). Emotional lability in children and adolescents with attention deficit/hyperactivity disorder (ADHD): clinical correlates and familial prevalence. J. Child Psychol. Psychiatry Allied Discipl. 51, 915–923. 10.1111/j.1469-7610.2010.02217.x
10. Yazgan Y. Hiperaktif Çocuk Okulda (2017) sf.140-141.
11. Faraone S. V., Rostain A. L., Blader J., Busch B., Childress A. N., Connor D. F., et al. (2019). Practitioner Review: emotional dysregulation in attention-deficit/hyperactivity disorder - implications for clinical recognition and intervention. J. Child Psychol. Psychiatry. 60, 133–150. 10.1111/jcpp.12899
12. Surman C. B., Biederman J., Spencer T., Miller C. A., McDermott K. M., Faraone S. V. (2013). Understanding emotional self-regulation in adults with attention deficit hyperactivity disorder: a controlled study. ADHD Attent. Deficint Hyperact. Disord. 5, 273–281. 10.1007/s12402-012-0100-8
13. Barkley R. A. (2015). Emotional dysregulation is a core componentof ADHD. In R.A. Barkley (Ed.), Attention-Deficit Hyperactivity Disorder: A Handbook for Diagnosis and Treatment (4th edn). New York, NY: The Guilford Press.
14. Corbisiero S., Stieglitz R.-D., Retz W., Rösler M. (2013). Is emotional dysregulation part of the psychopathology of ADHD in adults? Attent. Deficit Hyperact. Disord. 5, 83–92. 10.1007/s12402-012-0097-z
15. Gisbert, Laura, et al. "The impact of emotional lability symptoms during childhood in adults with ADHD." Journal of Attention Disorders 22.6 (2018); 581-590.
16. Faraone, Stephen V., et al. "Practitioner Review: Emotional dysregulation in attention-deficit/hyperactivity disorder–implications for clinical recognition and intervention." Journal of Child Psychology and Psychiatry 60.2 (2019); 133-150.
17. Shoham, Rachel, et al. "ADHD is associated with a widespread pattern of risky behavior across activity domains." Journal of attention disorders 25.7 (2021); 989-1000.

18. Tatlow-Golden, Mimi, et al. "Transitioning from child and adolescent mental health services with attention-deficit hyperactivity disorder in Ireland: Case note review." Early intervention in psychiatry 12.3 (2018); 505-512.
19. Ustun, Berk, et al. "The World Health Organization adult attention-deficit/hyperactivity disorder self-report screening scale for DSM-5." Jama psychiatry 2017; 74.5: 520-526.
20. Genç, Herdem Aslan, et al. "Validity and reliability of the Turkish version of the adult ADHD Self-Report Screening Scale for DSM-5." Balkan Medical Journal 2021; 38.2: 111-125.
21. Swanson JM, Kraemer HC, Hinshaw SP, Arnold LE, Conners CK, Abikoff HB, et al. Clinical relevance of the primary findings of the MTA: success rates based on severity of ADHD and ODD symptoms at the end of treatment. J Am Acad Child Adolesc Psychiatr 2001; 40:168-179
22. Cherkasova MV, Roy A, Molina BSG, Scott G, Weiss G, Barkley RA, Biederman J, Uchida M, Hinshaw SP, Owens EB, Hechtman L. Review: Adult Outcome as Seen Through Controlled Prospective Follow-up Studies of Children With Attention-Deficit/Hyperactivity Disorder Followed Into Adulthood. J Am Acad Child Adolesc Psychiatry. 2022 Mar;61(3):378-391. doi: 10.1016/j.jaac.2021.05.019. Epub 2021 Jun 8. PMID: 34116167.
23. Adler LA, Faraone SV, Spencer TJ, Berglund P, Alperin S, Kessler RC. The structure of adult ADHD. Int J Methods Psychiatr Res. 2017;26(1):e1555
24. Stevens, A. E., Abu-Ramadan, T. M., & Hartung, C. M. (2021). Promoting academic success in college students with ADHD and LD: A systematic literature review to identify intervention targets. Journal of American College Health, 1–14. doi:10.1080/07448481.2020.1862127
25. Sibley, Margaret H et al. “Academic impairment among high school students with ADHD: The role of motivation and goal-directed executive functions.” Journal of school psychology vol. 77 (2019): 67-76. doi:10.1016/j.jsp.2019.10.005
26. Morsink, Sarah et al. “Task-related motivation and academic achievement in children and adolescents with ADHD.” European child & adolescent psychiatry vol. 30,1 (2021): 131-141. doi:10.1007/s00787-020-01494-8
27. Smith, Zoe R et al. “Academic Motivation Deficits in Adolescents with ADHD and Associations with Academic Functioning.” Journal of abnormal child psychology vol. 48,2 (2020): 237-249. doi:10.1007/s10802-019-00601-x
28. Smith, Z. R., Langberg, J. M., Cusick, C. N., Green, C. D., & Becker, S. P. (2019). Academic Motivation Deficits in Adolescents with ADHD and Associations with Academic Functioning. Journal of Abnormal Child Psychology, 48(2), 237–249. doi:10.1007/s10802-019-00601-x
29. DuPaul, George J et al. “Academic Trajectories of College Students with and without ADHD: Predictors of Four-Year Outcomes.” Journal of clinical child and adolescent psychology : the official journal for the Society of Clinical Child and Adolescent Psychology, American Psychological Association, Division 53 vol. 50,6 (2021): 828-843. doi:10.1080/15374416.2020.1867990
30. Austerman, Joseph. “ADHD and behavioral disorders: Assessment, management, and an update from DSM-5.” Cleveland Clinic journal of medicine vol. 82,11 Suppl 1 (2015): S2-7. doi:10.3949/ccjm.82.s1.01
31. https://data.tuik.gov.tr/Bulten/Index?p=Istatistiklerle-Kadin-2021-45635
32. Gnanavel S, Sharma P, Kaushal P, Hussain S. Attention deficit hyperactivity disorder and comorbidity: A review of literature. *World J Clin Cases*. 2019;7(17):2420-2426. doi:10.12998/wjcc.v7.i17.2420
33. Klein RG, Mannuzza S, Ramos Olazagasti MA, et al. Clinical and functional outcome of childhood attention-deficit/hyperactivity disorder 33 years later. Arch Gen Psychiatry. 2012;69:1295-1303.
34. Li, Lin et al. “Association Between Pharmacological Treatment of Attention-Deficit/Hyperactivity Disorder and Long-term Unemployment Among Working-Age Individuals in Sweden.” JAMA network open vol. 5,4 e226815. 1 Apr. 2022
35. Altszuler AR, Page TF, Gnagy EM, et al. Financial dependence of young adults with childhood ADHD. J Abnorm Child Psychol. 2016;44:1217-1229.
36. https://data.tuik.gov.tr/Kategori/GetKategori?p=istihdam-issizlik-ve-ucret-108&dil=1

37. Ramos-Olazagasti MA, Klein RG, Mannuzza S, et al. Does childhood attention-deficit/ hyperactivity disorder predict risk-taking and medical illnesses in adulthood? J Am Acad Child Adolesc Psychiatry. 2013;52:153-162.e4.
38. Cortese S, Ramos Olazagasti MA, Klein RG, Castellanos FX, Proal E, Mannuzza S. Obesity in men with childhood ADHD: A 33-year controlled, prospective, followup study. Pediatrics. 2013;131:e1731-e1738.
39. Pliszka, Steven R. "Attention-Deficit Hyperactivity Disorder Across the Lifespan." Focus (American Psychiatric Publishing) vol. 14,1 (2016): 46-53.
40. Aduen, Paula A et al. "The role of top-down attentional control and attention-deficit/hyperactivity disorder symptoms in predicting future motor vehicle crash risk." Neuropsychology vol. 34,8 (2020): 894-905.
41. Umeda, Maki et al. "Comorbidity and sociodemographic characteristics of adult autism spectrum disorder and attention deficit hyperactivity disorder: epidemiological investigation in the World Mental Health Japan 2nd Survey." International journal of developmental disabilities vol. 67,1 58-66. 15 Mar. 2019, doi:10.1080/20473869.2019.1576409
42. Dirks, Henrike et al. "ADHS im Erwachsenenalter und substanzbezogene Störungen – Prävalenz, Diagnostik und integrierte Behandlungskonzepte" [ADHD in Adults and Comorbid Substance Use Disorder: Prevalence, Clinical Diagnostics and Integrated Therapy]. Fortschritte der Neurologie-Psychiatrie vol. 85,6 (2017): 336-344.
43. Hammerness, Paul et al. "Do Stimulants Reduce the Risk for Alcohol and Substance Use in Youth With ADHD? A Secondary Analysis of a Prospective, 24-Month Open-Label Study of Osmotic-Release Methylphenidate." Journal of attention disorders vol. 21,1 (2017): 71-77.
44. Capuzzi, Enrico et al. "Screening for ADHD Symptoms among Criminal Offenders: Exploring the Association with Clinical Features." Healthcare (Basel, Switzerland) vol. 10,2 180. 18 Jan. 2022
45. Roy A, Hechtman L, Arnold LE, et al. Childhood predictors of adult functional outcomes in the Multimodal Treatment Study of Attention-Deficit/Hyperactivity Disorder (MTA). J Am Acad Child Adolesc Psychiatry. 2017;56:687-695.e7.
46. Rajeh A, Amanullah S, Shivakumar K, Cole J. Interventions in ADHD: A comparative review of stimulant medications and behavioral therapies. Asian J Psychiatr. 2017 Feb;25:131-135. doi: 10.1016/j.ajp.2016.09.005. Epub 2016 Sep 12. PMID: 28262134
47. Swanson JM, Arnold LE, Molina BSG, et al. Young adult outcomes in the follow-up of the multimodal treatment study of attention-deficit/hyperactivity disorder: Symptom persistence, source discrepancy, and height suppression. J Child Psychol Psychiatry Allied Discip. 2017;58:663-678.
48. Williamson, D., & Johnston, C. (2015). Gender differences in adults with attention-deficit/hyperactivity disorder: A narrative review. Clinical psychology review, 40, 15-27.

[Abstract:0201] [Autism Spectrum Disorders]

0201 - Toward the detection of reduced emotion expression: a multicenter broad autism phenotype study

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OBJECTIVE: Although more than 23 years have passed since the first investigation into the BAP, the lack of standardized criteria for BAP complicates attempts to engage in comparative studies of relevant research, although it also inspires researchers to find new methods for exploring this area. Different approaches have been proposed to characterize and detect BAP; however, just as BAP has been defined in various ways, so have a wide range of structured interviews, observational tools, and scales have been used in its assessment [1-4]. Assessment of ASD is far more specific than that of BAP. For instance, while facial analysis, emotion recognition, and mimicry analysis are prominent in the definition of ASD and help to separate its features from the general population, these approaches have barely been applied to research into BAP. The central aim of this paper is to propose a novel methodology for investigating deficits in facial emotional expression in the non-ASD siblings of children with ASD using an open-source software and a validated stimulus task. A secondary aim is to confirm facial expression deficiency in children with ASD as compared with typically developed children and to assess whether this deficit is related to ASD symptom severity.

METHODS:

Setting and Study Design

This prospective, non-interventional, multicenter study was conducted at four centers in Turkey and was approved by the local medical ethics board. Written informed consent was obtained from parents and from children over the age of 12 before the procedure commenced.

Participants

A sample of 60 children with high functioning ASD, 60 non-ASD siblings of children with ASD, and 60 typically developed (TD) children were included in the study. Data from these children were collected between December 2019 and December 2021.

All the children were between 8 and 17 years of age. Exclusion criteria for the groups were a measured IQ score on the Wechsler Intelligence Scale for Children–Revised of < 70 (during recruitment or from a recent IQ evaluation), epilepsy, neurological disorders, or any known genetic disorders such as Down's or Fragile X syndrome, and comorbid psychiatric disorders. The diagnosis of children in the autism group was made by two child and adolescent psychiatrists with the DSM-5-based clinical examination. Similarly, the diagnosis of ASD was excluded by the DSM-5-based clinical examination of the sibling group. The children already clinically diagnosed with ASD, siblings, and the TD children were all screened for the presence of comorbid disorders using both a DSM-5 based clinical examination and the Schedule for Affective Disorders and Schizophrenia for School-Age Children–Present and Lifetime Version, DSM-5, Turkish Adaptation (K-SADS-PL-DSM-5-T). IQ data were not available for the sibling and TD groups, but all participants were

functioning in age-appropriate settings (social, academic, etc.) and were within the normal functioning range. Children in the sibling group are not siblings of the children in the ASD group. Because, although the sibling meets the eligibility criteria, their siblings with ASD may not or vice versa.

Procedure

Participants were told that they would now look at some short scenes to which they should direct their attention entirely. They were told to look directly at the 17" monitor screen, which was approximately 60 centimeters away from the child. Compliance with these instructions was confirmed with video recordings. After each scene, a 10-second break was given before the next scene was presented. The doctor did not tell the children that the webcam was recording them. During the procedure, the participants' faces were recorded with a webcam capable of shooting video at 1920×1080p resolution and at 30fps (frames per second). Figure 1 shows the operation scheme for the study.

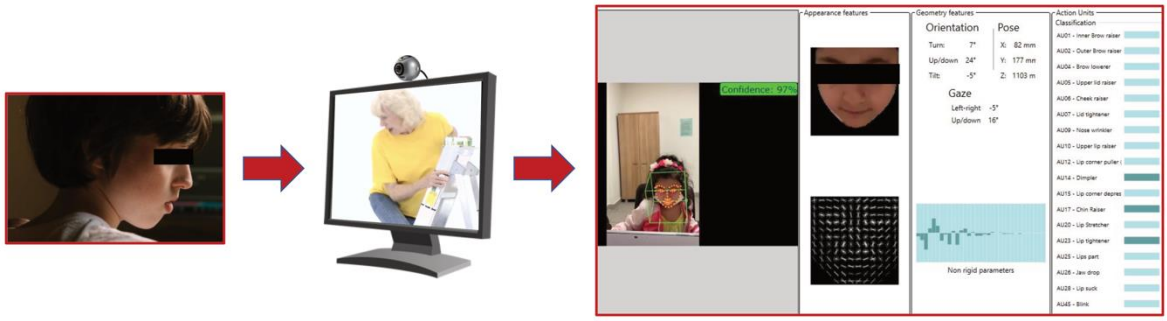

Figure 1. Operation scheme for the study

1.1. Automatic analysis and feature extraction of facial expressions

The facial action coding system (FACS) is widely used as a coding approach for assessments in automatic facial expression analysis and generally in behavioral discipline. FACS analysis facial expressions into 44 observable muscle movements, called action units (AUs). With this aspect, via the face recognition software libraries, a face recognition problem (by observing a still and/or a moving image) is modelled as a multi-class and multi-label classification problem for which the relevant AU (or AUs) is (are) detected at the corresponding image frame. Throughout this study, we used a free and open-source Python and Torch (not to be confused with PyTorch) implemented platform for face recognition with deep neural networks (via utilization of algorithms such as Convolutional Neural Networks supported by other methods such as L_2 normalization) (OpenFace 2.0)[5] in order to obtain facial AUs from the records of the participants' faces. It is Owing to the fast-scripting language LuaJIT (Lua Just In Time), Torch framework enables the use of a variety of machine learning algorithms on the Graphical Processing Units (GPUs) in addition to the Central Processing Units (CPUs) of the computers. This yields the programme to outperform against other similar face recognition platforms in terms of accuracy and the number of evaluations/operations; as demonstrated via the Labeled Faces in the Wild (LFW) database, which is a widely used academic test set for face verification [6]. Thanks to this powerful infrastructure, though not being an official gold standard, the system is a very accurate and rapid face recognition tool, and hence a very feasible tool for the purpose of our study.

Throughout the AU extraction process (from the videos); the following methodology was followed:

- Each video consists of consecutive frames with relatively small movements of the relevant children (mostly his/her facial expressions/mimics) accompanied by still/static background and landmarks.
- OpenFace 2.0 calculates the intensity (on a scale from 0 to 5) of 18 AUs from each video frame.
- Since there is no abrupt change in the consecutive video frames (thanks to the limited movement of the child and the still/static background) for a specific episode, the intensity values of AUs extracted by OpenFace for consecutive frames were averaged throughout the duration of the relevant episode. This is a very common approach referred to as "time-average filtering" which falls in the class of temporal filtering, and is a fundamental technique applied in almost all video compression algorithms; and hence academically and scientifically unarguably accepted. The AUs chosen were based on the emotion FACS (EmFACS) mapping of emotion to AUs.

- The extracted AUs typically were associated with the expression of a specific emotion (Table 1).

Table 1. Task content, associated emotion, and action unit encodings

Stimulus Task	Emotion	Action Unit	FACS Name
Scene 1: An elderly woman is surprised to see an old photograph falling from in a book.	Surprise	AU5 + AU26	Upper lid raiser + Jaw Drop
Scene 2: A boy sits sadly at the table. A girl older than him comes up and pats him on the back.	Sadness	AU1 + AU15	Inner brow raiser + Lip corner depressor
Scene 3: An old woman is afraid to climb the stairs with a box in her hand, and she waits for a while in the middle of the stairs, fearfully.	Fear	AU4 + AU5	Brow lowerer + Upper lid raiser
Scene 4: A boy is lining up chess pieces alone. An older man comes to him holding out a chocolate, the boy smiles, they start playing chess together, the boy smiles and looks happy.	Happiness	AU6 + AU12	Lip corner puller + Cheek raiser
Scene 5: While a woman is drinking something from a glass, another person, who is busy looking at their own phone, comes past and hits her on the shoulder, the woman gets angry.	Anger	AU4 + AU23	Brow lowerer + Lip tightener with risorius
Scene 6: A person opens and smells the milk to prepare herself a coffee, then she is disgusted by the smell.	Disgust	AU9 + AU10	Nose wrinkler, Upper lip raiser

FACS: Facial acting coding system, AU: Action Unit

Emotion Stimulus Task

The EU-Emotion Stimulus Set was created as part of the Autism Spectrum Condition (ASC)-Inclusion project within the European Community's Seventh Framework Programme (FP7/2007-2013; www.ascinclusion.eu; [7]. The purpose of the ASC-Inclusion project was to produce an online socio-emotional training instrument for children with a diagnosis of ASC. The EU-Emotion Stimulus Set is a validated compilation of 418 dynamic multimodal emotion and mental state portrayals exhibited through body gestures, facial expressions, and contextual social scenes. We used the contextual social scenes in this study. For these scenes, one to three actors are requested to perform a social scenario. Each contextual social scene depicts one emotion. In the current study, a 3 minutes 50 seconds contextual social scene, consisting of the six best validated scenes (without any verbal language), were watched. These included six core emotions (surprise, sadness, fear, happiness, anger, and disgust) with 10 second pauses between them (Table 1). The validation (recognition task and emotional impression) study for this evidence-based set has been published [7]. Official permission was obtained from the developers for its use.

Statistical Analysis

The action unit values for the study groups (ASD, Sibling, and TD) were compared using the Kruskal-Wallis test because nonparametric assumptions were met. A post hoc comparison was carried out using the Dunn-Bonferroni test. Epsilon squared was used as effect size measure.

First, spontaneous emotion expression intensity was investigated across the groups: the participants' responses were examined to see whether they expressed relevant AUs in response to the social context videos involving surprise (AU5 and AU26), sadness (AU1 and AU15), fear (AU4 and AU5), happiness (AU6 and AU12), anger (AU4 and AU23), and disgust (AU9 and AU10). P values lower than 0.05 were regarded as statistically significant. The relationships between the CARS scores and the Autism Groups's AU values were assessed by the Spearman Test. The Statistical Package for Social Sciences (SPSS) version 24.0 was used for the data

analysis. Boxplots representing post-hoc compassion (Figure 2) were formed using GraphPad Prism version 9 (San Diego, USA).

RESULTS: Table 2 presents the statistics for the sociodemographic data of the 180 participants. The three groups did not differ significantly in terms of age or sex distribution.

Table 2. Participants' characteristics

	ASD Group (n = 60)	**Sibling Group** (n = 60)	**TD Group** (n = 60)	**p**
Age (months), (mean ± SD)	126 ± 25.7	126 ± 32.1	126 ± 17.1	0.378[b]
Gender (n, %)				
Female	30 (50.0)	30 (50.0)	30 (50.0)	0.999[a]
Male	30 (50.0)	30 (50.0)	30 (50.0)	
Consanguineous marriage (n, %)	6 (10.0)	5 (8.3)	5 (8.3)	0.934[a]
Age at diagnosis (months), (mean ± SD)	35.45 ± 59.7			
IQ Scores (mean ± SD)	81.56 ± 7.63			

a: Chi-squared test, b: Kruskal Wallis test

Table 3 presents a comparison, between groups, of the evidence for each emotion from the specific AUs identified. There were statistically significant differences in the spontaneous emotion expression intensity of the ASD, sibling, and TD groups in the relevant AUs for social context videos involving surprise ($p < 0.001$, effect size = 0.09), sadness ($p = 0.048$, effect size = 0.03), fear ($p = 0.003$, effect size = 0.06), happiness ($p < 0.001$, effect size = 0.19), anger ($p < 0.001$, effect size = 0.07), and disgust ($p = 0.02$, effect size = 0.04) (Table 3).

Table 3. Group comparison of prespecified action units for each emotion

	ASD Group (n=60)		**Sibling Group (n=60)**		**Typically Developed Group (n=60)**		**Kruskal-Wallis p value**	**Effect Size**
	Mean ± SD	**Median (25-75 percentile)**	**Mean ± SD**	**Median (25-75 percentile)**	**Mean ± SD**	**Median (25-75 percentile)**		
AU5+AU26 (Surprise)	0.509 ± 0.315	0.456 (0.252-0.688)	0.533 ± 0.456	0.419 (0.169-0.848)	0.905 ± 0.601	0.887 (0.382-1.336)	<0.001	0.093
AU1+AU15 (Sadness)	0.492 ± 0.388	0.411 (0.172-0.688)	0.620 ± 0.663	0.303 (0.162-0.900)	0.839 ± 0.756	0.551 (0.254-1.365)	0.048	0.034
AU4+AU5 (Fear)	0.376 ± 0.398	0.200 (0.059-0.539)	0.292 ± 0.372	0.150 (0.068-0.346)	0.725 ± 0.808	0.367 (0.119-1.183)	0.003	0.067
AU6+AU12 (Happiness)	0.356 ± 0.398	0.274 (0.065-0.440)	0.246 ± 0.336	0.115 (0.045-0.323)	0.940 ± 0.838	0.723 (0.273-1.532)	<0.001	0.197
AU4+AU23 (Anger)	0.462 ± 0.510	0.366 (0.079-0.641)	0.659 ± 0.668	0.374 (0.106-1.081)	1.065 ± 1.004	0.686 (0.220-1.808)	<0.001	0.079

AU9+AU10 (Disgust)	0.254 ± 0.276	0.147 (0.037-0.481)	0.180 ± 0.334	0.040 (0.010-0.173)	0.198 ± 0.317	0.068 (0.013-0.245)	0.024	0.042

ASD: Autism Spectrum Disorder, AU: action unit, Effect size (epsilon squared): small, medium, and large effect sizes correspond to 0.01, 0.06 and 0.14

Although there was a significant difference between the groups for all scenes, there were no significant differences in the post hoc analyses for Scene 2 (sadness) and Scene 6 (disgust); however, the effect sizes for these scenes were small. When the comparisons with medium and large effect sizes were examined, there was no difference between the ASD and Sibling, but the TD expressed more intense spontaneous emotion expression compared to the other groups, and this difference was statistically significant. Post hoc analyses are shown in Figure 2.

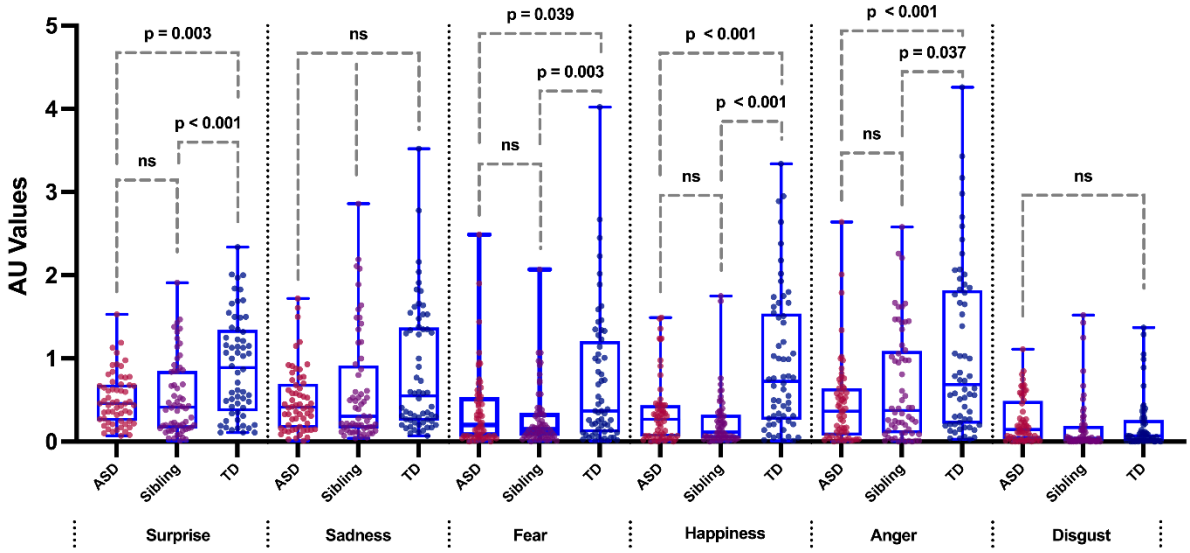

Figure 2. Group comparisons of post-hoc analysis of prespecified action units for each emotion

Table 4 shows the correlation analysis between the childhood autism rating scale (CARS) and the AU values for the ASD group. Although autism severity and emotion expression were not found to be related in the correlation analyses, a weak correlation was observed between the CARS score and anger (r = − 0.279, p = 0.031).

Table 4. Correlation between prespecified action units for each emotion and CARS in the ASD group

	ℝS Score	
	lue	
+AU26 (Surprise)	5	9
+AU15 (Sadness)	)	83
+AU5 (Fear)	)	4
+AU12 (Happiness)	3	)3
+AU23 (Anger)	1	'9
+AU10 (Disgust)	9	)1

r: Spearman's rho, weak, moderate, and strong correspond to 0.39, 0.69 and 0.89, AU: action unit, CARS: Childhood Autism Rating Scale

DISCUSSION: This project was undertaken to design a methodology combining a computer-vision-based program involving emotion recognition with evidence-based social context videos and to evaluate the BAP by

investigating spontaneous emotion expression. The results of the study suggest that the computer-based automated analysis with a validated task of facial expressions holds potential for measuring ability to express emotions through spontaneous emotion expression and that it supports the traditional clinical assessment of phenotypical social behavioral deficits. To the best of our knowledge, our methodology offers the first fully standardized and computer-based measure of non-verbal social behavioral deficits in sibling groups. For some years now, studies assessing the broad autism phenotype have focused on emotion recognition; however, it is only recently that spontaneous emotion expression studies, which offer a more sophisticated understanding of the precise nature and limits of emotional expression, have been investigated [8].

REFERENCES

1. Bolton P, Macdonald H, Pickles A, et al. A case-control family history study of autism. Journal of child Psychology and Psychiatry. 1994;35(5):877-900.
2. Dawson G, Estes A, Munson J, Schellenberg G, Bernier R, Abbott R. Quantitative assessment of autism symptom-related traits in probands and parents: Broader Phenotype Autism Symptom Scale. Journal of autism and developmental disorders. 2007;37(3):523-536.
3. Baron-Cohen S, Wheelwright S, Skinner R, Martin J, Clubley E. The autism-spectrum quotient (AQ): Evidence from asperger syndrome/high-functioning autism, malesand females, scientists and mathematicians. Journal of autism and developmental disorders. 2001;31(1):5-17.
4. Hurley RS, Losh M, Parlier M, Reznick JS, Piven J. The broad autism phenotype questionnaire. Journal of autism and developmental disorders. 2007;37(9):1679-1690.
5. Baltrusaitis T, Zadeh A, Lim YC, Morency L-P. Openface 2.0: Facial behavior analysis toolkit. IEEE; 2018:59-66.
6. Huang GB, Ramesh M, Berg T, Learned-Miller E. Labeled faces in the wild: a database for studying face recognition in unconstrained environments. Univ. Massachusetts, Amherst, MA, USA. 2007;
7. O'Reilly H, Pigat D, Fridenson S, et al. The EU-emotion stimulus set: a validation study. Behavior research methods. 2016;48(2):567-576.
8. Trevisan DA, Hoskyn M, Birmingham E. Facial expression production in autism: A meta-analysis. Autism Research. 2018;11(12):1586-1601.

[Abstract:0204] [Schizophrenia and other psychotic disorders]

0204 – Vortioxetine improved negative and cognitive symptoms-like behaviors on MK-801 induced schizophrenia model in rats

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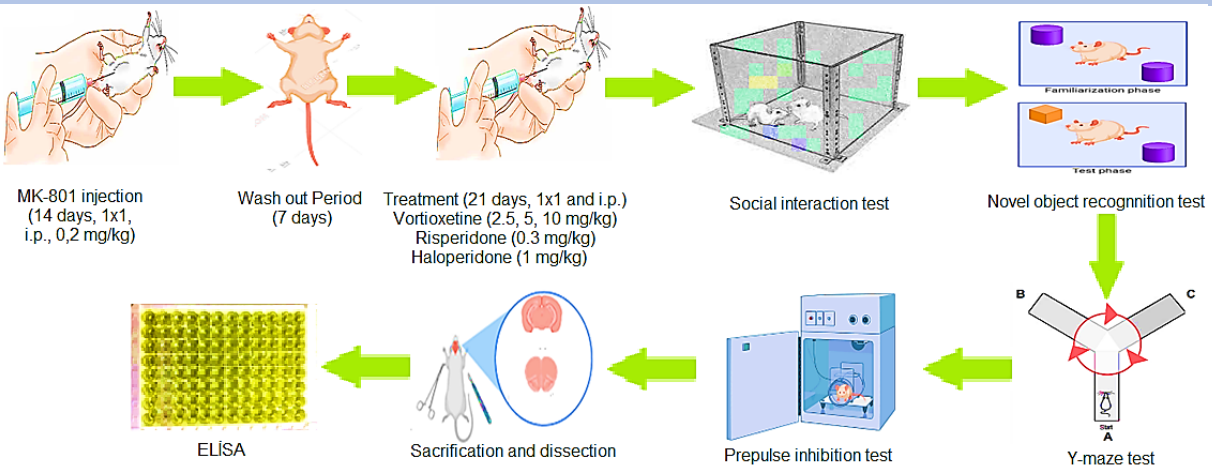
INTRODUCTION: Schizophrenia is one of the important neuropsychiatric diseases with complex symptoms and neurobiology, affecting approximately 1% of the world's population. Although dopaminergic and glutamatergic systems are thought to have central roles in neurobiology, serotonergic dysregulation is known to contribute to the pathogenesis of schizophrenia. Although positive symptoms can be significantly reduced with current treatment approaches in schizophrenia, no significant success can be achieved in the treatment of negative and cognitive symptoms. Therefore, researches have focused on novel therapeutic approaches for better treatment for schizophrenia [1].
Glutamatergic hypoactivity is one of the most debated hypotheses about the pathophysiology of schizophrenia. Studies have shown that administration of NMDA receptor antagonists such as Ketamine and MK-801 causes psychosis-like expressions in healthy volunteers and schizophrenia-like behavioral and neurobiological

changes in rodents. Acute administration of NMDA receptor antagonists has been shown to be useful in screening for the antipsychotic-like effects of new therapeutic approaches in rats [2].
Vortioxetine; It is a new multimodal antidepressant with 5-HT1A receptor agonist, 5-HT1B receptor partial agonist, 5-HT3, 5-HT7 and 5-HT1D receptor antagonist and inhibitory effect on serotonin reuptake pumps. It has been thought that vortioxetine may have a beneficial effect on schizophrenia due to its multimodal regulatory role in the serotonergic system in the brain, and limited studies suggest that vortioxetine may have a potential therapeutic effect, especially on the negative and cognitive symptoms of schizophrenia. Therefore, in this study, it was aimed to investigate the effects of vortioxetine on schizophrenia-like behaviors in a schizophrenia model induced with MK-801 in rats [3].
MATERIAL AND METHODS: Adult female Wistar albino rats were used in our study. Rats were obtained from Erciyes University Experimental Research Application and Research Center. All experiments were conducted in this study were approved by the Erciyes University Animal Research Ethics Committee. Wistar albino rats were grouped as saline, MK-801 (0,2 mg/kg), MK-801+vortioxetine (2,5 mg/kg), MK-801+vortioxetine (5 mg/kg), MK-801+vortioxetine (10 mg/kg), MK-801+haloperidol (1 mg/kg) and MK-801 + risperidone (0,3 mg/kg). The eight rats were used in each group.
MK-801 Hydrogen Maleate (Sellect Chemical) and Vortioxetine (Lundbeck, Denmark) were dissolved in saline. Risperidone (Janssen, Belgium) and Haloperidol (Aris, Turkey) were diluted with saline. The injection volume of chemicals was 0.1 mL/100 g. The study flowchart is summarized in Figure 1.
GraphPad Prism8.0 program was used for all statistical analysis. Data are presented as mean ± standard error, and our data was considered statistically significant when $p<0.05$.

Keywords: GAD67, Novel object recognition test, Parvalbumine, Schizophrenia, Social interaction test, Vortioxetine



RESULT

Vortioxetine increased the discrimination index in the NOR task

All groups spent more time with the new object (Figure 1).

The discrimination indexes increased in the Vortioxetine (5 mg/kg) ($p<0.001$), vortioxetine (10 mg/kg) ($p<0.001$) and risperidone ($p<0.001$) groups (Figure 2).

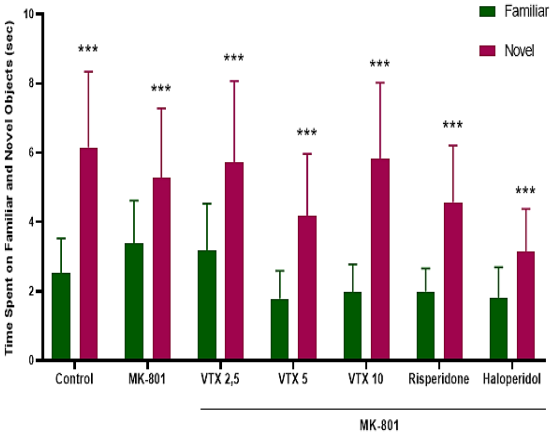


Figure 1. The time spent by experimental groups with familiar and novel objects in the novel object recognition test. The values were shown as mean ± standard error. The time spent with old and new objects was compared with the Student's-t test, which was paired within each group. Compared with older objects ***: $p<0.001$.

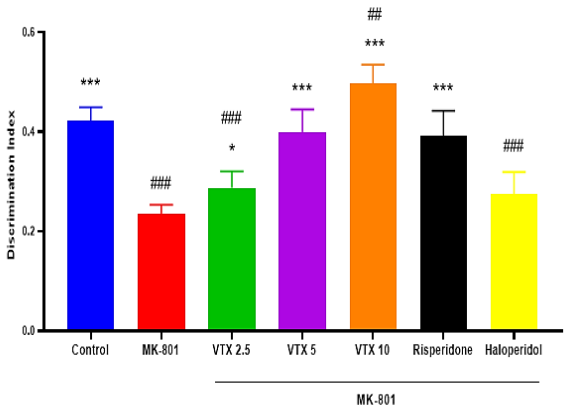


Figure 2. Comparison of the effect of the treatment groups on the discrimination index in the novel object recognition test with the control and MK-801 groups. Values were expressed as mean ± standard error. Comparisons between groups were made using one-way ANOVA and post hoc Dunnett's test. Compared with the control group, it is ###: $p<0.001$ and ##: $p<0.01$, when compared with the MK-801 group, ***: $p<0.001$ and *: $p<0.05$.

Vortioxetine increased sniffing, climbing and following behaviors while decreasing avoiding behavior

MK-801+vortioxetine (5 mg/kg) (p<0.001), MK-801+ vortioxetine (10 mg/kg) (p<0.001) and MK-801+ risperidone (p<0.001) groups increased sniffing (Figure 3).

MK-801+vortioxetine (2.5 mg/kg) (p<0.001), MK-801+vortioxetine (10 mg/kg) (p<0.001) and MK-801+ risperidone (p<0.001) groups increased following (Figure 4).

MK-801+vortioxetine (2.5 mg/kg) (p<0.001), MK-801+vortioxetine (5 mg/kg) (p< 0.01) MK-801+vortioxetine (10 mg/kg) (p<0.001) and MK-801+risperidone (p<0.001) groups increased climbing (Figure 5).

Vortioxetine (5 mg/kg) (p<0.001), vortioxetine 10 mg/kg (p<0.001), risperidone (p< 0.001) and haloperidol (p<0.001) decreased avoiding (Figure 6).

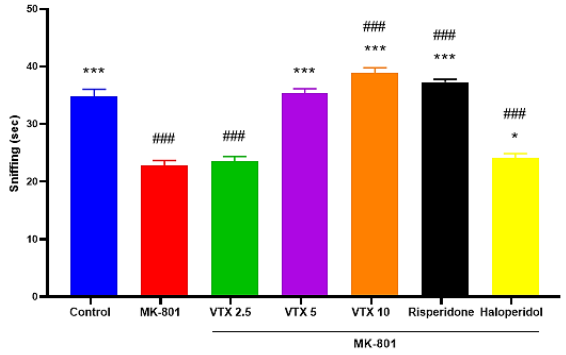


Figure 3. Comparison of the effect of treatment groups on sniffing time in social interaction test with control and MK-801 groups. Values were expressed as mean ± standard error. Comparisons between groups were made using one-way ANOVA and post hoc Dunnett's test. Compared to the control group, it is ###: p<0.001, compared to the MK-801 group, ***: p<0.001 and *: p<0.05.

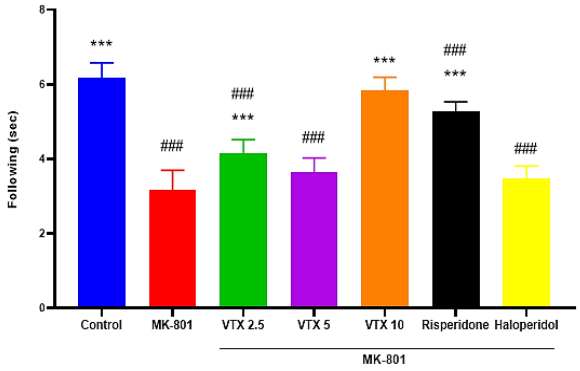


Figure 4. Comparison of the effect of treatment groups on following time in social interaction test with control and MK-801 groups. Values were expressed as mean ± standard error. Comparisons between groups were made using one-way ANOVA and post hoc Dunnett's test. Compared to the control group, it is ###: p<0.001, compared to the MK-801 group ***: p<0.001.

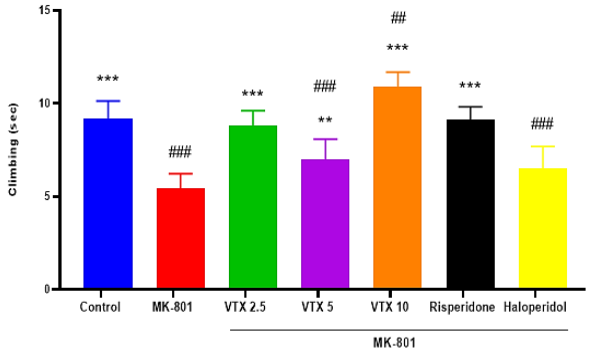


Figure 5. Comparison of the effect of treatment groups on climbing time in social interaction test with control and MK-801 groups. Values were expressed as mean ± standard error. Comparisons between groups were made using one-way ANOVA and post hoc Dunnett's test. Compared with the control group, it is ###: p<0.001 and ##: p<0.01, when compared with the MK-801 group, ***: p<0.001 and **: p<0.01.

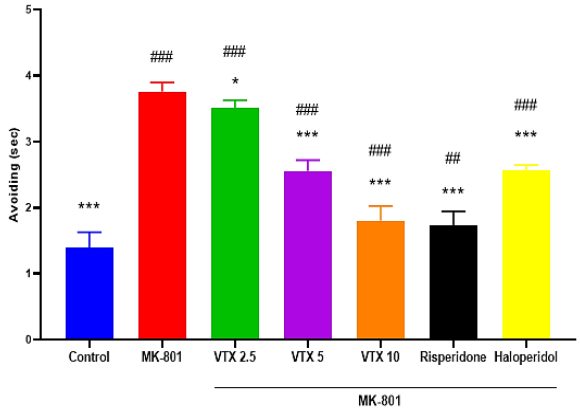


Figure 6. Comparison of the effect of treatment groups on avoidance time in social interaction test with control and MK-801 groups. Values were expressed as mean ± standard error. Comparisons between groups were made using one-way ANOVA and post hoc Dunnett's test. Compared with the control group, it is ###: p<0.001 and ##: p<0.01, when compared with the MK-801 group, ***: p<0.001 and *: p<0.05.

Vortioxetine increased the percentage of alternation in the y-maze test

When we compare the percentage of alternation of the MK-801 group with the control group, a significant decrease is observed in the MK-801 group ($p<0.001$). Vortioxetine (5 mg/kg) ($p<0.001$), vortioxetine (10 mg/kg) ($p<0.001$) and risperidone ($p<0.001$) improved percentage of alternation (Figure 7).

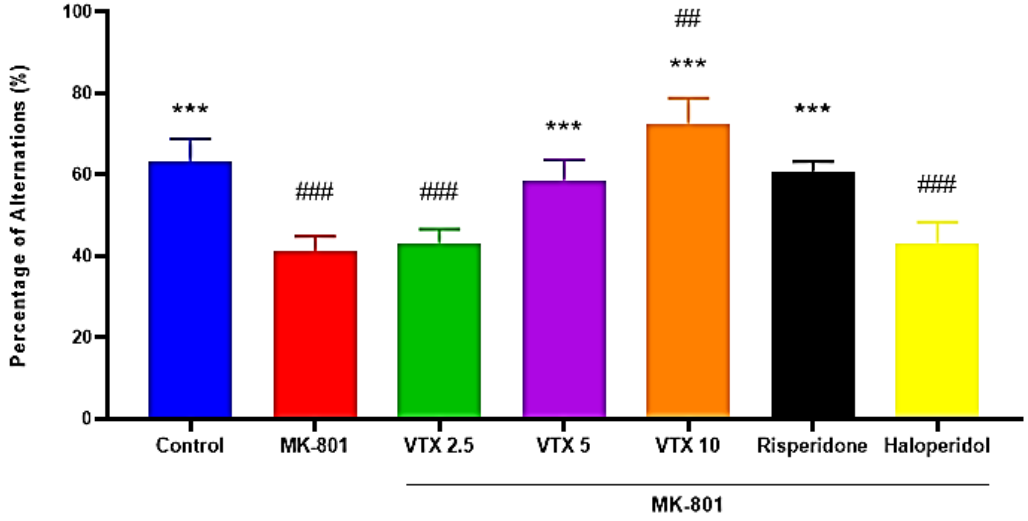


Figure 7. Comparison of the effect of the treatment groups on the percentage of alternation in the Y-maze test with the control and MK-801 groups. Values were expressed as mean ± standard error. Comparisons between groups were made using one-way ANOVA and post hoc Dunnett's test. Compared to the control group, it is ###: $p<0.001$ and ##: $p<0.01$, compared to the MK-801 group, ***: $p<0.001$.

Vortioxetine worsened the MK-801 induced deficits in the PPI test

The results indicated that MK-801 administration decreased the prepulse inhibition (%) compared to saline in +4 dB ($p<0.001$), +8 dB ($p<0.0001$), and +16 dB ($p<0.001$) prepulse intensities in the PPI test. It was determined that the rats treated with MK-801 inhibited startle less than +4 dB ($p<0.001$), +8 dB ($p<0.0001$) and +16 dB ($p<0.001$) stimulus at prepulse intensities compared to the control group. Among the treatment groups, risperidone's impairment in MK-801's inhibition mediated by prepulse was at +4 dB prepulse intensity ($F (6, 49) = 18.22$ and $p<0.001$), +8 dB prepulse intensity ($F (6, 49) = 40.22$ and ($p<0.0001$) and +16 dB prepulse intensity ($F (6, 49) = 29.05$ and $p<0.001$). Haloperidol, one of the treatment groups, caused the impairment of MK-801 in inhibition mediated by prepulse at +4 dB prepulse intensity ($F (6, 49) = 18.22$ and $p<0.01$), +8 dB prepulse intensity ($F (6, 49) = 40.22$ and $p<0.01$) and +16 dB prepulse intensity ($F (6, 49) = 29.05$ and $p<0.5$). It was determined that MK-801 did not reverse the decrease in prepulse inhibition, on the other hand, treatment groups treated with vortioxetine (Figure 8).

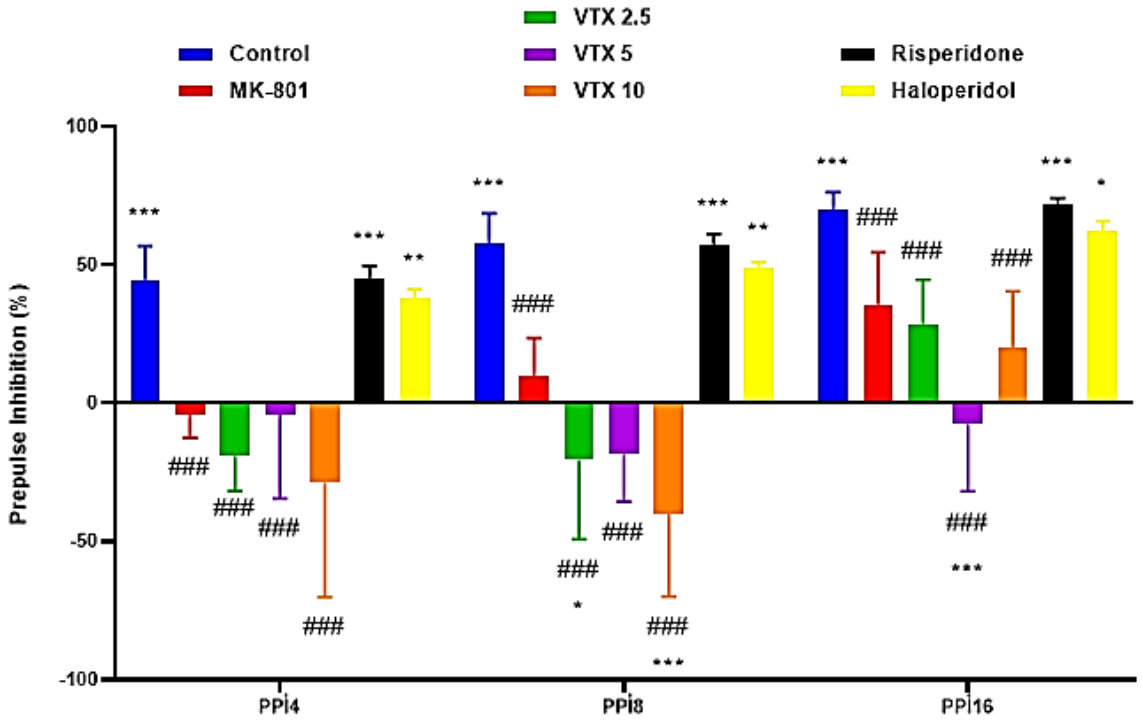


Figure 8. Comparison of the effect of treatment groups on percent inhibition in prepulse inhibition test with control and MK-801 groups. Values were expressed as mean ± standard error. Comparisons between groups were made using one-way ANOVA and post hoc Dunnett's test. Compared to the control group, it is ###: $p<0.001$, compared to the MK-801 group ***: $p<0.001$, **: $p<0.01$ and *: $p<0.05$.

Brain GAD67 levels in ELISA test

The level of GAD67 in the frontal cortex ($p<0.001$), prefrontal cortex ($p<0.001$) and ventral hippocampus ($p<0.01$) was decreased in the MK-801 group compared to the control group ($p<0.001$).

Vortioxetine (5 mg/kg) ($p<0.001$), vortioxetine (10 mg/kg) ($p<0.001$), haloperidol ($p<0.001$) and risperidone ($p<0.001$) increased GAD67 level (Figure 9).

Vortioxetine (5 mg/kg) ($p<0.001$), vortioxetine (10 mg/kg) ($p<0.001$) and haloperidol ($p<0.001$) and risperidone ($p<0.001$) increased GAD67 level (Figure 10).

When the GAD67 levels in the dorsal hippocampus were examined, no statistical difference was found between the control group and the MK-801 group (Figure 11).

Vortioxetine (2.5 mg/kg) ($p<0.001$), vortioxetine (5 mg/kg) ($p<0.001$), vortioxetine (10 mg/kg) ($p<0.001$), haloperidol ($p<0.001$) and risperidone ($p<0.001$) increased GAD67 level (Figure 12).

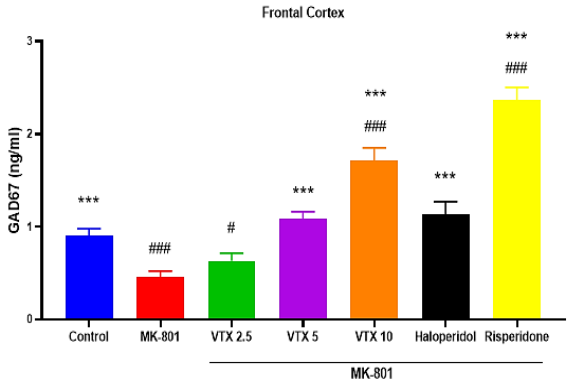


Figure 9. Comparison of the effect of treatment groups on GAD67 levels in frontal cortex with control and MK-801 groups. Values were expressed as mean ± standard error. Comparisons between groups were made using one-way ANOVA and post hoc Dunnett's test. Compared to the control group, it is ###: p<0.001, #: p<0.05, compared to the MK-801 group ***: p<0.001 and **: p<0.01.

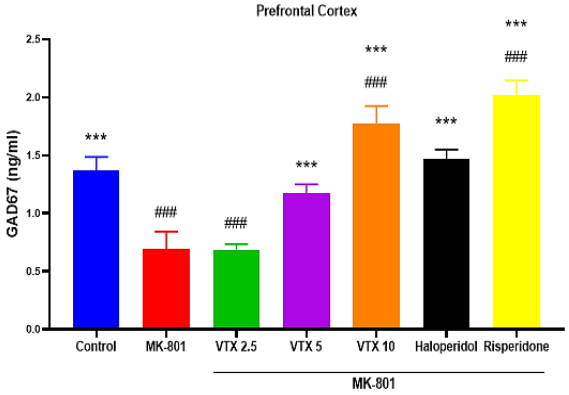


Figure 10. Comparison of the effect of treatment groups on GAD67 levels in the prefrontal cortex with control and MK-801 groups. Values were expressed as mean ± standard error. Comparisons between groups were made using one-way ANOVA and post hoc Dunnett's test. Compared to the control group, it is ###: p<0.001, compared to the MK-801 group ***: p<0.001.

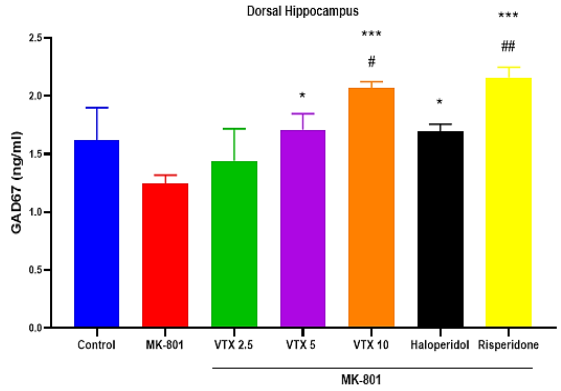


Figure 11. Comparison of the effect of treatment groups on GAD67 levels in the dorsal hippocampus with control and MK-801 groups. Values were expressed as mean ± standard error. Comparisons between groups were made using one-way ANOVA and post hoc Dunnett's test. Compared to the control group, it is ##: p<0.01, #: p<0.05, compared to the MK-801 group ***: p<0.001, *: p<0.05.

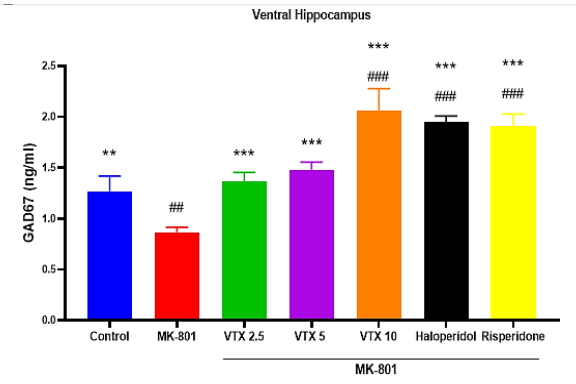


Figure 12. Comparison of the effect of treatment groups on GAD67 levels in the ventral hippocampus with control and MK-801 groups. Values were expressed as mean ± standard error. Comparisons between groups were made using one-way ANOVA and post hoc Dunnett's test. Compared to the control group, it is ###: p<0.001, ##: p<0.01, compared to the MK-801 group ***: p<0.001, **: p<0.01.

Brain parvalbumine levels in ELISA test

Parvalbumin level in the frontal cortex ($p<0.001$), prefrontal cortex ($p<0.001$), dorsal hippocampus ($p< 0.01$) and ventral hippocampus ($p<0.001$) was decreased in the MK-801 group compared to the control group.

Vortioxetine (5 mg/kg) ($p<0.001$), vortioxetine (10 mg/kg) ($p<0.001$) and haloperidol ($p<0.001$) and risperidone ($p<0.001$) increased parvalbumin levels (Figure 13).

Vortioxetine (5 mg/kg) ($p<0.01$), vortioxetine (10 mg/kg) ($p<0.001$) and haloperidol ($p<0.001$) and risperidone ($p<0.5$) increased parvalbumin levels (Figure 14).

Vortioxetine (5 mg/kg) ($p<0.001$), vortioxetine (10 mg/kg) ($p<0.001$) and risperidone ($p<0.001$) increased parvalbumin levels (Figure 15).

Vortioxetine (10 mg/kg) ($p<0.001$), haloperidol ($p<0.001$) and risperidone ($p<0.001$) increased parvalbumin level (Figure 16).

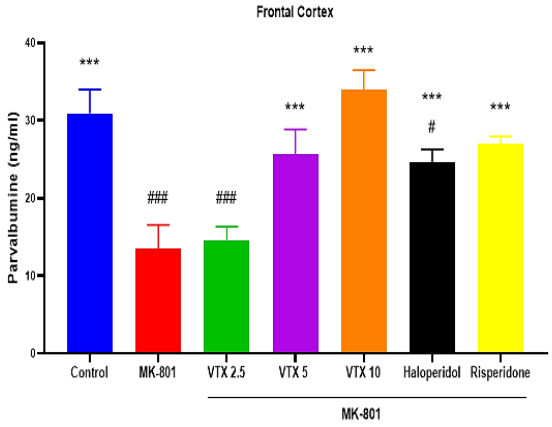


Figure 13. Comparison of the effect of treatment groups on parvalbumin levels in the frontal cortex with control and MK-801 groups. Values were expressed as mean ± standard error. Comparisons between groups were made using one-way ANOVA and post hoc Dunnett's test. Compared to the control group ###: p<0.001, #: p<0.05, compared to the MK-801 group ***: p<0.001.

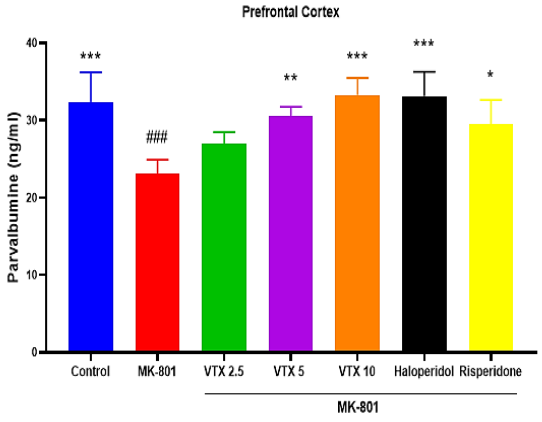


Figure 14. Comparison of the effect of treatment groups on parvalbumin levels in prefrontal cortex with control and MK-801 groups. Values were expressed as mean ± standard error. Comparisons between groups were made using one-way ANOVA and post hoc Dunnett's test. Compared with the control group, it is ### : p<0.001, when compared with the MK-801 group ***: p<0.001, **: p<0.01, *: p<0.05.

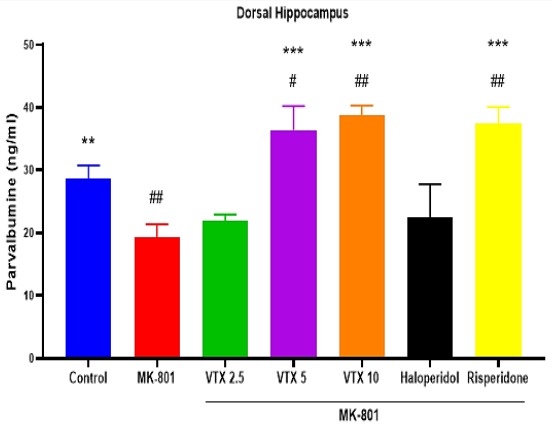


Figure 15. Comparison of the effect of treatment groups on parvalbumin levels in the dorsal hippocampus with control and MK-801 groups. Values were expressed as mean ± standard error. Comparisons between groups were made using one-way ANOVA and post hoc Dunnett's test. Compared with the control group, it is ##: p<0.01, when compared with the MK-801 group, it is ***: p<0.001, **: p<0.01.

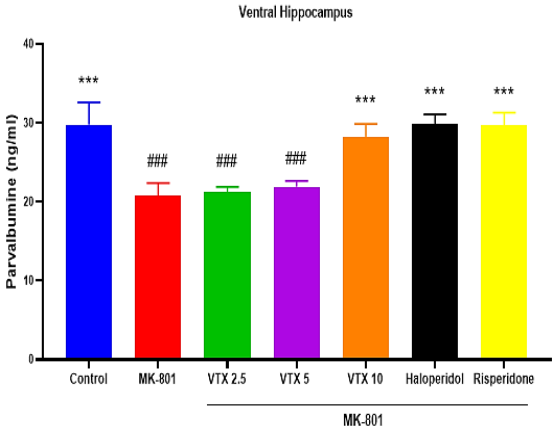


Figure 16. Comparison of the effect of treatment groups on parvalbumin levels in ventral hippocampus with control and MK-801 groups. Values were expressed as mean ± standard error. Comparisons between groups were made using one-way ANOVA and post hoc Dunnett's test. Compared to the control group, it is ###: p<0.001, compared to the MK-801 group ***: p<0.001.

DISCUSSION: In this study, we evaluated the potential beneficial effects of vortioxetine, a new multimodal antidepressant, in the acute MK-801 schizophrenia model in rats. Our results showed that acute administration of MK-801 induced schizophrenia-like behaviors in rats. MK-801 administration impaired the cognitive performance, social behavior and sensorimotor gating mechanisms of the rats. However, vortioxetine improved visual learning and memory, spatial memory, and social deficits in rats. In addition, vortioxetine exacerbated the MK-801-induced sensorimotor gating deficit in rats. These results suggest that

vortioxetine improves negative and cognitive symptoms, but not the sensorimotor gating deficit, in the acute MK-801 model of schizophrenia in rats.

Acute or chronic administration of NMDA receptor antagonists such as MK-801, ketamine has been shown to impair visual learning and memory. Unal et al. (2020) reported that ketamine impairs visual learning and memory in a ketamine-induced schizophrenia model in rats, while vortioxetine 10 mg/kg treatment reverses this situation. In previous studies, the procognitive effects of vortioxetine were tried to be explained by serotonergic, glutamatergic, GABAergic or histaminergic enrichments in the prefrontal cortex [4]. Our study is the first study in which 3 different doses of vortioxetine were administered in a schizophrenia model created with MK-801 in rats and the procognitive effect of vortioxetine was demonstrated at these 3 doses.

Sams Dodd et al. (1999) reported that social deficits occur in rats as a result of NMDA receptor antagonism, and that models created with NMDA receptor antagonists have preliminary and facet validity [5]. Unal et al. (2021) reported that vortioxetine did not have a significant effect on tracking and sniffing behaviors in a ketamine-induced schizophrenia model in rats, but it improved avoidance behavior [4]. The reinforcing effect of vortioxetine in social interaction was pharmacologically attributed to its inhibition of SERT, being a 5-HT1B partial agonist, and being a 5-HT7 antagonist [4].

One of the behavioral experiments to evaluate cognitive performance is the Y-maze test. This test evaluates learning and short memory . When the literature is reviewed, many studies have reported that NMDA antagonists such as ketamine and MK-801 negatively affect spatial learning and memory performance in rodents. Jiang et al. (2020) in a transgenic Alzheimer's mouse model, it was shown that vortioxetine corrects the deterioration in recognition and spatial memory [6]. In a study conducted by Samur et al (2022) in a rotenone-induced Parkinson's model, impairment in recognition and spatial reference memory was improved with vortioxetine [7]. To the best of our knowledge, this is the first study to investigate the effect of vortioxetine on spatial memory in a model of MK-801-induced schizophrenia.

It has been demonstrated that sensorimotor gating, which plays a role in attention, cognitive functions and maintaining daily life, is impaired in individuals with schizophrenia. Prepulse inhibition includes sensory stimuli, as well as motor response. Therefore, prepulse inhibition is a well-validated translational model that demonstrates the sensorimotor gating function and is valid in humans and rodents such as rats and mice. Dopaminergic receptor agonists such as apomorphine and glutamatergic receptor antagonists such as ketamine, MK-801 mimic the disruption in the cortico-thalamo-pallido-striatal neuronal loop in rats and mice, allowing the modeling of positive symptoms in schizophrenia [17]. Ünal et al. (2020) reported that vortioxetine did not change the sensorimotor gating function when administered alone. However, ketamine-induced sensorimotor gating disorder was exacerbated by vortioxetine [4]. Increased serotonergic activity in subcortical regions such as the limbic system has been blamed for positive symptoms in schizophrenia [18]. When the multimodal serotonergic enhancing effects of vortioxetine and the cortico-pallido-striatal-thalamic control of sensorimotor gating are considered together, it is seen that the synergistic destructive effect of vortioxetine and MK-801 on sensorimotor gating is in parallel with the theoretical knowledge [4].

In postmortem studies, it has been shown that the gene level expression of GAD, which is the major component of GABA synthesis in the prefrontal cortex, is decreased in schizophrenia [9]. In addition, studies have shown that GABAergic araneurons carrying parvalbumin are decreased in both the prefrontal cortex and the hippocampus [10]. It is assumed that these changes seen in the physiopathology of schizophrenia may lead to neuronal synchronization disorders and in this case, may cause errors in working memory [9]. GABAergic neurons containing parvalbumin, whose number is significantly reduced in schizophrenia, cannot suppress the activity of pyramidal cells, and the excessive stimulation of tissues such as the nucleus accumbens, basolateral amygdala and prefrontal cortex by these neurons, which originate from the hippocampus, causes positive, negative and cognitive symptoms of schizophrenia [10]. It has been shown that GAD65 and GAD67, the isoforms of the GAD enzyme responsible for GABA synthesis, are decreased in the hippocampus of schizophrenia patients. Many studies have shown that acute or chronic administration of NMDA receptor antagonists in rodents caused loss of GABAergic neurons containing parvalbumin in the hippocampus and caused a decrease in GAD65 and GAD67 expressions [9-10]. When these findings obtained from previous studies were examined, it was shown in our study that the decrease in parvalbumin and GAD67 levels that

occurred with subchronic MK-801 administration was compatible with the literature. The fact that the decrease in parvalbumin and GAD67 expression is accepted among the reproducible findings of schizophrenia and the results obtained from our study are parallel to this shows that the model we used meets the structural validity criteria. Our study is the first to investigate the effects of three different doses of vortioxetine on GAD67 and parvalbumin levels in a schizophrenia model induced with MK-801 in rats. According to the findings we obtained in our study, the decrease in parvalbumin and GAD67 levels that occurred with MK-801 administration was reversed with vortioxetine 5 mg/kg and vortioxetine 10 mg/kg.

Keywords: GAD67, Novel object recognition test, Parvalbumine, Schizophrenia, Social interaction test, Vortioxetine

REFERENCES

[1] van Os J, Kapur S. Schizophrenia. Lancet. 2009; 374(9690): 635-645. [CrossRef]
[2] Unal G, Aricioglu F. Famotidine Improved Schizophrenia-Like Behaviors in Acute Ketamine Model of Schizophrenia in Rats. Psychiatry and Behavioral Sciences. 2020; 10(2): 45-54. [CrossRef]
[3] D'Agostino A, English CD, Rey JA. Vortioxetine (brintellix): a new serotonergic antidepressant. P T. 2015; 40(1): 36–40.
[4] Unal, G., and M. Taskiran. "Vortioxetine improved social and cognitive deficits in acute ketamine model of schizophrenia in rats." J Res Pharm 24.5 (2020): 648-55.
[5] Sams-Dodd, F. Phencyclidine in the social interaction test: an animal model of schizophrenia with face and predictive validity. Rev Neurosci. 1999; 10: 59–90.
[6] Jiang, LX., Huang, GD., Su, F. et al. Vortioxetine administration attenuates cognitive and synaptic deficits in 5×FAD mice. Psychopharmacology 237, 1233–1243 (2020).
[7] Nemutlu Samur D, Akçay G, Yıldırım S, Özkan A, Çeker T, Derin N, Tanrıöver G, Aslan M, Ağar A, Özbey G. Vortioxetine ameliorates motor and cognitive impairments in the rotenone-induced Parkinson's disease via targeting TLR-2 mediated neuroinflammation. Neuropharmacology. 2022 May 1;208:108977.
[8] Mansbach RS, Geyer MA. Effects of phencyclidine and phencyclidine biologs on sensorimotor gating in the rat. Neuropsychopharmacol. 1989;2:299-308.
[9] Lewis DA, Gonzalez-Burgos G. Pathophysiologically based treatment interventions in schizophrenia. Nat Med. 2006;12:1016-1022.
[10] Heckers S, Konradi C. GABAergic mechanisms of hippocampal hyperactivity in schizophrenia. Schizophr Res. 2015;167:4-11.

[Abstract:0235] [Epidemiology]

0235 - Beyond the conferment: meta-analysis of the risk of 17q12 deletion for autism and schizophrenia

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OBJECTIVE: To our knowledge, the prevalence of the 17q12 recurrent deletion is extremely low with the number from 0.002% (1:50,000) to 0.007% (1:14,000). Notwithstanding, the phenotype of the 17q12 recurrent deletion is defined as a variable expressivity, this deletion has a high penetrance and it could cause considerable pathological conditions. In-depth, the recurrent deletion on 17q12 causes a syndrome having the involvement of different organs including the kidney, pancreas, and central nervous system (CNS). According to a review published by Mitchel et al., the syndrome is a diverse combination of maturity-onset diabetes of the young type 5 (MODY5), kidney and urinary tract abnormalities, and neurodevelopmental or neuropsychiatric disorders. In clinically suspected patients, a definitive diagnosis of the syndrome is established by detection of 1.4 Mb deletion with genomic testing methods that identify the copy number [1].
Regarding deletion in the 17q12 region, central nervous system (CNS) involvement results in a wide range of neuronal and psychiatric conditions epilepsy, intellectual and learning disabilities, autism spectrum disorder (ASD), and schizophrenia (SCZ). In their large case-control study, Moreno-De-Luca et.al. claimed that the 17q12 deletion confers a high risk for SCZ and ASD [1]. Besides, the existing literature on the 17q12 deletion syndrome lacks clarity regarding providing a risk estimation for ASD, and SCZ. For this aim, we systematically reviewed the existing literature and calculated the overall effect size of case-control studies with the meta-analytical method.
METHODS: This study was performed according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [2] and informed by the MOOSE (Meta-analyses of Observational Studies in Epidemiology) guidelines. Following keywords as ("DNA Copy Number Variations"[MeSH Terms] OR "deletion"[Title/Abstract] OR "17q12"[Title/Abstract] OR ("17q12"[Title/Abstract] AND "syndrome"[Title/Abstract]) OR "rcad"[Title/Abstract] OR "chromosome 17"[Title/Abstract] OR "17q12 deletion syndrome"[Title/Abstract]) AND ("Autism Spectrum Disorder"[MeSH Terms] OR "autism"[Title/Abstract] OR "autistic"[Title/Abstract] OR "autistic features"[Title/Abstract] OR "neurodevelopmental disorder"[Title/Abstract]) for autism and ("DNA Copy Number Variations"[MeSH Terms] OR "deletion"[Title/Abstract] OR "17q12"[Title/Abstract] OR ("17q12"[All Fields] AND "syndrome"[Title/Abstract]) OR "rcad"[Title/Abstract] OR "chromosome 17"[Title/Abstract] OR "17q12 deletion syndrome"[Title/Abstract]) AND ("Autism Spectrum Disorder"[MeSH Terms] OR "autism"[Title/Abstract] OR "autistic"[Title/Abstract] OR "autistic features"[Title/Abstract] OR "neurodevelopmental disorder"[Title/Abstract]) AND ("Schizophrenia Spectrum and Other Psychotic Disorders"[MeSH Terms] OR "schizophrenia"[Title/Abstract] OR "schizophrenic"[Title/Abstract] OR "schizophren*"[Title/Abstract] OR "psychosis"[Title/Abstract] OR "psychotic"[Title/Abstract] OR "psycho*"[Title/Abstract]) for schizophrenia were used.
Eligible studies were required to meet the following criteria (i) be a case-control and family-based study (ii) had more than five participants (iii) conducted with patients who had already confirmed diagnosis of autism or schizophrenia (iv) included control subjects having no history of mental disorder, other neurological disorder, alcohol dependence, or drug dependence. The coordinates of the 17q12 deletion were considered as the existence of a recurrent 1.4-Mb deletion at the position of 36,46-37,85 (GRCh38/hg38). Also, we considered deletion at Chr17:31.8-33.2 Mb (NCBI36) because that evidence suggests the presence of

syndrome caused by deletion at the mentioned site (#614527). On the other hand, the exclusion criteria were defined as (i) case-only studies, case reports, and case series (ii) studies with non-human subjects (iii) CNVs that do not meet the canonical regions and type of mutation (iv) studies which were not provided to adequate information for genotyping of the specified gene. In addition, to avoid bias originating from overlapped samples due to the use of the same database, studies with the largest and most complete data collections were included only.

We extracted the number of copy number variations (CNVs) for cases and controls. The meta-analyses were carried out using Cochran–Mantel–Haenszel (CMH) test, and the CMH-adjusted odds ratios (ORs) and two-sided p values were calculated. Considering heterogeneity between selected studies fixed-effect models or random-effect models were employed to calculate pooled estimates.

The heterogeneity between studies was assessed with the Cochrane Q test and I2 statistic. In accordance with Cochrane recommendations, we considered the heterogeneity if the p-value of the Cochrane Q test was smaller than 0.05. When $I2 \geq 50\%$ or the p-value of the Cochrane Q test is <0.05, the heterogeneity was considered substantial and in such cases, the random effect models were used to pool the mean differences. The fixed effect models were employed in the absence of significant heterogeneity. Forrest plots were used to graphically display the results and effect measures and corresponding 95% confidence intervals (CI) were presented.

RESULTS: For ASD, the search in MEDLINE, EMBASE, PsychINFO, and Google Scholar databases returned 3,127 records. 324 were duplicates and after a title and abstract screening, 2,796 articles were excluded for not fully meeting the inclusion criteria. Full texts were assessed in the 7 remaining articles for eligibility, and 3 were excluded. Finally, four articles were found to fulfill the selection criteria. Our results revealed that a total of 38 events were observed in 34,824 cases and six were found in 84,461 controls. There was no significant statistical heterogeneity between studies quantified as I2 = 0% and p = 0.85, and we selected the fixed-effect model for our pooled estimate OR. The calculated CMH-adjusted OR was 8.56 (95 % CI 2.75, 26.67; p = 0.0002).

For SCZ, the search in MEDLINE, EMBASE, PsychINFO, and Google Scholar databases returned 723 records. 112 were duplicates and after a title and abstract screening, 605 articles were excluded for not fully meeting the inclusion criteria. Full texts were assessed in the 6 remaining articles for eligibility, and 2 were excluded. Finally, four articles were found to fulfill the selection criteria. Our results revealed that a total of seven events were observed in 18,772 cases and none were found in 56,663 controls. There was no significant statistical heterogeneity between studies quantified as I2 = 0% and p = 0.42 and we selected the fixed-effect model for our pooled estimate OR. The calculated CMH-adjusted OR was 8.06 (95 % CI 1.86, 34.98; p = 0.005).

DISCUSSION: In reviewing the literature, at least 309 cases of 17q12 deletion syndrome have been described in cohort studies and clinical series, 55 of which suffered from neurodevelopmental and/or neuropsychiatric conditions. In terms of neuropsychiatric diseases, the syndrome grounds a wide range of clinical phenotypes such as autism, SCZ, ADHD, bipolar disorder, etc. In-depth, whereas intellectual and learning disability (number of 38 and 30 patients, respectively) predominantly represents the neuropsychiatric phenotype of the syndrome, 27 ASD and four SCZ cases were designated. Other demonstrated neuropsychiatric and neurodevelopmental disorders in the literature include developmental disorder, oppositional and deviant disorder, epilepsy, ADHD, OCD, BPD, OCD, and MDD with the number of 24, 5, 5, 6, 3, 5, and 5 patients, respectively. One of the most important characteristics of the syndrome, concurrently displaying two or more neuropsychiatric disorders/neurodevelopmental disorders (NPDs/NDDs) in nearly all patients. Although the severity of the disease due to widespread organ involvement was associated with the degree of gene loss dosage, no clear interpretation was suggested for the high prevalence of neuropsychiatric comorbidity [3]. It could be hypothesized that the greater burden of functional gene loss, some of which have a critical role in neuronal developmental processes, lead to comorbidity of developmental and psychiatric conditions. Moreover, along with functional genes, the loss of non-coding regulatory genes could cause psychiatric comorbidity by epistatic interactions.

In this meta-analysis, we tried to confirm the associations of the deletion at the 17q12 locus with autism and schizophrenia. For this purpose, we used statistical models trained in the general population and performed

meta-analyses of case-control studies using disease cohorts and control subjects. Our results showed that 17q12 deletion may increase the risk for the development of ASD and SCZ by nearly 8 times. We state that haploinsufficiency in the 17q12 gene is a great risk factor for ASD and SCZ. How this CNV causes ASD and SCZ could explain by losses of genes harbored in the deleted interval. HNF1B, LHX1, and ACACA are the most candidate genes to develop CNS conditions because of their critical roles in neurogenesis and neurotransmission. If the debate is to be moved forward, a better understanding of association of the 17q12 deletion and psychiatric conditions needs to be further elaborated.

Keywords: 17q12 deletion, genetic, autism, schizophrenia, odds ratio, meta-analysis

REFERENCES

1. Mitchel MW, Moreno-De-Luca D, Myers SM, Levy RV, Turner S, Ledbetter DH, et al. 17q12 Recurrent Deletion Syndrome. In: Adam MP, Everman DB, Mirzaa GM, Pagon RA, Wallace SE, Bean LJH, et al., editors. GeneReviews(®). Seattle (WA): University of Washington, Seattle Copyright © 1993-2022, University of Washington, Seattle. GeneReviews is a registered trademark of the University of Washington, Seattle. All rights reserved.; 1993.
2. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. Bmj. 2021;372:n71. doi:10.1136/bmj.n71
3. Wu HX, Li L, Zhang H, Tang J, Zhang MB, Tang HN, et al. Accurate diagnosis and heterogeneity analysis of a 17q12 deletion syndrome family with adulthood diabetes onset and complex clinical phenotypes. Endocrine. 2021;73(1):37-46. doi:10.1007/s12020-021-02682-5

[Abstract:0244] [Schizophrenia and other psychotic disorders]

0244 - The effect of implict learning on neuroplasticity-related resting-state activity in patients with schizophrenia: a graph theory network analyses

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INTRODUCTION: Postmortem, genetic and restricted neuroimaging research on schizophrenia patients shows that neuroplasticity defects in schizophrenia patients and causal effects of neuroplasticity defects on decreasing cognitive functions and distortions in higher cortical functions. Our current research aims comparison of implicit learning effects on neuroplasticity-related activity between schizophrenia patients and healthy controls. It is aimed to use the findings as a diagnostic biomarker in the clinical high-risk group.
METHOD: A computerized implicit learning task named Serial Reaction Time Task "SRTT" was applied to schizophrenia patients and healthy controls that matched age, gender, and educational level. In the SRTT, each block consisted of 96 trials. Blocks 5, 6, 7, 8, and 9 are called "fixed -sequence blocks" During “fixed-sequence blocks”, the stimuli appeared according to one-of-four fixed 12-item sequences, which repeated 8 times (e.g. 3-4-1- 2-3-1-4-3-2-4-2-1). “Sequential motor learning” takes place in these blocks. Particularly, the motivation of the patient group was tried to be increased by giving feedback as “you made money” to the participants

who made less than 5% mistakes between the blocks in a fixed order. The same sequential sequence is seen in the 3rd and 11th blocks, and the remaining blocks consist of random trials. The research aims to investigate alterations in cortical and subcortical structures. It is envisioned that alterations of neural plasticity cause task-related activations and increased signal in regions with increased blood supply. Resting state functional magnetic resonance (fMRI) was applied to participants before and after task and task- related activations in brain regions detected in schizophrenia and healthy control groups. The connectivity of brain regions with increased task-related activity was compared between the two groups using graph theory-based network analysis. Behavioral data were analyzed between two groups regarding accuracy and reaction time. In order to investigate the relationship between behavioral data and functional connectivity, Pearson correlation analysis was applied. First, to examine whether there was a difference between the groups in the mean RT and accuracy in the pre-test and post-test sequential and random blocks, 2 (group: control and schizophrenia) x 2 (type: random and sequential) x 2 (test time: pre-test and post-test) mixed pattern analysis of variance was applied. Finally, in order to look at the change in mean RT and accuracy as the trial progressed, each block was divided into 2 (group: control and schizophrenia) x 5 (fixed-sequence blocks) across 5 blocks of a fixed sequence between the groups. It was included in the analysis by ANOVA. In addition, Bonferroni correction was applied for the analysis of main effects. Finally, the results for all analyzes were considered significant at the 0.05 alpha level and the effect size was reported as partial eta square. The difference between groups of brain regions with increased pre- and post-task functional connectivity between the two groups was compared between groups using graph theory connectivity analyses. In the resting state functional imaging graph theory analysis, all graph parameters were analyzed for ROI regions. Cerebellum, left premotor cortex, left thalamus, left caudate nucleus, which play an active role in implicit learning, were selected as ROI regions. 2 (group: control and schizophrenia) X 2 (time: before and after task) Mixed Pattern Analysis of Variance was performed. Finally, Pearson r correlation analysis was performed between behavioral data and neuroimaging functional connectivity data for the two groups.

RESULTS: Total of 60 participants, 33 schizophrenia and 27 healthy controls involved in the study. Six participants were excluded from behavioral and neuroimaging analysis. Fifty-four participants proceeded to analysis. Resting-state functional connectivity analysis investigates implicit sequential motor learning (SMO)-related activity alterations and relationships between relevant regions. Behavioral data during the task was analyzed in accuracy and reaction time (RT). During SRTT, when fixed serial blocks that implicit learning happened, RT decreases for both groups. In accuracy, lower number of correct answers is detected in schizophrenia group than control group. When pre- test post-test RT compared with each other, post-test trials' RT lower than pre-test trials within both group. Schizophrenia patients exhibit lower number of correct answers than control group in pre-test/post-test comparison. In the resting state fMRI graph analyses, the mean local efficiency for the cerebellum increased in both groups after the learning task compared to before. ($F = 5.36$, $p = 0.026$) For the local efficiency parameter, the group*time joint effect in the left anterior premotor region was significant ($F = 7.94$, $p = 0.007$). In the control group, the average local efficiency in the left anterior premotor region increased after learning; decreased in the schizophrenia group. For the global activity parameter, the group*time joint effect was found to be significant in the right cerebellum ($F = 4.56$, $p = 0.037$). While the global activity average in the right cerebellum decreased after learning in the control group; increased in the schizophrenia group. For the global efficiency parameter, the time*group joint effect was found to be significant in the left anterior premotor region, ($F = 4.31$, $p = 0.043$). While the global efficiency average before and after learning decreased in the control group; increased in the schizophrenia group.

DISCUSSION: Consequently, our research analysis is completed with a total of 54 subjects consisting of 28 schizophrenia and 26 healthy controls. Decreasing RT in proceeding of fixed serial blocks that implicit learning happened, decreasing RT in a pre-test/ post-test analysis, no significant difference between groups' RT prove implicit learning happened in both groups. However, fewer correct answers in fixed serial blocks and pre-test/post-test analysis exhibit implicit learning problems compared to healthy controls, even though implicit learning happened in both. In our study, we focused on the left PMC and cerebellum in the resting state fMRI data graph theory analysis. In the control group, while the local efficiency parameter in the left anterior premotor cortex increased as a result of motor consolidation due to neuroplasticity developing

secondary to learning, it was determined that the global efficiency parameter decreased. In the patient group, the decrease in the local efficiency parameter in the left anterior premotor cortex suggests that this group could not achieve localization in sequential motor learning in parallel with the neuronal dysfunction hypothesis. The global activity parameter increased in the left anterior premotor cortex in the patient group; supports that the global activity parameter continues to increase after learning in the cerebellum, and the local interaction between regions in the implicit learning task of patients with schizophrenia is low, and the patients cannot increase their neural input signal efficiency and remain stuck in global information processing. **CONCLUSION:** In our study, neuroplasticity-related problems in schizophrenia showed by both implicit serial motor tasks and resting-state fMRI graph theory network analysis. In behavioral data, a lower number of correct answers in the schizophrenia group, albeit as good RT as the control group, exhibited that implicit learning happened but was flawed in schizophrenia. In the functional connection graph analyzes performed, the decrease in the left anterior PMC local activity parameter in schizophrenia patients, the increase in the global activity parameter, and the increase in the global activity parameter in the cerebellum after learning supports that there is a problem in neuroplasticity in schizophrenia patients and they cannot increase the neural input signal efficiency and are stuck in global information processing.

Keywords: schizophrenia; neuroplasticity; serial reaction time task; resting state fMRI; implicit motor sequence learning; premotor cortex

[Abstract:0247] [Schizophrenia and other psychotic disorders]

0247 - The effect of long-acting ınjectable antipsychotics on qtc ınterval

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BACKGROUND AND OBJECTIVE: Long-acting injectable (LAI) antipsychotics are frequently used agents in the treatment of schizophrenia and other psychotic disorders in order to maintain a stable plasma antipsychotic level and increase treatment adherence. Considering the burden of relapse and recurrence of patients and the cost of hospitalizations, LAIs seem to be preferable medications for both the patient and the physician.
Antipsychotics have adverse effects that are usually seen in the neurological system, cardiovascular system and endocrinological system. Side effects of antipsychotics that used in the treatment of psychotic disorders should follow-up regularly, considering the presence of high levels of comorbid medical diseases in these patients.
Among the cardiac side effects of antipsychotics, QTc interval prolongation is known as an important side effect of antipsychotics, and can cause sudden death in patients with psychiatric disorders.
The aim of this study is to examine the effects of LAI antipsychotics on the QTc interval in the early period and estimate the probable risk factors for QTc prolangation.

METHODS: The study included the patients diagnosed with psychotic disorder or bipolar disorder according to 5th edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) and hospitalized in the psychiatry service and treated with a LAI antipsychotics between 2019-2021.
The electrocardiography (ECG) examinations of the patients were performed before the antipsychotic treatment and on the 7th-14th days of the treatment which is generally accepted as the highest plasma peak concentration time for LAIs. These ECG records were analyzed retrospectively and QTc intervals were calculated according to Bazzett’s formula.

IBM SPSS 22.0 statistical software was used for data processing. Normally distributed variables were tested by Kolmogorov-Smirnov Test. Descriptive statistics of the numerical data were indicated as the median, interquartile range (Q1-Q3). The Willcoxon test was used for non parametric variables. For the multivariate analysis, the possible factors identified with chi-square and Mann-Whitney U test were further entered into the logistic regression analysis. $P < 0.05$ was set as the statistical test level.

RESULTS: The study included 48 patients. Of those patients, 27 (56.3%) were diagnosed with schizophrenia, 10 (20.8%) were other psychotic disorders, 6 (12.5%) were bipolar affective disorder, and 5 (10.4%) were schizoaffective disorder. The mean age of the patients was 39.8 ± 11.2 years, and the mean duration of illness was 14.06 ± 10.2 years. There was a comorbid medical disease in 22 (45.8%) of the patients, two (4.2%) of them had a cardiovascular disease.
In the patients that were using first generation LAI antipsychotics, seven (58%) of them were using haloperidol decanoate and five (42%) of them were using Zuclopenthixol decanoate. The patients that were using second-generation LAI antipsychotics were consist of 15 (42%) paliperidone palmitate, 11 (30%) aripiprazole and 10 (28%) risperidone.
The comparison of QTc values of the patients before and after LAI injection is given in Table 1. A statistically significant prolongation in the QTc interval was found in patients who received second-generation LAI antipsychotics.

Table 1. Comparison of QTc values before and after long-acting injectable (LAI) antipsychotic treatment

	QTc values (ms) Median [Q1-Q3]			
	Before injection	7-14 days after injection	z	p
All of the LAI antipsychotics	418 [398-430]	421 [408-435]	-2.412	**0.016***
First generation LAI antipsychotics	426 [400-442]	407 [403-438]	-0.236	0.814
Second generation LAI antipsychotics	417 [398-427]	422 [411-434]	-2.680	**0.007***

Wilcoxon test; *p<0.05 statistically significant; ms=milliseconds

QTc values according to combined antipsychotic use and presence of a comorbid medical disease are presented in Table 2. There was no difference in terms of QTc values before and after LAI antipsychotic treatment between LAI monotherapy and combined oral+LAI antipsychotic therapy. Wen the patients Similarly, when the patient groups with and without comorbid medical disease were compared, no statistically significant difference was found between these patient groups in terms of QTc values of both pre-treatment and after LAI antipsychotic administration.

Table 2. Comparison of some clinical data in terms of QTc values

	QTc values (ms)					
	Before LAI Antipsychotic Injection			After LAI Antipsychotic Injection		
	QTc Median [Q1-Q3]	z	p	QTc Median [Q1-Q3]	z	p
LAI antipsychotics (n=36)	423[409-430]	-0.965	0.335	422 [408-435]	-0.703	0.482
Oral+LAI antipsychotic combination (n=12)	413[394-426]			417 [403-434]		

Comorbid Medical Disease No (n=26) Yes (n=22)	425[399-430] 413[398-423]	-1.501	0.133	421[407-436] 421[408-435]	-0.114	0.909

Mann-Whitney U test

The pre- and post-treatment QTc values of the patient groups with and without comorbid medical disease were evaluated within themselves (Table 3 and 4). A statistically significant prolongation of the QTc interval was found after treatment in the patient group with comorbid medical disease. There was no statistically significant change in QTc value after LAI antipsychotic treatment in patients without comorbid medical disease.

Table 3. The effect of LAI antipsychotic treatment on QTc values in patients with comorbid medical disease (n=22)

QTc values (ms) Median [Q1-Q3]			
Before Treatment	After Treatment	z	p
413 [398-423]	421 [407-435]	-2.796	**0.005***

Wilcoxon test; *p<0.05 statistically significant; ms=milliseconds; n: number of patients

Table 4. Effect of LAI antipsychotic treatment on QTc values in patients without comorbid medical disease (n=26)

QTc values (ms) Median [Q1-Q3]			
Before Treatment	After Treatment	z	p
425[399-430]	421[407-436]	-2.796	0.485*

Wilcoxon test; *p<0.05 statistically significant; ms=milliseconds; n: number of patients

CONCLUSIONS: In our study, QTc interval in patients with comorbid medical disease was found to be statistically significantly increased during the acute period after LAI antipsychotic injection. It is known that some electrolyte disorders and cardiovascular system diseases predispose to rhythm disorders such as antipsychotic related ventricular tachycardia. However, there is not any study examining the effect of LAI antipsychotics on QTc prolongation in the acute period.

Our study has some limitations. The study was designed in a retrospective design and was conducted with a limited number of participants. Equivalent doses of antipsychotics were not calculated were not considered as a variable. In addition, comorbid medical conditions were not evaluated by dividing them into subcategories. The patients with comorbidity may be at increased risk of QTc interval prolongation, which may be a risk factor for drug-induced sudden cardiac death. Therefore, frequent ECG monitoring and close follow-up of the patient at the early period after injection are important in patients who are switched to long-acting antipsychotics, especially in patients with medical comorbidities.

REFERENCES

Leung JY, Barr AM, Procyshyn RM, Honer WG, Pang CC. Cardiovascular side-effects of antipsychotic drugs: the role of the autonomic nervous system. Pharmacology & therapeutics. 2012 Aug 1;135(2):113-22.

Nielsen J, Graff C, Kanters JK, Toft E, Taylor D, Meyer JM. Assessing QT interval prolongation and its associated risks with antipsychotics. CNS drugs. 2011 Jun;25(6):473-90.

Schneider-Thoma J, Chalkou K, Dörries C, Bighelli I, Ceraso A, Huhn M, Siafis S, Davis JM, Cipriani A, Furukawa TA, Salanti G. Comparative efficacy and tolerability of 32 oral and long-acting injectable antipsychotics for the maintenance treatment of adults with schizophrenia: a systematic review and network meta-analysis. The lancet. 2022 Feb 26;399(10327):824-36.

[Abstract:0252] [Schizophrenia and other psychotic disorders]

0252 - The role of anxiety, experiential avoidance and perspective taking in persecutory delusions

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OBJECTIVE: Theoretical models of persecutory delusions have been emphasising negative emotions and emotion regulation strategies (1). There is an extensive literature on the relationship between anxiety and paranoia but our knowledge about the nature of this relationship is still controversial. While some models suggest that anxiety directly paves the way for paranoia, some suggests that paranoia emerges in order to avoid negative internal experiences (2). On the other hand, Theory of Mind (ToM) and perspective taking deficits are consistently demonstrated in psychotic disorders but there is contradictory data about their relationship with delusions (3). In this experimental study, it's aimed to investigate the relationship between anxiety and paranoia, to evaluate the mediator role of experiential avoidance (EA) and the moderator role of Perspective Taking (PT) on this relationship.
METHODS: This study has been approved by Bakırköy Prof. Dr. Mazhar Osman Mental Health and Neurology Training and Research Hospital Ethics Committee on 06.02.2018 with protocol number 133. Participants were recruited from both outpatient and inpatient clinic of Bakirkoy Prof. Dr. Mazhar Osman Mental Health and Neurological Diseases Training and Research Hospital, between December 2018 and January 2019. The inclusion criteria were as follows: aged between 18 and 65, able to read and write, having a diagnosis of psychotic disorder according to DSM-V, a current persecutory delusion (rated ≥ 3 on the positive subscale of PANSS). The exclusion criteria were having a diagnosis of organic brain disorder, alcohol or drug dependency, physical disability and agressive or hostile manner.
Informed consent for participation was obtained at the start of the session. At the baseline, the Sociodemographic Data Form, Positive Symptoms Subscale of Positive and Negative Symptoms (PANNS) Scale, Acceptance and Action Questionnaire-II (AAQ-II), Depression Anxiety Stress Scale-21 (DASS-21), Peters Delusion Inventory (PDI) – Paranoia Items, PT Task and Stroop Test were administered. The order of measures was randomized to avoid the order effect. The assessment was completed in approximately 45 minutes.
There were two experimental conditions in the study. While Anxiety Group (AG) was exposed to an anxiety inducing scenario with virtual reality (VR), Mindfullness Group (MG) was exposed to a mindfullnes task. After baseline measurements, participants were randomly assigned to either an AG (n=37) or MG (n=32). Before experimental manipulation, they were asked to fill in the Visual Analog Scale (VAS) for Emotions and State Adapted Paranoia Checklist - Short Version in order to evaluate state emotion and paranoia. Immediately after the experimental manipulation, state emotion and paranoia scales were administered again, as well as the State Inventory of EA (Figure 1).
All statistical analysis were made using the Statistical Package for Social Sciences (SPSS) 20.0. After descriptive statistical analyzes, it was investigated whether there was a statistically significant difference between the groups in terms of baseline measurements. The difference between groups was analyzed using Chi-Square tests for qualitative and the Independent Samples T-Test or Mann Whitney-U test for quantitative measurements. The effect of anxiety manipulation on emotions was analyzed using two-way mixed ANOVA (Analysis of Variance). One-way between-group ANCOVA (Analysis of Covariance) was used to compare the paranoia levels of the groups after anxiety manipulation. Mediation and moderation analyzes were performed using the PROCESS plugin developed by Hayes (4). The statistical significance level for the results was accepted as $p<0.05$.
RESULTS: 69 individuals with current persecutory delusions, 37 in the AG and 32 in the MG, took part in the study. There were no significant differences between groups according to sociodemoghraphic and clinical

characteristics of the patients. The independent sample t-tests had shown that there were also no statistically significant differences according to baseline measurements.
When conducting a two-way Mixed ANOVA for exploring effects of manipulation on emotions, pre-manipulation (t1) and post-manipulation (t2) emotions were considered as within and experimental groups (AG, MG) as between-group factors. While there was a statistically significant main effect for group x time interaction [$F(1, 67)=11.68$, $p=0.001$, $\eta 2_{partial} =0.149$] for anxiety, group [$F(1,67)=0.49$, $p=0.483$, $\eta 2_{partial} =0.07$] or time effect [$F(1,67)=3.76$, $p=0.057$, $\eta 2_{partial}=0.053$] were not found significant. It means that anxiety manipulation is successful and there is a significant increase in anxiety levels in the AG compared to MG. For other emotions (sadness, anger, shame, happiness), neither group nor time effect nor group x time interaction were found significant ($p>0.05$).

One-way ANCOVA was conducted to compare paranoia levels of the groups after manipulation. In the analysis, the experimental group (AG, KG) was considered as independent and the post-manipulation (t2) paranoia score as dependent variable. When the effect of paranoia scores before manipulation was controlled, paranoia levels in AG were found significantly higher [$F(1,66)=4.42$, $p=.039$, $\eta 2_{partial}=0.06$].
Simple mediation analysis was performed to investigate whether anxiety manipulation affects paranoia through EA. It was found that anxiety manipulation did not affect EA ($a=-.93$, $p=.723$) when state paranoia levels before manipulation were controlled. However anxiety ($c=5.10$, $p=0.003$) and EA ($b=.32$, $p=.003$) was found to predict the increase in paranoia. While the direct effect of anxiety manipulation on paranoia levels was significant ($c'=5.40$, $p=.021$), there was no effect on paranoia through EA ($ab=-.30$, Bootstrap CI: -2.18 to 1.41).
In order to investigate whether PT has a moderator role on the relationship between anxiety and paranoia, the effect of PT on both anxiety-paranoia and EA-paranoia relationship were analyzed. It has shown that AnxietyxPT interaction did not predict paranoia ($p=0.72$). Likewise, it was determined that the EAxPT interaction did not have a predictive effect on paranoia levels (Bootstrap CI: -.27 to .19). Therefore, it was concluded that there was no effect of PT on anxiety-paranoia or EA-paranoia relationship.
DISCUSSION: This is the first experimental study designed to investigate the role of anxiety on paranoia in the clinical population with persecutory delusions in Turkey. It is also the first experimental study in the literature designed to investigate the role of EA and PT in the relationship between anxiety and paranoia. It also shows that the VR is feasible and safe in psychotic patients and has a strong potential to understand the mechanism of psychotic symptoms.
The absence of a statistically significant difference between the experimental groups in terms of sociodemographic and clinical characteristics indicates that the randomization was successful.
Our findings support the literature that anxiety has a central place in paranoia (1). Although the statistical analyzes in our study are compatible with the hypothesis that anxiety causes paranoia and a scenario without social elements was used for manipulation in order to exclude social influence, the possibility of this causality occurring in the opposite direction cannot be excluded. However, longitudinal studies support the argument that anxiety causes paranoia (5).
The results also support the role of EA in paranoia formation but contrary to our hypothesis, anxiety did not predict EA and EA did not have a mediating role in the relationship between anxiety and paranoia. This may mean that psychotic patients use EA strategies only in the presence of certain stressors or emotions other than anxiety. In other words, while anxiety directly paves the way for the formation of paranoia, other emotions may cause the development of paranoia through avoidance. Because the findings in the literature shows that there isn't a single mechanism in the formation of psychotic symptoms, more than one mechanism with many factors may be effective.
There was also no significant effect of PT on the relationship between anxiety and paranoia. This finding may be due to very low accuracy of PT skills in our sample. However, our study was conducted in a chronic patient group and therefore PT may have an effect only on delusion formation at the first stages of psychosis.
In conclusion, our findings support the role of anxiety and EA in paranoia formation and reveal the importance of the interventions for negative emotions and emotion regulation strategies in patients with PD. However,

considering that different causal factors may be at play in different stages of delusional belief formation and maintenance, the hypotheses in our study should also be investigated in healthy, high-risk populations and first episode psychosis. In addition, studies using different stressors will be beneficial in understanding the contribution of both different stressors and different emotions. And also further research is needed which includes behavioral and physiological measurements in the methodolody.

Keywords: Psychosis, Paranoia, Anxiety, Experiential Avoidance, Perspective Taking, Virtual Reality

REFERENCES

Freeman D. Suspicious minds: The psychology of persecutory delusions. Clin Psychol Rev 2007; 27: 425–457.

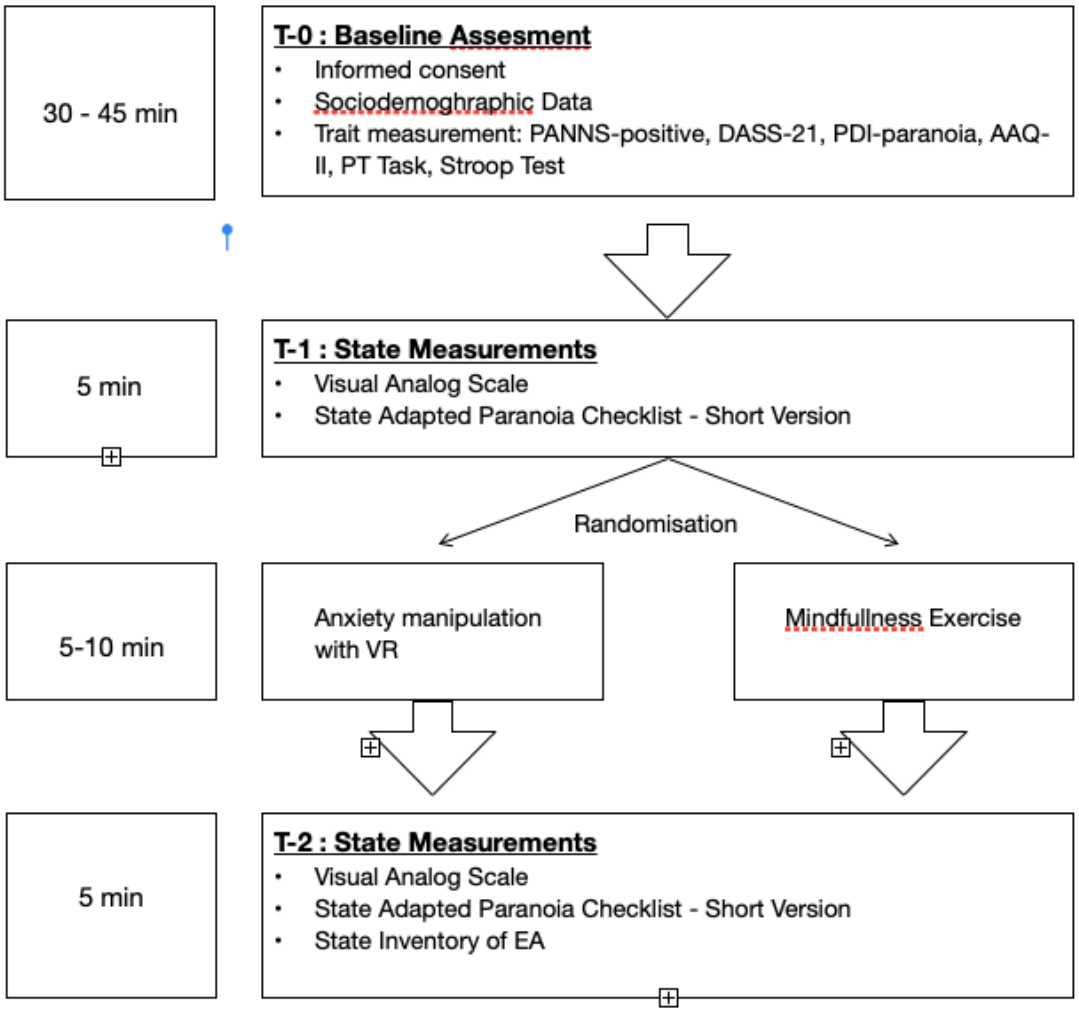
Bentall RP, Corcoran R, Howard R, Blackwood N, Kinderman P. Persecutory delusions: A review and theoretical integration. Clin Psychol Rev 2001; 21: 1143–1192.

Bore, E. (2009). Theory of Mind in Schizophrenia Spectrum Disorders, Turkish Journal of Psychiatry, 20(3).

Hayes AF. The PROCESS macro for SPSS and SAS [Internet]. 2016, Available from: http://processmacro.org/index.html

Oliver JE, O‟Connor JA, Jose PE, McLachlan K, Peters E. The impact of negative schemas, mood and psychological flexibility on delusional ideation - mediating and moderating effects. Psychosis 2012; 4:6–18.

Figure 1. Study Procedure



[Abstract:0262] [Anxiety disorders]

0262 - Examination of inflammation and oxidative stress in children and adolescents with anxiety disorders

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OBJECTIVE: The aim of this study is to evaluate the inflammation and oxidative stress (OS) parameters in children and adolescents with anxiety disorders (AD) by comparing them with healthy controls (HC) and to reveal the effects of the 3-month treatment period on these parameters in AD patients. OS and inflammation parameters as thiol-disulfide, ischemia-modified albumin (IMA), nitric oxide (NO), inducible nitric oxide synthase (iNOS), nitrosothiol, neutrophil lymphocyte ratio (NLR), mean platelet volume (MPV), platelet lymphocyte ratio (PLR), C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), T_3, T_4, TSH, and ferritin levels were evaluated.
METHODS: Our research was designed as a case-control study. The study was approved by the Ankara City Hospital Ethics Committee. This study was supported by Ankara Yıldırım Beyazıt University Scientific Research Projects Commission. The study was conducted in Yenimahalle Training and Research Hospital Child and Adolescent Psychiatry Outpatient Clinic. The case group included forty children aged 7-17 years diagnosed with AD according to DSM-5 criteria with no other psychiatric diseases. HC group consisted of forty-one healthy children without any psychiatric disorder according to DSM-5 criteria. Exclusion criteria for the case and HC groups: Abnormal mental capacity, with any chronic disease, taking another treatment or supplement, having an infection in the last 2 weeks, and receiving related treatment, having used psychotropic drugs before, having anormal body mass index, having used cigarettes, alcohol, or drugs, not accepting to participate in the study. In addition, cases who did not use AD treatment regularly, took another treatment or supplement within 3-month, and had an infection in the 2 weeks before giving a second venous blood sample were excluded from the study. Routine polyclinic controls were performed by applying all modules of K-SADS-PL-DSM-5-T for diagnostic interview to the cases participating in the study. General information was obtained from the case information form and parent and subject report by the researchers. The Screen for Child Anxiety Related Emotional Disorders (SCARED) was given to the children to complete, filled with the clinician. The clinician filled Clinical Global Impression-Severity (CGI-S) to evaluate the severity of the disease at monthly controls. Afterwards, the cases diagnosed with AD were referred to the polyclinic where they were evaluated for routine follow-up and treatment. Later, it was learned that selective serotonin reuptake inhibitor treatment, which was recommended as the first choice in the treatment guidelines, was started in all cases. It was learned that some of the cases had mild gastrointestinal complaints (n=3), inappetence (n=2), headache (n=2), for which treatment was continued by reducing the drug dose in these cases. However, some cases were excluded due to the follow-up process at the request of their legal representatives (n=5), not coming to outpatient clinic controls (n=2), inability to get a second blood sample because they had an active infection (n=2), did not use the treatment regularly (n=4), and did not show clinical improvement over 3-months (n=4). Blood samples were taken from the antecubital vein, on an empty stomach, between 09.00-10.00 in the morning, twice, in the 0_{th} and 3_{rd} months, from the participants in the case group. These samples were taken once in the same procedure from the HC group and then immediately sent to the laboratory. The participants' complete blood count, CRP, ESR, ferritin, and thyroid hormones were routinely studied in the hospital biochemistry laboratory. Approximately 10 ml of venous blood sample taken into a yellow-capped biochemistry tube was centrifuged for 10 minutes and then serum samples were separated. These samples were transferred to two eppendorf and kept in a refrigerator at -80°C until biochemical analysis. At the end of the study, the stored serum samples were taken to Ankara City Hospital Medical Biochemistry Laboratory in accordance with the cold chain rules. Serum samples were thawed simultaneously and thiol-disulfide, IMA, NO, iNOS, and nitrosothiol levels were studied. Parameters related to thiol-disulfide hemostasis were

determined by the new automatic and spectrophotometric method found by Erel and Neselioglu [1]. IMA levels were determined by the spectrophotometric measurement method developed by Bar-Or et al. [2]. The measurement of NO level was carried out based on the Griess method. ELISA Kit (Cloud Clone Corp.) was used for iNOS. Nitrosothiol levels were studied based on the Saville method. From the results obtained, the NLO was found by the ratio of the neutrophil level to the lymphocyte level, and the PLO was found by the ratio of the platelet level to the lymphocyte level.

IBM SPSS.26 program was used in the statistical analysis of the data. Sociodemographic and clinical characteristics of the participants; number, percentage, mean, standard deviation, median, minimum, and maximum values. The suitability of numerical data to normal distribution was evaluated by visual and analytical methods. Independent samples t-test and Mann Whitney U test were used to compare data between two independent groups. Paired samples t-test and Wilcoxon test were used to compare data between two dependent groups. Repeated measures analysis of variance and Friedman test were used to compare the data between three dependent groups. In paired comparisons made in post hoc tests, Bonferroni correction was made and $p<0.008$ was considered significant. Chi-square test and Fisher's exact test were used in the comparison of categorical variables between two independent groups. In the statistical analysis of all data, values of $p<0.05$ were considered significant.

RESULTS: There was no significant difference between the cases and HCs in terms of age, gender, and socioeconomic status ($p=0.059$, $p=1.000$, $p=0.206$, respectively). Distribution of the case group was as follows: generalized anxiety disorder 45% (n=18), social phobia 32.5% (n=13), specific phobia 15% (n=6), separation anxiety disorder 7.5% (n=3).

When the OS and inflammation parameters of pre-treatment AD patients and HCs were compared, the significantly higher results in AD patients are as follows: IMA ($p=0,021$), NO ($p=0,028$), disulfide ($p=0,006$), disulfide/native thiol ($p=0,021$), disulfide/total thiol ($p=0,035$), NLR ($p=0,016$), PLR ($p=0,043$), ESR ($p=0,034$). Parameters are elaborated in Table-1 and Table-2.

When the OS and inflammation parameters of AD patients before and after treatment were compared, the results that decreased significantly after treatment in AD patients are as follows: disulfide ($p=0,019$), T_3 ($p<0,001$), T_4 ($p<0,001$), CRP ($p=0,001$), ESR ($p=0,041$). Parameters are elaborated in Table-3 and Table-4.

According to the CGI-S scale, there was a clinically significant improvement in the monthly follow-up of the participants in the case group ($p<0.001$). According to the SCARED, it was determined that there was a significant decrease in the anxiety level of the participants in the case group every month ($p<0.001$).

DISCUSSION: There are previous studies evaluating OS and inflammation in AD in children and adolescents [3,4]. However, there is not any study about changes in OS and inflammation during the treatment process of AD in children and adolescents. For this reason, it is thought that our study will contribute to the literature.

IMA, NO, iNOS, and nitrosothiol are all markers of OS [2,5,6]. The thiol-disulfide balance represents the antioxidant (thiol) and oxidant (disulfide) load in the organism [1]. In our study, among the parameters related to OS in pre-treatment AD patients; disulfide, disulfide/native thiol, disulfide/total thiol, IMA, and NO levels being significantly higher than HC's may indicate increased OS in childhood AD.

In a study by Güney et al., examining the change in OS with treatment in children diagnosed with ADHD, it was found that thiol levels were significantly lower in the case group before treatment compared to the control group, and there was a significant increase after treatment [7]. In our study, the significant decrease in disulfide levels in AD patients after treatment is an important finding indicating that OS decreases with the improvement of the disease.

It is stated that thyroid hormones, which can accelerate basal metabolism in mitochondria and change respiratory rate, play a role in the production of reactive oxygen radicals and hyperthyroidism induces OS [8]. Therefore, the significant decrease in T_3 and T_4 levels after treatment in AD patients in our study may indicate a decrease in OS.

ESH, CRP, NLR, PLR are parameters that indicate inflammation [3,9]. In a recent study, NLR and PLR levels were found to be significantly higher in children and adolescents with AD, like our study, and it was suggested that there is a relationship between AD and inflammation [3]. In our study, the fact that the levels of inflammation markers NLR, PLR, and ESR were found to be higher in AD patients before treatment compared

to HCs can be interpreted as an increase in inflammation in AD patients. Also, the significant decrease in ESR and CRP levels after treatment in AD patients in our study may indicate that inflammation decreased with AD treatment in children.
The limitations of our study were the small sample size of the case and control groups, and the lack of a second blood sample because the HC group was not followed up. Studies with larger samples are needed to evaluate post-treatment inflammation and OS change in children and adolescents with AD.

REFERENCES

1) Erel O, Neselioglu S. A novel and automated assay for thiol/disulphide homeostasis. Clin Biochem 2014;47(18):326-32.
2) Bar–Or D, Lau E, Winkler JV. A novel assay for cobalt-albumin binding and its potential as a marker for myocardial ischemia—a preliminary report. The Journal of emergency medicine 2000;19(4):311-5.
3) Uzun N, Akıncı MA. Hemogram parameters in childhood anxiety disorders: Could anxiety disorders be related with inflammation?. Med Hypotheses 2021;146(2021):110440.
4) Guney E, Ceylan MF, Tektas A, Alisik M, Ergin M, Goker Z, et al. Oxidative stress in children and adolescents with anxiety disorders. J Affect Disord 2014;156:62-6.
5) Cinelli MA, Do HT, Miley GP, Silverman RB. Inducible nitric oxide synthase: Regulation, structure, and inhibition. Medicinal research reviews 2020;40(1):158-89.
6) Giustarini D, Milzani A, Colombo R, Dalle-Donne I, Rossi R. Nitric oxide and S-nitrosothiols in human blood. Clin Chim Acta 2003;330(1-2):85-98.
7) Guney E, Cetin FH, Alisik M, Tunca H, Torun YT, Iseri E, et al. Attention deficit hyperactivity disorder and oxidative stress: a short term follow up study. Psychiatry Res 2015;229(1-2):310-7.
8) Villanueva I, Alva-Sánchez C, Pacheco-Rosado J. The role of thyroid hormones as inductors of oxidative stress and neurodegeneration. Oxid Med Cell Longev 2013;2013.
9) Lapić I, Padoan A, Bozzato D, Plebani M. Erythrocyte sedimentation rate and C-reactive protein in acute inflammation: meta-analysis of diagnostic accuracy studies. Am J Clin Pathol 2020;153(1):14-29.

Table-1. Comparison of oxidative stress parameters of anxiety disorder patients and healthy controls

	Healthy Control n=41, (mean ± sd)	**Case Group n=40, (mean ± sd)**	**p**
Native thiol (µmol/L)	380.1 ± 86.6	356.2 ± 32.3	0.104*
Total thiol (µmol/L)	426.3 ± 87.7	405.6 ± 33.6	0.164*
Native thiol/total thiol	88.8 ± 2.4	87.8 ± 1.7	**0.035***
Disulfide (µmol/L)***	22.8 (17.4-33.2)	24.6 (14.8-32.2)	**0.006****
Disulfide/native thiol***	6.1 (4.1-10.3)	7.0 (4.2-9.6)	**0.021****
Disulfide/total thiol	5.6 ± 1.2	6.1 ± 0.8	**0.035***
IMA (ABSU)	0.9 ± 0.2	1.0 ± 0.2	**0.021***
NO (µmol/L)	3.5 ± 1.8	4.6 ± 2.4	**0.028***
iNOS (pg/mL)	1310.5 ± 305.4	1441.7 ± 426.5	0.115*
Nitrosothiol (µmol/L)***	0.62 (0.10-0.74)	0.65 (0.30-1.33)	0.09**
TSH (mlU/L)***	1.9 (0.8-4.1)	1.6 (0.4-4.0)	0.441**
T_3 (ng/dl)	3.7 ± 0.6	3.5 ± 0.5	0.104*
T_4 (ng/dl) ***	1.0 (0.8-15.2)	1.0 (0.7-1.5)	0.517**

*Student t test
**Mann whitney u
***Median (min-max)
IMA: Ischemia-modified albumin
NO: Nitric oxide
iNOS: inducible nitric oxide synthase

Table-2. Comparison of oxidative stress parameters before and after treatment in anxiety disorder patients.

	Pre-treatment Case Group n=40, (mean ± sd)	**Post-treatment Case Group n=40, (mean ± sd)**	**p**
Native thiol (µmol/L)	356.2 ± 32.3	343.9 ± 29.7	0.057*
Total thiol (µmol/L)	405.6 ± 33.6	392.4 ± 31.5	0.055*
Native thiol/total thiol	87.8 ± 1.7	87.6 ±2.0	0.689*
Disulfide (µmol/L)	24.7 ± 3.4	23.2 ± 3.1	**0.019***
Disulfide/native thiol	7.0 ± 1.1	6.8 ± 0.8	0.230*
Disulfide/total thiol	6.1 ± 0.8	5.9 ± 0.7	0.175*
IMA (ABSU)***	1.0 (0.6-1.2)	1.0 (0.4-1.4)	0.422**
NO (µmol/L)	4.6 ± 2.4	4.6 ± 2.6	0.990*
iNOS (pg/mL)***	1367.6 (795.7-2601.9)	1473.7 (910.2-2821.7)	0.192**
Nitrosothiol (µmol/L)	0.7 ± 0.2	0.6 ± 0.2	0.061*
TSH (mlU/L)***	1.6 (0.4-4.0)	1.5 (0.4-5.5)	0.089**
T_3 (ng/dl)***	3.5 (2.5-4.5)	3.1 (2.5-4.5)	**<0.001****
T_4 (ng/dl)	1.0 ± 0.1	0.9 ± 0.1	**<0.001***

*Paired sample t test
**Wilcoxon test
***Median (min-max)
IMA: Ischemia-modified albumin
NO: Nitric oxide
iNOS: inducible nitric oxide synthase

Table-3. Comparison of inflammation parameters of anxiety disorder patients and healthy controls.

	Healthy Control n=41, median (min-max)	**Case Group n=40, median (min-max)**	**p**
NLR	1.2 (0.6-7.0)	1.5 (0.6-5.6)	**0.016****
MPV (fL)***	9.6 ± 1.2	9.7 ± 0.9	0.619*
PLR	117.6 (75.0-220.1)	140.6 (73.1-279.8)	**0.043****
CRP (g/L)	0.5 (0.0-5.7)	0.4 (0.1-19.0)	0.306**
ESR (mm/h)	9.0 (1.0-38.0)	11.0 (2.0-28.0)	**0.034****
Ferritin (µg/L)	24.0 (7.2-114.4)	19.7 (3.1-71.4)	0.162**

*Student t test
**Mann whitney u test
***Mean ± sd
NLR: Neutrophil lymphocyte ratio
MPV: Mean platelet volume
PLR: Platelet lymphocyte ratio
CRP: C-reactive protein
ESR: Erythrocyte sedimentation rate

Table-4. Comparison of oxidative stress parameters before and after treatment in anxiety disorder patients

	Pre-treatment Case Group n=40, median (min-max)	**Post-treatment Case Group n=40, median (min-max)**	**p**
NLR	1.5 (0.6-5.6)	1.6 (0.7-3.2)	0.893*
MPV (fL)***	9.7 ± 0.9	9.6 ± 0.8	0.452**
PLR***	145.9 ± 44.3	151.6 ± 44.2	0.227**
CRP (g/L)	0.4 (0.1-19.0)	0.3 (0.1-7.0)	**0.001***
ESR (mm/h)	11.0 (2.0-28.0)	10.0 (3.0-20.0)	**0.041***
Ferritin (µg/L)	19.7 (3.1-71.4)	15.1 (2.0-82.9)	0.667*

*Wilcoxon test
**Paired sample t test
***Mean ± sd
NLR: Neutrophil lymphocyte ratio
MPV: Mean platelet volume
PLR: Platelet lymphocyte ratio
CRP: C-reactive protein
ESR: Erythrocyte sedimentation rate

[Abstract:0273] [Psychopharmacology]

0273 - Effects of royal jelly on depression, anxiety, learning and memory in mice

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INTRODUCTION: Royal jelly (RJ) is secreted from the hypopharyngeal and mandibular glands of worker honey bees of the genus Apis mellifera. RJ is an indispensable food for the development of the queen honey bee [1]. RJ is a substance that contains a combination of proteins, sugars, lipids, amino acids, vitamins and minerals [2]. Further more it contains the unsaturated fatty acid 10 hydroxy trans 2 decenoic acid (HDEA), which is an important component of RJ [3]. Due to antioxidant, anti-inflammatory, neurotrophic, hypotensive, antidiabetic, antihypercholesterolemic, antirheumatic, antitumor, anti-fatigue, antimicrobial and anti-aging properties; effects of RJ is used in many diseases such as cancer, diabetes, hypertension, hyperlipidemia and skin diseases [4]. And also the effectiveness of RJ had been showed on improving learning and memory tasks in animal models of Alzheimer's disease [5]. Brain derived neurotrophic factor (BDNF) has a role in processes such as neuronal maturation, synapse formation and synaptic plasticity among others in the brain [6]. Antidepressant and anxiolytic like effect of BDNF have been showed [7]. Nowadays used highly most of the antidepressants increases the level of BDNF [8]. It is suppented that HDEA, a component of RJ, has a BDNF-like effect by crossing the blood-brain barrier [9,10]. In the present study we aimed to investigate whether the RJ has an effect on depression, anxiety, learning and memory.
METHODS: We investigated the effects of RJ on depression, anxiety, learning and memory by using forced swimming test (FST), elevated plus maze test (EPM), passive avoidance (PA) and morris water maze (MWM) in mice. FST is the most widely used, fast, low cost and simple behavioral test for the screening of antidepressant drugs, EPM is one of the tests used to evaluate anxiety in animals, the PA and MWM tests are useful for the evaluation of cognitive performance (learning and memory). Sixty male inbred BALB/c ByJ mice (Sakarya University Faculty of Medicine Experimental Medicine Applications and Research Center -

SÜDETAM, Sakarya, Türkiye) aged 7 weeks upon arrival to the laboratory were used in this study. Mice were randomly divided into experimental groups in the FST: saline, imipramine 30 mg/kg, RJ 50, 100 and 200 mg/kg; in the EPM test: saline, diazepam 2 mg/kg, RJ 50, 100 and 200 mg/kg; in the PA test: saline, scopolamine 0,6 mg/kg, RJ 50, 100 and 200 mg/kg, RJ 200 mg/kg + scopolamine 0,6 mg/kg; in the MWM test: saline, scopolamine 0,6 mg/kg, RJ 50, 100 and 200 mg/kg, RJ 200 mg/kg + scopolamine 0,6 mg/kg. Mice were treated chronically with RJ (50, 100 and 200 mg/kg) for 15 days. Each group consisted of 8-10 mice. All experiments were performed between 10:00 and 12:00 a.m. Since compounds altering motor activity may give false positive/negative effects in behavioral tests; spontaneous locomotor activity of mice was evaluated by monitoring the activity of the animals in an open field. The locomotor activity was evaluated by measuring the total distance moved of the animals.

RESULTS: Imipramine and all doses of RJ significantly reduced immobility time in FST. Diazepam and all doses of RJ significantly increased the time spent in open arms; and diazepam but not RJ significantly increased the number of entries to the open arms in EPM test. Scopolamine has caused a decrease in latency time in PA test; furthermore, cognitive performance impaired with scopolamine has been significantly improved with 200 mg/kg RJ. RJ (50, 100 and 200 mg/kg) significantly increased the time spent in the target quadrant in naive mice. Again, 200 mg/kg RJ reversed scopolamine-induced decrease in time spent in the target quadrant. All doses of RJ had no effect on mean distance traveled to the platform; on the other hand, 200 mg/kg RJ significantly reversed scopolamine-induced increase in mean distance traveled to the platform. Neither RJ (50, 100 and 200 mg/kg) nor other drugs modified the total distance moved in the open field test.

DISCUSSION: In a previous study; HDEA has been showed protective effects against depression and anxiety [10]. Queen bee acid (QBA; 10-hydroxy-2-decenoic acid) is the predominant fatty acid in RJ and it is showed that QBA, increases neuron growth, protects neurons from damage and reduces anxiety-like behaviors [11], just as we showed the anxiolytic activity of RJ in our study. The basis of neurodegenerative diseases is the increase of free radicals and oxidant molecules. Recent studies have revealed that RJ reduces free radicals and has an antioxidant effect by disrupting lipid peroxidation [12,13]. RJ also has a BDNF-like effect by crossing the blood-brain barrier [10]. BDNF plays an important role in learning and memory, such as long-term potentiation, synaptic plasticity, axonal sprouting and proliferation of the dendritic arbor, particularly in the hippocampus [14]. In addition, it was observed that the average lifespan of mice fed with RJ increased [15]. In the FST, we understood that the immobile times of the mice that received RJ were considerably reduced, that is, they showed an antidepressant effect. In EPM, on the other hand, we saw an increase in the number of entrances to open arms, that is, the anxiolytic effect. In MWM, we found that mice given RJ had learning and memory levels better than the control group. At the same time, we observed that RJ improved scopolamine-impaired memory in the MWM and PA test. When we evaluate all these experimental results, we can say that RJ increases the learning memory level, especially in chronic use, and also has an antidepressant and anxiolytic effect.

CONCLUSION: RJ might be clinically useful for the treatment of depression and anxiety, without disrupt learning and memory. These results demonstrate that RJ is are effective in ameliorating the symptoms of depression and anxiety and suggest that they may become a promising tool as a new antidepressant/anxiolytic. This natural food source is promising in terms of treatment in elderly patients with depression and anxiety.

Keywords: Royal jelly, depression, anxiety, learning, memory, mice

REFERENCES

[1] Hashimoto M, Kanda M, Ikeno K, Hayashi Y, Nakamura T, Ogawa Y, Fukumitsu H, Nomoto H and Furukawa S. Oral administration of royal jelly facilitates mRNA expression of glial cell line-derived neurotrophic factor and neurofilament H in the hippocampus of the adult mouse brain. Biosci Biotechnol Biochem. 2005;69:800-805.

[2] Hattori N, Nomoto H, Fukumitsu H, Mishima S and Furukawa S. Royal jelly-induced neurite outgrowth from rat pheochromocytoma PC12 cells requires integrin signal independent of activation of extracellular signal-regulated kinases. Biomed Res. 2007;28:139-146.

[3] Isidorov V. A, Bakier S and Grzech I. Gas chromatographic-mass spectrometric investigation of volatile and extractable compounds of crude royal jelly. J. Chromatogr. B: Anal. Technol. Biomed. Life Sci. 2012;885–886:109–116.
[4] Nakajima Y, Tsuruma K, Shimazawa M, Mishima S and Hara H. Comparison of bee products based on assays of antioxidant capacities. BMC Complement Altern Med. 2009;9:4.
[5] You M, Pan Y, Liu Y, Chen Y, Wu Y, Si J, Wang K and Hu F. Royal jelly alleviates cognitive deficits and β-amyloid accumulation in APP/PS1 mouse model via activation of the cAMP/PKA/CREB/BDNF pathway and inhibition of neuronal apoptosis. Frontiers in Aging Neuroscience. 2019;10:428.
[6] Park H and Poo MM. Neurotrophin regulation of neural circuit development and function. Nat. Rev. Neurosci. 2013;14(1):7–23.
[7] R. S. Duman. "Synaptic plasticity and mood disorders," Molecular Psychiatry. 2002;7(1):29–34.
[8] A. Russo-Neustadt, R. C. Beard and C. W. Cotman. "Exercise, antidepressant medications, and enhanced brain derived neurotrophic factor expression," Neuropsychopharmacology. 1999;21(5): 679–682.
[9] K. Athena, F. Mona, J. Melikasadat, J.B. Seyed and P. Vahid. Neurogenesis in the rat neonate's hippocampus with maternal short-term REM sleep deprivation restores by royal jelly treatment. Brain Behav. 2021;11(12):e2423.
[10] Ito S, Nitta Y, Fukumitsu H, Soumiya H, Ikeno K, Nakamura T and Furukawa S. Antidepressant-like activity of 10-hydroxy-trans-2-decenoic Acid, a unique unsaturated Fatty Acid of royal jelly, in stress-inducible depression-like mouse model. Evidence-Based Complementary and Alternative Medicine. 2012;(2012):6.
[11] Weiser MJ, Grimshaw V, Wynalda KM, Mohajeri MH and Butt CM. Long-Term Administration of Queen Bee Acid (QBA) to Rodents Reduces Anxiety-Like Behavior, Promotes Neuronal Health and Improves Body Composition. 2018;10(1):13.
[12] El-Nekeety AA, El-Kholy W, Abbas NF, Ebaid A, Amra HA and Abdel-Wahhab MA. Efficacy of royal jelly against the oxidative stress of fumonisin in rats. Toxicon. 2007;50(2):256-269.
[13] Jamnik P, Goranovic D and Raspor P. Antioxidative action of royal jelly in the yeast cell. Experimental Gerontology. 2007;42:594-600.
[14] Tan C.H, Low K.A, Chiarelli A.M, Fletcher M.A, Navarra R, Burzynska A.Z, Kong T.S, Zimmerman B, Maclin E.L, Sutton B.P, Gratton G and Fabiani M. Optical measures of cerebral arterial stiffness are associated with white matter signal abnormalities and cognitive performance in normal aging. Neurobiol Aging. 2019;84:200–207.
[15] Nagai T. and Inoue R. Preparation and the functional properties of water and alkaline extract of royal jelly. Food Chemistry. 2004;84(2):181–186.

[Abstract:0278] [Psychopharmacology]

0278 - Effects of vortioxetine on cognitive functions: naturalistic prospective study

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INTRODUCTİON: Cognitive dysfunction is frequently observed in patients suffering from Major Depressive Disorder (MDD) and is associated with poor response to treatment[1]. Cognitive dysfunction in MDD encompasses several domains, most commonly small to moderate deficits in attention, memory, learning, processing speed and executive function[2]. The serotonin (5-HT) system is thought to have a role in regulating prefrontal cortical circuitries involved in cognitive processing; several possible pathways whereby drugs acting through multiple serotonergic targets may robustly improve cognitive dysfunction have been postulated[2]. Vortioxetine is a novel multimodal antidepressant with two types of action towards the

serotonergic neurotransmitter system: it inhibits the serotonin transporter (SERT) and, additionally, modulates the effects of several serotonin (5-HT) receptors [2]. In recent literature, short-term treatment with vortioxetine 5–20 mg/day significantly improved cognitive functions in adults with MDD based on the results of various objective neuropsychological tests covering multiple domains [2]. In this study, we primarily aimed to evaluate the efficacy of vortioxetine 10-20 mg/day on cognitive function in adults with MDD at the beginning of treatment and after 8 weeks.

METHOD: A total of 19 patients with age range 18-55 who were consecutively presented to psychiatry outpatient clinics of Diskapi Yıldırım Beyazıd Training and Research Hospital and who were diagnosed as depression were included in the study. The patients were screened and diagnosed with the Structured Clinical Interview for DSM-V (SCID-5-CV). Patients with at least high school education were included in the study. The exclusion criteria were current alcohol and/or substance use disorder, presence of comorbid psychiatric disorder other than MDD, medications approved and/or employed off-label for cognitive dysfunction (e.g., psychostimulants), any medication for a general medical disorder that may affect cognitive function, use of benzodiazepines within 12 hours of cognitive assessments, physical, cognitive, or language impairments sufficient to adversely affect data derived from cognitive assessments, diagnosed reading disability or dyslexia, clinically significant learning disorder by history, electroconvulsive therapy (ECT) in the last 6 months, history of moderate or severe head trauma, other neurological disorders, or unstable systemic medical diseases that are likely to affect the central nervous system. All patients were evaluated before initiation of treatment and 8 weeks after treatment at the same hours. All participants were given vortioxetine 10 mg po as starting dosage. The dosage 10-20 mg po was maintained flexibly after the fourth week through the end of week 8. The severity of depression and anxiety as assessed using the Hamilton Depression (HAM-D) and Anxiety (HAM-A) scales. CGI (Clinical Global Impression) scale was used to assess the severity of the disease, the extent to which the patient responded to treatment, and compliance with treatment. Drug effects on cognition were evaluated cross sectionally at baseline and 8 weeks by using the neuropsychological tests. The cognitive functions were evaluated with Trail Making Test A and B (TMT A-B), Stroop Test TBAG form, Auditory Verbal Learning Test (AVLT). TMT A-B is a neuropsychological test of visual attention and task switching. It can provide information about visual search speed, scanning, speed of processing, mental flexibility, as well as executive functioning. Stroop Test is a neuropsychological test extensively used to assess the ability to inhibit cognitive interference that occurs when the processing of a specific stimulus feature impedes the simultaneous processing of a second stimulus attribute, well-known as the Stroop Effect. In AVLT, five presentations of a 15-word list (list A) are given, each followed by attempted recall. This is followed by a second 15-word list (list B), followed by recall of list A, and delayed recall and recognition are also tested. The analysis of the data has been performed by using a Statistical Package programmer for Social Science (SPSS) 20.0 statistical software. $p<0.05$ was considered significant. Wilcoxon test was used to compare the dependent groups that did not fit the normal distribution. The primary efficacy endpoint was a composite cognition score comprising the Trail Making Test A and B (TMT), Auditory Verbal Learning Test (AVLT) and Stroop Test TBAG form.

RESULTS: The demographic and clinical characteristics of the patients at baseline are summarized in Table 1. There was no patient who had a head trauma in the past, used alcohol and had an uncontrollable chronic disease. There was no patient who was hospitalized inpatient psychiatry clinics before or had an episode of depression. Comparison of cognitive functions before and after 8 weeks of vortioxetine treatment are summarized in Table 2. After the end of 8 weeks treatment, vortioxetine-treated patients exhibited significant improvement in both depression symptom and anxiety severity as assessed with the HAM-D ($p\leq0.0001$ r:0.62) and HAM-A scale ($p\leq0.0001$ r:0.62). Processing speed and executive function were evaluated with TMT-A and B. There was significant difference finishing duration in TMT-A ($p\leq0.01$ r:0.46) and TMT-B ($p\leq0.001$ r:0.54). In Stroop TBAG test, selective attention and executive function were evaluated. There was significant difference the duration for completion of 5 sections of Stroop TBAG test 1 ($p\leq0.01$ r:0.49), Stroop TBAG test 2 ($p\leq0.01$ r:0.40), Stroop TBAG test 3 ($p\leq0.0001$ r:0.62), Stroop TBAG test 4 ($p\leq0.0001$ r:0.57) and Stroop TBAG test 5 ($p\leq0.001$ r:0.53). Learning and memory were assessed with AVLT, number of words which were remembered truly increased significantly [(A1/L-FR:T $p\leq0.0001$ r:0.61), (A2/L-FR:T $p\leq0.0001$ r:0.57), (A3/L-FR:T $p\leq0.001$ r:0.52), (A4/L-FR:T $p\leq0.01$ r:0.46), (A5/L-FR:T $p\leq0.001$ r:0.52) (B/L-FR:T $p\leq0.001$

r:0.56), (A6/L-FR:T p≤0.0001 r:0.57), (A7/L-FR:T p≤0.001 r:0.55)]. In AVLT, true score from list A and B increased significantly [(A/RR: T p≤0.01 r:043), (B/RR:T p≤0.01 r:0.42), (A+B/RR:T p≤0.01 r:0.49)]. In AVLT, there was significant difference between number of semantic distractors [(A/SD p≤0.05 r:0.36), (B/SD p≤0.01 r:0.40)]. There was not significant difference between number of phonetic distractors.

DISCUSSION: According to results of our study, patients with diagnosed MDD showed a significant increase in severity of depressive symptoms and showed significant improvement in cognitive function which are processing speed, executive function, attention, learning and memory after 8 weeks of vortioxetine treatment. There are few studies that assessed the efficacy of the application of vortioxetine on cognitive functions in the treatment of patients with MDD in recent literature. In this respect, our study is an important study with its prospective feature and number of inclusive cognitive tests. In previous literature; McIntyre et al. (2014) found that Vortioxetine significantly improved objective and subjective measures of cognitive function in adults with recurrent MDD and these effects were largely independent of its effect on improving depressive symptoms [3]. According a review and a meta-analysis, across three large, placebo-controlled studies in adults with recurrent MDD, short-term treatment with vortioxetine improved performance on the DSST and RAVLT, two objective measures that together cover a broad range of cognitive domains, including executive function, attention, processing speed, learning and memory[4, 5]. Results of our study are in line with the previous studies that showed a positive change in cognitive function after receiving vortioxetine in patients with MDD. Limitations of our study are duration of treatment for only 8 weeks, small sample size, lack of the control group and results only pertain to the two doses evaluated. In this study, it could not be concluded whether the effect of the efficacy of both doses of vortioxetine on cognitive function was largely a direct and independent effect rather than an epiphenomenon of broad-based symptom improvement in depression. This effect can be measured by including other antidepressants and expanding the sample. There is a need for further studies on effects of vortioxetine on cognitive function in patients with MDD.

Keywords: vortioxetine, major depressive disorder, cognitive function

REFERENCES

1. Rock, P.L., et al., Cognitive impairment in depression: a systematic review and meta-analysis. Psychol Med, 2014. **44**(10): p. 2029-40.
2. McIntyre, R.S., et al., The prevalence, measurement, and treatment of the cognitive dimension/domain in major depressive disorder. CNS Drugs, 2015. **29**(7): p. 577-89.
3. McIntyre, R.S., S. Lophaven, and C.K. Olsen, A randomized, double-blind, placebo-controlled study of vortioxetine on cognitive function in depressed adults. Int J Neuropsychopharmacol, 2014. **17**(10): p. 1557-67.
4. Frampton, J.E., Vortioxetine: A Review in Cognitive Dysfunction in Depression. Drugs, 2016. **76**(17): p. 1675-1682.
5. Huang, I.C., et al., Effect of Vortioxetine on Cognitive Impairment in Patients With Major Depressive Disorder: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. Int J Neuropsychopharmacol, 2022.

Table 1. Demographic and clinical characteristics of patients at baseline

Variables	Value	
Age†	33.5±2.27	
Gender‡	19 (94.7) Female	1 (5.3) Male
Martial Status‡	7 (36.8) Married	6 (31.6) Single
Work Status‡	8 (41.2) Housewife	5 (26.3) Worker
Education Status‡	13 (68.4) High School	6 (31.6) University
Family Depression History‡	17 (89.5) Yes	2 (10.5) No
Smoking‡	9 (47.4) Yes	10 (52.6) No
Chronic Diseases‡	6 (31.6) Yes	13 (68.4) No
Depression age of onset*	29(23-37)	
Depression Duration(month) *	2(1-12)	

* Values presented as the median (25^{th}–75^{th} percentile)
† Values presented as the mean ± standard deviation.
‡ Values presented as the number of patients (percentage

	Week 0			Week 8			gative Ranks		Positive Ranks			Statistical Results			
	Percentiles			Percentiles											
	25th	50th (Median)	75th	25th	50th (Median)	75th	Mean Rank	Sum of Ranks		Mean Rank		Sum Ranks	Ties			
TMT-A	32.00	45.00	59.00	25.00	31.00	39.00	17	9.74	165.50	2	12.25	24.50	0	-2.839	0.46	≤0.01
TMT-B	75.00	111.00	155.00	69.00	89.00	124.00	15	10.87	163.00	2	2.67	8.00	1	-3.376	0.54	≤0.001
STROOP	8.00	10.00	13.00	8.00	9.00	10.00	14	9.96	139.50	3	4.50	13.50	2	-3.027	0.49	≤0.01
TBAG- 1																
STROOP	9.00	10.00	18.00	8.00	9.00	12.00	11	6.41	70.50	1	7.50	7.50	7	-2.477	0.40	≤0.01
TBAG-2																
STROOP	11.00	14.00	18.00	9.00	10.00	15.00	19	10.00	190.00	0	.00	.00	0	-3.846	0.62	≤0.0001
TBAG-3																
STROOP	15.00	22.00	22.00	12.00	16.00	19.00	17	9.76	166.00	1	5.00	5.00	1	-3.521	0.57	≤0.0001
TBAG-4																
STROOP	22.00	28.00	31.00	19.00	22.00	27.00	14	10.39	145.50	3	2.50	7.50	2	-3.273	0.53	≤0.001
TBAG-5																
A1/L-FR: T	4.00	5.00	6.00	6.00	8.00	9.00	0	.00	.00	18	9.50	171.00	1	-3.772	0.61	≤0.0001
A2/L-FR: T	6.00	7.00	10.00	9.00	10.00	11.00	1	2.50	2.50	16	9.41	150.50	2	-3.536	0.57	≤0.0001
A3/L-FR: T	8.00	9.00	11.00	9.00	11.00	12.00	2	7.75	15.50	17	10.26	174.50	0	-3.247	0.52	≤0.001
A4/L-FR :T	7.00	10.00	13.00	10.00	12.00	14.00	2	8.50	17.00	15	9.07	136.00	2	-2.868	0.46	≤0.01
A5/L-FR:T	8.00	10.00	12.00	12.00	13.00	14.00	1	15.00	15.00	18	9.72	175.00	0	-3.236	0.52	≤0.001
B/L-FR:T	3.00	4.00	6.00	6.00	7.00	7.00	2	5.00	10.00	17	10.59	180.00	0	-3.470	0.56	≤0.001
A6/L-FR:T	7.00	8.00	11.00	10.00	11.00	13.00	1	2.50	2.50	16	9.41	150.50	2	-3.531	0.57	≤0.0001
A7/L-FR:T	6.00	7.00	9.00	9.00	10.00	12.00	1	3.00	3.00	15	8.87	133.00	3	-3.422	0.55	≤0.001
A/RR: T	8.00	12.00	14.00	13.00	14.00	15.00	1	13.00	13.00	14	7.64	107.00	4	-2.681	0.43	≤0.01
B/RR: T	3.00	9.00	12.00	8.00	10.00	13.00	5	6.20	31.00	14	11.36	159.00	0	-2.600	0.42	≤0.01
A+B/RR: T	14.00	18.00	25.00	21.00	24.00	27.00	2	7.75	15.50	16	9.72	155.50	1	-3.058	0.49	≤0.01
A/SD	.00	.00	1.00	.00	.00	.00	5	3.00	15.00	0	.00	.00	14	-2.236	0.36	≤0.05
B/SD	.00	1.00	1.00	.00	.00	.00	9	5.61	50.50	1	4.50	4.50	9	-2.484	0.40	≤0.01
HAMD	16.00	21.00	25.00	3.00	5.00	6.00	19	10.00	190.00	0	.00	.00	0	-3.825	0.62	≤0.0001
HAMA	6.00	7.00	7.00	1.00	2.00	3.00	19	10.00	190.00	0	.00	.00	0	-3.835	0.62	≤0.0001

Table 2.Change from baseline to week

[Abstract:0282] [Others]

0282 - Evaluation of medical students' knowledge and attitudes towards LGBTQIA ındividuals

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AIM: The concept of homophobia has been introduced to define the prejudices and discriminations LGBTI+ individuals face in society.The number of homophobia studies has increased significantly in recent years.It can be assumed that academic curiosity and knowledge on this subject are invisible, as are the difficulties LGBTI+ individuals experience due to homophobic attitudes and concerns.
LGBTI+: It is an abbreviation consisting of the initials of Lesbian, Gay, Bisexual, Trans, and Intersex identities. Lesbian, Gay, and Bisexual is a sexual orientation; trans is a gender identity; intersex is a gender status/characteristic. In recent years, a plus sign, meaning "more", has been added to the end of the abbreviation to include sexual orientation and gender identities other than these definitions.The plus sign indicates that the diversity of sexual orientation and gender identity is much more than the identities in this abbreviation (1).
Gender identity is the individual's perception and acceptance of his own body and self in a certain gender.On the other hand, sexual orientation is the attraction of an individual's wishes, feelings and behaviors to a certain gender.In the Yogyakarta Principles (2007) document, the concept of gender identity is defined by expanding its content.The Yogyakarta Principles state, "Gender identity is understood to refer to each person's deeply felt internal and individual experience of gender, which may or may not correspond with the sex assigned at birth, including the personal sense of the body (which may involve, if freely chosen, modification of bodily appearance or function by medical, surgical or other means) and other expressions of gender, including dress, speech and mannerisms."According to this definition, gender identity, in addition to bodily consciousness and functions, is basically experiencing private and personal satisfaction and sexuality regardless of whether they conform to what is expected of their birth sex, and it is being outside of gender stereotypes and judgments(2,3). Sexual orientation expresses the nature of emotional and sexual attraction towards others(4).
In the previous studies in the literature, it seems that there is lack of education at health services.The aim of this study is to reveal the knowledge level of medical students about LGBTI+ individuals, their sexual attitudes, and their interaction with professional equipment at a university in the southeast of Turkey with a questionnaire consisting of sociodemographic data, Hudson and Ricketts homophobia scale and Hendrick Sexual Attitudes scale.
METHODS: This cross-sectional study was undertaken in a university hospital with a sample of medical faculty students.Anonymous data were collected with a link which google form of a self-administered,online survey sent to whatsapp group via group of medical students. Participants gave their informed consent before the questionnaire was administered.The study was carried out per good scientific standards and was approved by the university's ethics committee.Besides the established questionnaires and scales, the survey consists of questions on sociodemographics.**Hendrick Sexual Attitudes Scale:**It is a comprehensive scale to measure attitudes towards different aspects of sexuality.The Turkish version of the Hendrick Brief Sexual Attitudes Scale has validity and reliability study.Reliability analysis and item analysis was made of the scale with acceptable internal consistency coefficient for the scale items measuring out to show proficiency.We used the Turkish adaptation of this 23-item version in our study.**The Attitudes Toward Lesbians and Gay Men Scale:**The Attitudes Toward Lesbians and Gay Men (ATLG) Scale is a brief measure of heterosexuals' attitudes toward gay men and lesbians.The original scale consists of 20 different statements, 10 about gay men and 10 about lesbians.The ATLG can be self-administered (presented on paper or on a computer) or administered orally (as in a telephone survey).Five response options are offered:strongly disagree,disagree

somewhat,neither agree nor disagree ,agree somewhat,strongly agree.Scoring is accomplished by summing numerical values.Duyar and colleagues examined the Turkish version of the ATLG for reliability, validity.(1)**Hudson and Ricketts Homophobia Scale:**The scale was developed to assess the cognitive, affective, and behavioral components of homophobia.A high score on the scale indicates a high level of homophobia. In research.The Turkish form of the scale, which consists of 24 items adapted by Sakallı and Uğurlu(2001), was used(2).

RESULTS: The average age of the 324 students participating in the study was 21.97±2.12(min-max=18.0-30.0). In the research, 84%(n=272) of the students were heterosexual, 5.6%(n=18) bisexual, 0.6%(n=2) lesbian, 3.7%(n=12) gay, and 0.9%(n=9) asexual. Among the students who give a score of 5 or more to the question asked; the rate of those who consider the level of knowledge about homosexuals as sufficient or very good is 75.9%(n=246), the rate of those who think they know the health needs of homosexuals sufficiently or very well is 57%(n=187), and the rate of those consider that there is enough or too much information about homosexuals in the medical school curriculum is 19.4%(n=63). The median value of the scores collected from the Hudson Ricketts scale was 58.50. Those below this value were associated with low homophobia level, and those above it with high homophobia. For the Attitudes towards Lesbian and Gays(LGYT) and Hendrick Sexual Attitude Scale, students were compared only based on their total scores. Female students showed significantly lower homophobia than male students($p=0.001$, $p<0.05$). The scores of the female students on the LGYT scale were significantly higher than the male students($p=0.001$, $p<0.05$). Homophobia scores for gays in the LGYT scale were found to be higher in both male students($p=0.001$, $p<0.05$) and female students($p=0.001$, $p<0.05$) compared to the homophobia scores for lesbians.

DEBATE: Today, the idea that assumes the binary gender system as a social norm is still valid. In many countries, because of the gender identity and sexual orientation, some people are excluded or even ignored in various fields such as health, education, employment, legal rights. In our research, we investigated the relationship between the knowledge, opinions and attitudes of physician candidates and their homophobia levels.

Heteronormativity based on patriarchal structure in the Southeastern region of Turkey, individuals who are not seen as "acceptable" and who do not comply with common social norms are excluded from society. In the southeast region, the low or no education level, the fact that economic independence is generally for men, religious and cultural life differences, and honor killings carried out due to custom as in the feudal structure have led to the emergence of a male-dominated understanding. Therefore, it has become inevitable for women and LGBTI+ individuals to become “invisible” in this region. Studies conducted around the world also show that LGBTI+ individuals experience several health inequalities and barriers to quality health care. There are studies showing that one reason for this is insufficient integration into the medical curriculum, and the other reason is limited knowledge and awareness about LGBTI+ individuals(7). Although the results of our study are largely compatible with the existing literature examining homophobic attitudes, the proportion of participants who stated that they were heterosexual(84%) was found to be lower than predicted. The rate of those who find the Faculty of Medicine curriculum sufficient(19.4%) is quite low, as expected. In a study conducted in our country, it was seen that participants who had social contact with gay people before had more positive attitudes. This study showed that social contact with homosexual people enables the individual to have a more realistic and holistic perspective and to attribute homosexuality to preferences rather than pathology. In our study, it was determined that students with homosexual acquaintances showed lower homophobia with the scores they got from both Hudson Ricketts and LGYT scales. In this study, the most negative attitudes are against the label "gay", and as a result of this and some other studies, it has been shown that the concept of homosexuality is associated with men for many individuals, and the concept of homosexuality has a stronger relationship with male homosexuality than female homosexuality(6). In our study, the homophobia scores for gays were found to be higher than the homophobia scores for lesbians in both female and male students in the evaluation made according to the scores obtained from the Attitudes Towards Lesbian and Gays Scale, which once again showed the negative point of view towards gay individuals. Another significant difference was found that students studying in the English program showed a lower level of homophobia than those in the Turkish program($p=0,001$, $p<0,05$). When we examined the

relationship between the increase in the education level of the parents (the group with higher education and higher education) and homophobic attitudes, it was observed that the scores obtained from the Hudson and Ricketts scale were significantly lower in the students whose parents had a high education level. The main determinants of mental health are to exist together with diversity, with the assurance of our universal rights. The findings of our study support that medical students consider their knowledge of the health needs of LGBTI+ individuals and the education they receive in this regard inadequate. Our study is a preliminary study in which opinions and attitudes can be evaluated for future studies in larger groups, including physicians with specialty training. It should be aimed to review educational activities and to make health services inclusive with different research to be conducted on this subject.

REFERENCES

1.Güven, U.(2021). LGBTİ+ temel kavramlar atölye kolaylaştırıcı kılavuzu. https://kaosgldernegi.org/images/library/kolaylas-tirici-kilavuz.pdf,04.04.2022
2.Jogjakarta İlkeleri (2007). Uluslararası İnsan Hakları Mevzuatının Cinsel Yönelim ve Cinsiyet Kimliği Alanlarında Uygulanmasına İlişkin İlkeler.
3. Kayır GÖ. Sosyolojik değerlendirme: LGBT bireyler açısından cinsiyet kimlikleri meselesi. Eğitim Bilim Toplum Dergisi 2015;13(51):73-97.
4. Yarns BC, Abrams JM, Meeks TW, Sewell DD The mental health of older LGBT adults. Curr Psychiatry Rep 2016;18:60 DOI 10.1007/s11920016-0697-y.
5.Duyan, Veli, Selahattin Gelbal, and Veli Duyan. "Lezbiyen ve geylere yönelik tutum (LGYT) ölçeği: Güvenirlik ve geçerlik çalışması." HIV/AIDS Dergisi 7.3 (2004): 106-112.
6.Sakalh, Nuray, and Ozanser Ugurlu. "Effects of social contact with homosexuals on heterosexual Turkish university students' attitudes towards homosexuality." Journal of homosexuality 42.1 (2002): 53-62.
7. .https://onlinelibrary.wiley.com/doi/10.1111/hsc.13130
Grant, Ruby, et al. "Tasmanian healthcare professionals'& students' capacity for LGBTI+ inclusive care: A qualitative inquiry." Health & Social Care in the Community (2020).
8. Sakallı, N. (2002c). Relationship between sexism and attitudes toward homosexuality in a sample of Turkish university college students. Journal of Homosexuality, 43, 53–64.

[Abstract:0283] [Schizophrenia and other psychotic disorders]

0283 - Moodsoft-rita (mental health risks screening scale) preliminary study of the validity and reliability of the psychosis and bipolar story scales

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BACKGROUND AND OBJECTIVE: There are very few self-report scales to be used for screening psychotic experiences. It is especially important to distinguish ambiguous psychotic states. The aim of this study; To develop a short and easily applicable scale for screening psychotic symptoms.
METHOD: In the development of the Moodsoft-Rita psychosis scale, the questions included in the Research and Evaluation Form (ARDEF), which was used for screening purposes in prisons, were taken as the basis, and a form consisting of 4 questions was prepared. Response options were prepared as a 3-point likert. The developed scales were applied to 5 patients to test the comprehensibility of the scales.
Moodsoft-Rita Psychosis Scale and Psychic Experiences Assessment Scale were administered to 100 people who applied to Moodist Psychiatry and Neurology Hospital.
RESULTS: The correlation between the Psychic Experience Rating Scale and the Moodsoft-Rita Psychosis Scale was 0.66 ($p<0.01$). In the exploratory factor analysis, a single factor with an eigenvalue greater than 1

was obtained and explains 67.15% of the total variance. The internal consistency Cronbach alpha coefficient of the scale was found to be 0.83.
DISCUSSION AND CONCLUSION: As a result, we believe that the Moodsoft-Rita Psychosis Scale has adequate psychometric properties, is valid and reliable, and can be used as a risk screening scale in its current form.
Keywords: psychosis screening, psychosis questionnaire, validity and reliability, moodsoft-rita, risk screening

REFERENCES
[1] Sevi OM, Ustamehmetoğlu F, Gülen M, Zeybek Z. Toplumda Psişik Yaşantıları Değerlendirme Ölçeği Türkçe Formu'nun Güvenilirlik ve Geçerliliği Yeni Symposium Dergisi. Eylül 2019, Cilt: 57, Sayı: 3
[2] Konuk N, Kıran S, Tamam L, Karaahmet E, Aydın H, Atık L. Duygudurum Bozuklukları Ölçeği'nin Türkçe Uyarlamasının Bipolar Bozukluk Taramasında Geçerliği. Türk Psikiyatri Dergisi 2007; 18(2):147-154
[3] Ögel K, Başabak A, Kamer Vk, Görücü S. Yetişkin Hükümlüler için Risk ve İhtiyaç Belirleme Formunun (YARDEF) geliştirilmesi. Anadolu Psikiyatri Derg 2014; 15:132-140
[4] Peters ER, Joseph SA, Garety PA. Measurement of delusional ideation in the normal population: introducing the PDI (Peters et al. Delusions Inventory). Schizophr Bull 1999;25(3):553-576.
[5] Stefanis NC, Hanssen M, Smirnis NK, Avramopoulos DA, Evdokimidis IK, Stefanis CN ve ark. Evidence that three dimensions of psychosis have a distribution in the general population. Psychol Med 2002;32(2):347-358.

[Abstract:0284] [Obsessive-compulsive disorders (OCD)]

0284 - The validity and reliability study of the moodsoft-rita (mental health risks screening scale) obsession scale

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Background and Objective: OCD scales are examined, most of them have a high number of questions and take a lot of time to complete. The aim of current study is to scan the risk factors of the obsessive compulsive symptoms and to develop a short and easily applicable scale for screening obsessive compulsive symptoms.
Method: The questions of the SCL-90 obsession subscale were used as the basis for the development of the Moodsoft-Rita obsession scale. Among these questions, a smaller number of questions that could represent the whole subscale were selected. response options: It was prepared as a 3-point likert.
The Moodsoft-Rita Obsession Scale and the SCL-90 Obsession Scale were administered to 280 people, who applied to the Moodist Psychiatry and Neurology Hospital.
Results: Correlation between SCL-90 obsession subscale and Moodsoft-Rita obsession scale was found to be 0.95 ($p<0.01$).
In the exploratory factor analysis, a single factor with an eigenvalue greater than 1 was obtained, and it explains 79.11% of the total variance.
The internal consistency Cronbach alpha coefficient of the whole scale was found to be 0.89. Based on the SCL-90 obsession subscale, the area under the curve (AUC) at the cut-off point for the Moodsoft-Rita obsession scale is 0.94, the sensitivity is 0.88, and the specificity is 0.84.
Discussion and Conclusion: As a result, we believe that the Moodsoft-Rita obsession scale has adequate psychometric properties, is valid and reliable, has satisfactory sensitivity and specificity values, and can be used as a risk screening scale in this state.

Keywords: obsessive compulsive disorder, obsession scale, psychometric properties, moodsoft-rita, risk screening

REFERENCES
[1] Beşiroğlu, L. ve Ağargün, M.Y. (2006). Obsesif kompulsif bozuklukta sağlık yardımı arama davranışı ile ilişkili etmenler: Hastalık ile ilişkili ve genel etmenlerin rolü. Türk Psikiyatri Dergisi; 17:213-22.
[2] Dağ, İ. (1991). Belirti tarama listesi (SCL-90-R)'nin üniversite öğrencileri için güvenirliği ve geçerliği. Türk Psikiyatri Dergisi, 2, 5-12.
[3] Derogatis. L. R., Lipman, R. S. SC Covi. L. (1973). SCL-90. an outpatient psvchiatric rating scale-oreliminarv renort. Psychopharmacology Bulletin, 9, 13-28.
[4] Derogatis, L. R. & Cleary, P. A. (1977). Factorial invariance across gender for the primary symptom dimensions of the SCL-90. British Journal of Social and Clinical Psychology, 16, 347-356.
[5] Erol N, Savaşır. I: Maudsley Obsesif-Kompulsif Soru Listesi. 24. Ulusal Psikiyatri ve Nörolojik Bilimler Kongresi. Bilimsel Çalışma Kitabı. Ankara, 1988; s:107-114

[Abstract:0286] [Others]

0286 - The validity and reliability study of the moodsoft-rita (mental health risks screening scale) psychological resilience scale

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Background and Objective: Psychological resilience is a prominent factor influencing mental health outcomes after adversity. The aim of this study is to develop a short and easily applicable scale for screening psychological resilience.
Method: In the development of the Moodsoft-Rita Psychological Resilience Scale, other scales and literature knowledge were taken into consideration and 5-question was created. Response options: It was prepared as a 3-point likert.
The Moodsoft-Rita Psychological Resilience Scale and the Brief Resilience Scale (KPSÖ); were administered to 150 people who applied to the Moodist Psychiatry and Neurology Hospital.
Results: Correlation between KPSÖ and Moodsoft-Rita Psychological Resilience Scale was found to be 0.60 ($p<0.01$).
In the exploratory factor analysis, a single factor with an eigenvalue greater than 1 was obtained and explains 69.33% of the total variance.
The internal consistency Cronbach alpha coefficient of the whole scale was found to be 0.85. Based on the KPSÖ, the area under the curve (AUC) at the cut-off point for the Moodsoft-Rita Psychological Resilience scale is 0.77, the sensitivity is 0.78, and the specificity is 0.56 for a score of 1.1.
Discussion and Conclusion: As a result, we believe that the Moodsoft-Rita Psychological Resilience Scale has adequate psychometric properties, is valid and reliable, has satisfactory sensitivity and specificity values, and can be used as a risk screening scale in this state.

Keywords: psychological resilience, psychological resilience scale, validity and reliability, moodsoft-rita, risk screening

REFERENCES
[1] Doğan T. Kısa Psikolojik Sağlamlık Ölçeği'nin Türkçe uyarlaması: Geçerlik ve güvenirlik çalışması. The Journal of Happiness & Well-Being, 2015, 3(1), 93-102
[2] Smith, B. W., Dalen, J., Wiggins, K., Tooley, E., Christopher, P., & Jennifer Bernard, J. (2008). The brief resilience scale: Assessing the ability to bounce back. International Journal of Behavioral Medicine, 15, 194–200.

[3] Smith, B. W., Tooley, E. M., Christopher, P., & Kay, V. S. (2010). Resilience as the ability to bounce back: A neglected personal resource. Journal of Positive Psychology, 5, 166-176.
[4] Connor, K. M., & Davidson, J. R. (2003). Development of a new resilience scale: The Connor Davidson Resilience Scale (CD-RISC). Depression and Anxiety, 18, 76–82
[5] Taşğın, E. ve Çetin, F. Ç. (2006). Ergenlerde major depresyon: Risk etkenleri, koruyucu etkenler ve dayanıklılık. Çocuk ve Ergen Ruh Sağlığı Dergisi, 13(2), 87-94.

[Abstract:0287] [Attention deficit hyperactivity disorder (ADHD)]

0287 - The valıdıty and relıabılıty study of the moodsoft-rıta (mental health rısks screenıng scale) attentıon defıcıt hyperactıvıty scale

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Background and Objective: ADHD has many scales. These scales are based on category ratings. They focus on psychopathology and severe ADHD symptoms, which can lead to misjudgements that lead to overdiagnosis or, conversely, failure to identify individuals with mild ADHD symptoms. The aim of this study is to develop a short and easily applicable scale for screening Attention Deficit Hyperactivity.
Method: In the development of the Moodsoft-Rita Attention Deficit Hyperactivity (ADH) scale, a 6-item scale was prepared using Kessler's Adult Attention Deficit Hyperactivity Disorder Self-Report Scale (ASRS) as the basis.
Moodsoft-Rita ADH and ASRS; It was conducted on 280 patients who were admitted to Moodist Psychiatry and Neurology Hospital.
Results: The correlation between ASRS and Moodsoft-Rita ADH scale was 0.86 ($p<0.01$).
In the exploratory factor analysis (EFA), 2 factors were obtained with an eigenvalue greater than 1, and explained 48.08% of the total variance.
The internal consistency Cronbach alpha coefficient of the whole scale was found to be 0.74. Based on the KPSS, the area under the curve (AUC) at the cutoff point is 0.79, sensitivity 0.79, and specificity 0.84 for the Moodsoft-Rita ADH scale for 1.2 points.
Discussion and Conclusion: As a result, we believe that the Moodsoft-Rita ADH scale has adequate psychometric properties, satisfactory sensitivity and specificity values. It is valid and reliable, and can be used as a risk screening scale.

Keywords: attention deficit hyperactivity disorder, attention deficit hyperactivity screening, validity and reliability, moodsoft-rita, psychometric properties

REFERENCES

[1] Bicil Tokay, B., Başaran, I. ve Sorias, O. (2019). Brown dikkat eksikliği bozukluğu ölçeği yetişkin formunun Türkçeye uyarlanması. Nesne, 7(15), 254-268.
[2] Doğan, S., Öncü, B., Saraçoğlu, G. V., & Küçükgöncü, S. (2009). Erişkin dikkat eksikliği hiperaktivite bozukluğu kendi bildirim ölçeği (ASRS-v1.1): Türkçe formunun geçerlilik ve güvenilirliği. Anadolu Psikiyatri Dergisi. 2009; 10:77-87
[3] Günay, Ş., Savran, C., & Aksoy, U. M. (2005). Erişkin Dikkat Eksikliği Hiperaktivite Ölçeğinin (Adult Add/Adhd Dsm Iv- Based Diagnostıc Screenıng And Ratıng Scale) Dilsel Eşdeğerlilik, Geçerlik Güvenirlik Ve Norm Çalışması*. M.Ü. Atatürk Eğitim Fakültesi Eğitim Bilimleri Dergisi, 21(133–150).
[4] Silverman, Sarah Beth, "Assessing attention-deficit/hyperactivity disorder in adults: a review of rating scales" (2012). Theses and Dissertations. 251.

[5] World Health Organization (WHO). (2003). Adult ADHD Self-Report Scale-V1.1 (ASRS-V1.1) Symptoms Checklist from WHO Composite International Diagnostic Interview. https://www.hcp.med.harvard.edu/ncs/ftpdir/adhd/18Q_ASRS_English.pdf

[Abstract:0288] [Personality disorders]

0288 - The validity and reliability study of the moodsoft-rita (mental health risks screening scale) personality traits scale

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BACKGROUND AND OBJECTIVE: In the evaluation of personality traits, the big 5 Factor model to measure personality traits are widely used. Shorter scales have been developed in recent years. The aim of this study is to develop a short and easily applicable scale to determine the 5-factor personality traits.
METHOD: For the Moodsoft-Rita Personality Traits Scale, 2 questions were created for each of the dimensions of neuroticism, extraversion, openness to experience, agreeableness and self-control. The Moodsoft-Rita Personality Traits Scale and the Five Factor Personality Inventory (FFPI) Scale were administered to 280 outpatients who applied to the Moodist Psychiatry and Neurology Hospital.
RESULTS: Correlation between FFPI scale and subscales of Moodsoft-Rita Personality Traits Scale; 0.95 for neuroticism, 0.95 for extraversion, 0.97 for openness to experience, 0.96 for agreeableness, and 0.94 for conscientiousness ($p<0.01$). In the exploratory factor analysis, 4 factors were obtained and explained 43.05% of the total variance. The internal consistency Cronbach's alpha coefficient of the whole scale was found to be 0.96.
DISCUSSION AND CONCLUSION: As a result, we believe that the Moodsoft-Rita Personality Traits Scale has adequate psychometric properties in terms of validity and reliability, and can be used as a short personality scale.

Keywords: the big 5 factors, personality rating scale, psychometric properties, moodsoft-rita, validity and reliability

REFERENCES

[1] Benet-Martinez, V. ve John, O. P. (1998). 'Los Cinco Grandes' across cultures and ethnic groups: Multitrait-multimethod analyses of the Big Five in Spanish and English. Journal of Personality and Social Psychology, 75, 729–750.
[2] Çoklar Işıl. Kişilik özellikleri ile bağışlama eğilimi arasındaki İlişkinin intikam güdüsü ve adalete duyarlılık temelinde incelenmesi. Ankara Üniversitesi Sosyal Bilimler Enstitüsü Psikoloji (Sosyal Psikoloji) Anabilim Dalı Doktora Tezi. Ankara-2014
[3] Gosling, S. D., Rentfrow, P. J., & Swann, W. B.(2003). A very brief measure of the Big-Five personality domains. Journal of Research in Personality, 37, 504-528.
[4] Horzum, M. B., Ayas, T. ve Padır, M. A. (2017). Beş Faktör Kişilik Ölçeğinin Türk Kültürüne Uyarlanması. Sakarya University Journal of Education, 7(2), 398-408.
[5] Sümer, N., Lajunen, T. ve Ozkan, T. (2005, June). Big five personality traits as the distal predictors of road accident involvement. In Traffic and transport psychology: theory and application: proceedings of the ICTTP 2004 (p. 215). Elsevier Science Ltd.

[Abstract:0289] [Attention deficit hyperactivity disorder (ADHD)]

0289 - Effects of smoking on methylphenidate treatment in adult adhd: a magnetic resonance spectroscopy study

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OBJECTIVES: In this study, it was aimed to investigate the effects of smoking on the use of methylphenidate (MPH) and changes of creatine(Cr), choline(Cho) and N-acetyl-aspartate (NAA) in dorsolateral prefrontal cortex (DLPFC), striatum, cerebellum and anterior cingulate cortex(ACC) in adult attention deficit hyperactivity disorder (ADHD) patients.
METHODS: Sample of the study is consisted of 60 patients aged between 18-60 having ADHD according to DSM-IV criteria. Values of NAA, creatine and choline in ACC, cerebellum, striatum and DLPFC were measured with magnetic resonance spectroscopy. After the measurement, 10 mg oral MPH was given to the patients and the same metabolite levels were measured after 30 minutes interval.
RESULTS: A total of 60 patients (48 males,12 females) with a mean age of 28.98±7.66 years met the eligibility criteria for this study. Thirty-nine(%65) of the patients were smoking. Distribution of the patients according to the ADHD subtypes was as follows: 21 of them(35.0%) were in the inattentive type, 11 of them(18.3%) were in the hyperactive type and 28 of them were(46.7%) in the combined type. Higher levels of NAA($p<0,031$), Cr($p<0,024$) and Cho($p<0,035$) were determined in the striatum after MPH administration in the smokers according to the nonsmokers. Levels of Cr($p<0,037$) in the cerebellum and Cho($p<0,016$) in the striatum were found higher after MPH administration in the smokers according to the levels before MPH. Levels of NAA($p<0,014$) and Cho($p<0,045$) in the cerebellum were found higher and levels of NAA($p<0,043$) and Cr($p<0,004$) in the striatum were found lower after MPH administration in the nonsmokers according to the levels before MPH.
CONCLUSION: Increased levels of Cho and Cr in the smokers is thought to be involved with increased cellular destruction. Increased levels of NAA after MPH administration in the nonsmokers is thought to be involved with more neuronal healing and plasticity. In conclusion, it is thought that smoking effects MPH response.

Keywords: ADHD, Smoking, Methylphenidate