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# Candidates of TAP Outstanding Research Awards

**[Abstract:0089]** ***Child and adolescent mental and behavioral disorders***

## Retrospective analysis of patients with probable DSM-5 disruptive mood dysregulation disorder

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**OBJECTIVE:** In this study, we aim to present a retrospective analysis of cases with probable disruptive mood dysregulation disorder (DMDD) at a Turkish tertiary treatment center and discuss implications.

**METHODS:** Two hundred patients complaining of "irritability" and "temper tantrums" were evaluated at the time of their application with the Childhood Mania Rating Scale (CMRS), Parent Version of Young Mania Rating Scale (P-YMRS), the Children's Depression Inventory and the Screen for Anxiety and Related Disorders along with the Atilla Turgay Scale for DSM-IV-TR Disruptive Behavior Disorders. To differentiate those with probable DMDD, patients with a P-YMRS score of <20 (below cut-off), CDI<19 (below cut-off) and those with <4 criteria endorsed as "frequent" or "very frequent" in the ODD section of AT-Parent and AT-Teacher were selected.

**RESULTS:** Ninety-nine patients (63.6% male) were found to fulfill criteria for DMDD as per DSM-5. Eighty-five of the patients (87.6%) were prescribed drugs. Most commonly drugs used during lifetime were, in descending order, risperidone, methylphenidate, atomoxetine, OROS methylphenidate, sertraline and fluoxetine). Most common diagnoses according to DSM-IV-TR were ADHD (60.6%), GAD (33.3%), Learning Disability (31.3%), Social Phobia (18.2%), Separation Anxiety Disorder (14.1%), OCD (12.1%), Enuresis (11.1%), Tic Disorders (8.1%), MDD/ Dysthymia and BP-NOS (6.1% for each).

**CONCLUSION:** This study aimed to evaluate retrospectively patients with probable DSM-5 DMDD at a tertiary treatment center in Turkey according to socio-demographic and clinical variables in correspondence with DSM-IV-TR diagnoses. Patients had been prescribed stimulants, atomoxetine, risperidone and SSRIs during their lifetime. Anxiety disorders and ADHD were the most common DSM-IV-TR diagnoses while BP-NOS and Depression/ Dysthymia were rarer.

**Keywords:** disruptive mood dysregulation disorder, irritability, temper tantrums, treatment

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**[0117]** ***Schizophrenia and other psychotic disorders***

## Fractional anisotropic changes of the corpus callosum associated with antipsychotic treatment in first-episode antipsychotic drug-naive patients with schizophrenia

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**BACKGROUND:** Schizophrenia is a serious brain illness that indicates many abnormalities in the functions of the brain's fiber connections such as assessing the reality, thought, emotion and cognition. These fibers effect cognitional functions by connecting cortical and subcortical areas and networks formed by them. Aberrant brain connectivity especially in the prefrontal and temporal heteromodal cortex has been suggested as the essential mechanism underlying the disease. In this study, it is intended to investigate the post- and pre-treatment changes with diffusion tensor imaging MRI (DTI-MRI) in the splenium and genu regions of the corpus callosum in patients diagnosed with first-episode schizophrenia according to the DSM-IV-TR.

**METHOD:** Between June 2009 and February 2010, 18 patients with psychotic symptoms were recruited from the outpatient unit of the GMMA Haydarpasha Research and Training Hospital. These patients had been diagnosed with first-episode schizophrenia (n=7)

or schizophreniform disorder (n=11) and matched inclusion criteria. Patients with schizophreniform disorder as initial diagnosis were reevaluated after 6 months, and this time schizophrenia diagnosis was a ascertained. By means of implementation of SCID-II, additional diagnoses for personality disorder were excluded. Two of the 18 patients who had been admitted to the study were excluded because of being diagnosed with short-term psychotic disorder, and two patients were unable to proceed because of incompatibilitywith MRI device. Three participants with schizophrenia were excluded from this study because of unsatisfactory image data due to head and body movement in the follow-up MRI scan. DTI-MRI was obtained from participants at baseline and after 4 weeks of standard antipsychotic treatment follow-up. A 'difference color-coded fractional anisotropy (FA) map' for each of the 11 patients was calculated from the 4-week follow-up and the baseline splenium and genu FA ROI (Region of Interest)-based measurements. Finally, this study included participants of whom 14 had completed baseline, 11 both baseline and follow-up experiment and 16 control persons who had no organic or psychiatric disease and whose age, sex and education level was matched with the patient group.

Patients included in the study were hospitalized, all tests and measurements were implemented before starting on antipsychotics, then standard antipsychotic treatments (Risperidone (n=12), Paliperidone (n=2)) were continued. Patients' family histories were received and they were examined mentally, physically and neurologically. Initially liver, kidney and thyroid functions of all patients were examined. In addition, structural brain abnormalities were evaluated during the DTI measurements.

To be eligible, criteria of involvement for either patients or healthy control subjects were: between 18 and 45 years old, being right-handed, first application to psychiatry, at least primary school graduate, no abuse of nicotine or caffeine, no DSM-IV-TR Axis I and Axis II comorbidity, a written consent (for patients by first-degree relatives).

Criteria for being excluded: clinically conspicuous medical or neurological illness, having received antipsychotic treatment at the time of application or before or having used benzodiazepine longer than two weeks, for necessity of ECT (Electroconvulsive therapy), an incompatibility with MRI device and communication because of language problems and illnesses.

The study was started after submitting the study protocol to the Istanbul Clinical Research Ethics Board and receiving approval from there (Number of decision: 2009-CC-040/11.12.2009)

**DTI Image Analysis:** FA maps were calculated with Siemens® syngo VE27A SL0109 Syngo Multimodality Workplace AG 2007 according to Basser et al. Major eigenvector linear maps were transformed into color codes. In the second stage, in advance of measurements 3D correction (Eddy Current Correction) was implemented to remove artifacts of emerging images. ROI radiuses were determined as 2 mm in the genu, 3 mm in the splenium. Hereby FA values were calculated accurately.

**Statistic Evaluation:** Acquired parameters from the study were evaluated with Statistical package for Social Sciences for Windows 16.0 (SPSS 16.0). Study parameters were expressed with average±standard deviation and percentage values. Group differences were assessed at baseline using independent group Student's t-tests or $\chi^2$-tests, whereas longitudinal changes between the baseline and follow-up time points in the patients' group was examined using paired Student's t-tests. Significance level was based on $p<0.05$. Mean Callosal FA was exported to SPSS to be examined in relation to clinical symptom scores (using a cut-off value of $p<0.05$; two-tailed) using Pearson's or Spearman's rank (in the case of non-normally distributed data) correlations.

**FINDINGS:** All the subjects in the study were male. In terms of age (22.7±2.25 and 22.1±2.11 respectively) and education level (10.2±2.51 and 10.4±2.47 respectively) no significant difference was found between first episode schizophrenia group and control group ($t=0.906$, $p>0.05$). First-episode schizophrenia group's economic level was lower than in healthy controls ($\chi^2=5.275$, $p=0.022$). DUP was identified as 2.3±1.7 months. Family history for schizophrenia was identified as 28.6%.

In the first-episode schizophrenia group, an FA value of the genu region of the corpus callosum was determined as 0.690±0.124 and 0.834±0.042 for the control group. The FA value for the Splenium region was determined as 0.764±0.112 for the first-episode schizophrenia group and 0.852±0.031 for the control group. In the first-episode schizophrenia group, FA values detected both in the genu ($t15.6=4.1$, $p<0.001$) and the splenium ($t14.8=2.8$, $p<0.01$) were lower than in the control group. Follow-up measurements in the genu and splenium region of the corpus callosum determined FA values of respectively 0.711±0.133 and 0.790±0.056 for the FES group. There were mild fractional anisotropy increases respectively in genu and splenium ($t10=-0.646$, $p=0.533$; $t10=-1.051$, $p=0.318$) among FES patients following treatment.

A negative correlation (Pearson's $r=-0.569$, $p=0.034$) was detected between baseline splenium FA values and BPRS scores. The duration of illness prior to treatment was negatively correlated ($r=0.066$, $p=0.846$) between baseline and follow-up splenium FA changes.

There were no significant correlations between the change in genu and splenium FA value and the improvement in clinical symptoms, PANSS total ($r=-0.310$, $p=0.354$, $r=-0.583$, $p=0.060$) and BPRS score ($r=-0.087$, $p=0.800$, $r=-0.137$, $p=0.689$) after 4 weeks of treatment. Moreover, there were no significant correlations between the change in genu and splenium FA value and the dose of antipsychotic medications ($r=0.359$, $p=0.279$; $r=0.299$, $p=0.372$).

**DISCUSSION:** In our DTI study, a reduction in FA values in the genu and splenium regions of the corpus callosum and a more apparent decrease in the genu were determined in first-episode drug-naive schizophrenia patients. Also, a negative correlation was determined between BPRS scores and baseline splenium FA values. Although the callosal FA changes did not correlate with symptom improvement or the dose of antipsychotic medication statistically, there was a mild increase in follow-up FA measurements. Four weeks might be too short to observe changes in white matter integrity. However, a potential toxic effect of antipsychotic medication, including oxidative stress and

excitatory neurotoxicity, might be responsible for insufficient follow-up FA changes.

On the other hand, the existence of white matter changes even in first-episode drug-naive schizophrenia patients supports the view that these problems occurs in stages of development, because the degree of FA changes refers to the fiber tract organization's degree of function[1]. They have a positive correlation. Moreover, the reduction of FA values directly indicates histological abnormalities. Also, our findings overlap significantly with those described by Wang et al.[2] who reported that there was a significant decrease in absolute FA in the white matter in 35 first-episode drug-naive patients with schizophrenia and after 6 weeks of antipsychotic treatment that did not correlate with symptom reduction.

As a result of white matter studies, distensions were detected in schizophrenia patients, particularly in axonal atrophy and periaxonal oligodendrocyte in the prefrontal cortex. This was deemed compatible with increased radial permeability and decreased FA values in the white matter of schizophrenia patients. This also suggests a cause from changes in axons' skeletal structure or demyelinization rather than a big degeneration in axons[3].

These findings show that the CC, which is the main determiner of interhemispheric connection, is affected distinctly in schizophrenia patients. When all these findings are considered, all of them probably result in a neuro-developmental defect that creates a shortage in neurons' modulator capacity paving the way to changes in cellular morphology; then abnormal synaptic circuits come into existence.

Consequently, we report FA reductions especially in the posterior region, also insufficient FA increase in white matter after antipsychotic treatment in patients experiencing a first episode of psychosis. However, prospective collaborative studies are needed to clarify the potential long-term effects of antipsychotics on white matter microstructure and also its reversibility.

**Keywords:** corpus callosum, first episode schizophrenia, fractional anisotropy

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**[Abstract:0146]** ***Anxiety, stress, and adjustment disorders***

## Levels of Cortisol, Oxidative Stress, and DNA Damage in Victims of Childhood Sexual Abuse

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**INTRODUCTION**: Brain tissue continues to develop throughout childhood and during adolescence. Trauma experienced during these periods has been reported to have particularly serious consequences. With a few exceptions, most studies reported elevated cortisol levels in non-stressed circumstances in the child and adolescent victims of sexual abuse compared to controls[1]. Prolonged exposure to elevated cortisol levels has been shown to cause an increase in reactive oxygen species (ROS) at the cellular level and increased oxidative stress[2].

The aim of the present study was to evaluate cortisol levels, oxidative stress, and DNA damage in child and adolescent victims of sexual abuse versus healthy controls who did not have a history of trauma.

**MATERIALS AND METHODS:** The study was conducted in the Department of Child Psychiatry at Dicle University. Study data were collected between May 2012 and November 2012. The study included a total of 38 children (10 males and 28 females) aged between 9 and 17 years who had experienced childhood sexual abuse and 38 age- and gender-matched children as the control group. Children who reached an intelligence score below 70 points, who had a significant neurological or medical disorder, who received oral contraceptives, had previous or current cortisol therapy or used vitamins, and those who had morbid obesity or active infection were excluded in order to prevent interference with the biochemical parameters. In addition, patients with a history of psychiatric disorder before the latest trauma and those with a history of alcohol or substance abuse were excluded from the CSA group. Parents of all participants signed consent forms regarding their voluntary participation in the study. Approval for the study was obtained from the Non-Interventional Clinical Research Ethics Committee at Dicle University Faculty of Medicine. Sociodemographic features of the participants were obtained and

a clinical data form was completed. This was followed by the collection of 2 ml venous blood samples for biochemical tests. The blood samples were obtained in the morning between 10.00 and 12.00 am. Cortisol, glutathione peroxidase (GPx), Coenzyme Q, 8-Hydroxy-2-Deoxyguanosine (8-OHdG), and Superoxide dismutase (SOD) were tested using the ELISA method and commercial kits. The statistical analysis was performed using the SPSS 15.0 software package.

**RESULTS:** The mean age was 13.4±2.5 years (range 9-17 years) among the victims of sexual abuse. In the control group, the mean age was 13.5±2.6 years (range 9-17 years). There were ten males and 28 females in the CSA and control groups. The duration of education was lower in the victims of CSA and their parents compared to the control group. The number of siblings was higher. There was no significant difference between the groups in terms of their family history of psychiatric disorder and smoking/substance abuse. There was also no significant difference between the groups in terms of age at menarche and menstrual cycle.

Regarding the parameters related to sexual abuse, 61% (n=23) of the victims experienced sexual abuse involving penetration. Of those victims, 55% (n=21) experienced a single assault and 45% (n=17) experienced multiple assaults. Of the victims, 24% (n=9) experienced familial sexual abuse (incestuous) and 76% experienced sexual abuse committed by non-related persons.

Cortisol levels were significantly higher in the CSA group compared to the control group ($p<0.01$). There was no significant difference between the groups in terms of the levels of oxidative stress parameters (GPx, SOD, and coenzyme Q). Likewise, 8-OHdG levels as an indicator of DNA oxidation were not significantly different between the groups (Table 2). The mean time elapsed since the first sexual abuse until the date of examination was 20.6±22.4 months (3-95 months). The evaluation of the relationship between this time span and cortisol levels revealed that cortisol levels decreased as the time interval increased ($r=-0.279$, $p=0.04$). Similarly, 8-OHdG level decreased as the time elapsed since the sexual abuse increased ($r=-0.252$. $p=0.04$).

In the CSA group, there was no significant relationship between the sexual abuse involving penetration and the levels of GPx, SOD, coenzyme Q, and 8-OHdG. The coenzyme Q level was lower in the victims who sustained multiple assaults than the victims of a single assault ($p=0.04$). Cortisol and SOD levels were lower in the victims of familial sexual abuse ($p=0.03$ and $p=0.04$, respectively).

**DISCUSSION:** Studies conducted during childhood and adolescence on the victims of CSA report elevated cortisol levels; conversely, when studies on CSA victims are conducted after a significant amount of time has elapsed, cortisol levels are reported lower. This decrease in cortisol levels over time is referred to as attenuation hypothesis[3]. Consistent with the literature data, the present study reported higher cortisol levels in the CSA group. Furthermore, cortisol levels decreased as time since the sexual abuse increased.

In the present study, there was no significant difference between the control group and CSA group in terms of oxidative stress and DNA damage. In a recent study, increased oxidative stress has been shown in rats that were exposed to stress. In another study, oxidative stress was suggested to play a critical role in the development and exacerbation of post-traumatic stress disorder (PTSD). Consistent with the current results, a study conducted on 14 patients with PTSD reported no significant difference in terms of GPx and SOD levels when compared to the control group[4].

Both cortisol and 8-OHdG levels were found to be decreased as the time since sexual abuse increased. Although we did not find any difference between the groups in terms of 8-OHdG concentrations, this finding was considered to be a reflection of the relationship between cortisol and DNA damage. In addition, the decrease in cortisol levels over time was suggested to be reflective of an adaptive process preventing harmful effects of prolonged exposure to high cortisol levels on brain structures such as the hippocampus and frontal cortex[5].

In conclusion, no significant difference was found in children and adolescents who experienced sexual trauma in terms of oxidative stress level and DNA damage. Furthermore, some factors related to the trauma, such as sexual abuse within the family and multiple assaults, were found to have affected the level of oxidative stress. Because this is the first study that has been conducted in child and adolescent victims of sexual abuse, longitudinal studies on a larger scale are needed to confirm the results of the current study.

**Keywords:** DNA damage, oxidative stress, sexual abuse

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**[Abstract:0182]** ***Genetic psychiatry***

# No association of DRD3 and CNR1 polymorphisms in premenstrual dysphoric disorder

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**INTRODUCTION:** Premenstrual syndrome (PMS) is characterized by recurrent psychological and/or somatic symptoms occurring specifically during the luteal phase of the menstrual cycle and resolving during menstruation. Premenstrual dysphoric disorder (PMDD) is the extreme, predominantly psychological end of the PMS spectrum, and it is estimated that 5-10% of regularly ovulating women experience PMDD. The cause of PMDD is unknown. Studies attempting to elucidate the pathophysiology of the syndrome concentrate on the hypothalamic–pituitary–adrenal (HPA) axis, the γ-aminobutyric acid (GABA) system, the serotonergic system, and the opioid system. The dopamine D(3) receptor gene (DRD3) is a candidate for a number of psychiatric conditions. Rs6280, also known as Ser9Gly, is a SNP in the dopamine receptor D3 DRD3 gene. Polymorphisms in the DRD3 gene have associations with schizophrenia, depression, and nicotine dependence. DRD3Ser9Gly polymorphism affected response to antidepressant treatment in major depressive disorder[2]. The endocannabinoid system is widely distributed throughout the brain and involved in mood and related disorders. Genetic polymorphisms of the endocannabinoid system have been explored in mental disorders[3]. There are currently two known subtypes of endocannabinoid receptors, termed CB1 and CB2. CNR1 polymorphisms were found to be associated with substance use disorders, depression, and anxiety disorders[4]. Rs1049353 and rs12720071 are common variants of the CNR1 gene. Carriers of an rs1049353(G) allele were less likely to respond favorably to antidepressant treatment, particularly if they were females with comorbid anxiety[5]. Since polymorphisms in DRD3Ser9Gly and CB1 receptors seemed to be associated with anxiety and depressive disorders, and as it is known that PMDD shares a range of characteristics with depressive and anxiety disorders, our aim was to investigate whether DRD3Ser9Gly and CB1 receptor polymorphisms are related to PMDD.

**METHODS:**

**Study Population:** Patients were recruited from consecutive applications to the Harran University Research Hospital obstetrics and gynecology outpatient clinic. The control group was selected from the staff of the Faculty of Medicine. Fifty-one patients with PMDD and 51 healthy control subjects between the ages of 18 and 45 were included in this cross-sectional study. Anyone having an existing Axis I psychiatric disorder according to the DSM-4 criteria was excluded from the study. Clinical diagnosis was determined according to DSM-IV. Control subjects reported no significant premenstrual symptoms. All subjects were evaluated with a semi-structured interview form to determine their sociodemographic features. This form also evaluates the symptoms of Premenstrual Syndrome (PMS), family history of PMS, and nicotine use. Clinical categorization of PMDD patients and control subjects was determined by prospective symptom rating with the use of the Daily Record of Severity of Problems (DRSP) scale-short form.

**Procedures:** Venous blood samples were collected in EDTA-containing tubes. DNA was extracted from peripheral blood leukocytes by salting-out procedure.

Genotypic Analysis of the Dopamine Receptor D3 (DRD3) Gene Ser9Gly(rs6280) Polymorphism: Genotypes were determined using a TaqMan™ fluorogenic 5′-nuclease assay with TaqMan Probes. All reactions were carried out following the manufacturer's protocol.

Genotypic Analysis of CNR1 1359 G>A (codon Thr453Thr, rs1049353) Polymorphisms: The genotyping of CNR1 1359 G>A (codon Thr453Thr, rs1049353) polymorphisms was performed using predesigned TaqMan SNP Genotyping Assays (Applied Biosystems, Foster City, CA). The Assays-on-Demand SNP genotyping kit was used for the polymerase chain reaction (Applied Biosystems). Single nucleotide polymorphism amplification assays were performed according to the manufacturer's instructions. All procedures were conducted in a manner blind to the case status and other characteristics of the participants

**Statistical Analysis:** $\chi 2$ tests were performed to assess conformity to Hardy-Weinberg equilibrium and to detect any association between each genotype distribution and clinical category. Statistical significance was considered at exact probability values of $p<0.05$.

**RESULTS:** Fifty-one patients with PMDD (age range: 20-46; mean: 30.2) and 51 healthy control subjects (age range: 15-44; mean: 28.0) were included in the study. There was no significant difference in age, BMI, height, weight, or number of children between PMDD group and controls except for marriage rates. 5.9% of PMDD patients were single, against 29.4% of the controls. Allele and genotype frequencies were not different between PMDD patients and controls in DRD3Ser9Gly polymorphism ($\chi 2$: 0.356 and p: 0.837). Allele and genotype frequencies were not different between PMDD patients and controls in CNR1 polymorphism. Genotypes have Hardy-Weinberg equilibrium in DRD3Ser9Gly in the PMDD group (chi-square value=1.65 with 1 DF) but the other genotypes are not in Hardy-Weinberg

equilibrium. There was no significant difference of DRD3Ser9Gly polymorphism between PMDD patients and controls. Similarly, there was no significant difference of CNR1 polymorphism between PMDD patients and controls.

**DISCUSSION:** We genotyped the DRD3Ser9Gly (rs6280) and CNR1 polymorphisms in two groups of regularly ovulating women, one group with clinically diagnosed premenstrual dysphoric disorder and one group of normal healthy controls with no symptoms of premenstrual dysphoria. We found no association of DRD3Ser9Gly (rs6280) polymorphisms in PMDD. The D3 receptor is a candidate for being involved in mental disorders. Polymorphisms in the DRD3 gene have been studied in various psychiatric disorders. In a study of 88 patients being treated for schizophrenia with olanzapine, those who were rs6280(C;C) homozygote had greater positive symptom remission as compared with (C;T) or (T;T) genotypes. The ser9gly polymorphism has been associated with depression in different studies. A preliminary study showed that DRD3Ser9Gly polymorphism affected response to antidepressant treatment in major depressive disorder. Pharmacogenetic studies have reported that DRD3ser9gly polymorphism influenced antidepressant response in bipolar disorder patients treated with a combination of olanzapine and fluoxetine. Our first finding is the lack of an association of DRD3ser9Gly polymorphism in PMDD, and there is no other study looking for this association. As the etiology of PMDD is multifactorial, dopaminergic pathways may not be solely responsible in the pathophysiology of PMDD. Our second finding is a lack of association between CNR1 polymorphism and PMDD. The endocannabinoid system has been implicated in the pathogenesis of depression and anxiety.

Patients with depression are found to have reduced levels of circulating endocannabinoids, and an up-regulation of CB1R was observed in the prefrontal cortex of subjects with major depression who died by suicide. Since While polymorphism (rs1049353) is associated with depression and anxiety, we did not find an association between CNR1 polymorphism (rs1049353) and PMDD. The endocannabinoid system may not be the sole responsible in the pathophysiology of PMDD.

Previous genetic studies in premenstrual dysphoric disorder were mostly concerned with the serotonergic and noradrenergic systems. To our knowledge, this study is the first reported genotypic analysis of DRD3Ser9Gly (rs6280) and CNR1 polymorphisms in premenstrual dysphoric disorder. There may be several explanations for our negative findings. First, clinical categorization of patients with PMDD can be difficult because of the subjective nature of symptom interpretation. A second limitation is the possibility of population stratification. In studies comprising subjects taken primarily from a localized community, it is important to include healthy controls to determine typical genotype and allelic frequencies, although these may not be representative of the wider population.

Third, the lack of association between the DRD3Ser9Gly (rs6280) and CNR1 polymorphisms and PMDD may be affected by sample size. We were unable to identify either a single genetic marker or a combined polymorphic profile for susceptibility to PMDD. However, it is the first study evaluating DRD3Ser9Glyand CNR1 polymorphisms in PMDD. It is not plausible to expect a single polymorphism to be the sole factor responsible for PMDD. It is likely that PMDD is a polygenic disorder, but the relative contributions of the various implicated genes are unknown. Cautious interpretation of the present study is warranted, both by the preliminary nature of these findings and by their basis in simple association analysis. The polymorphisms that were studied here do not represent major risk factors for PMDD. Confirmation of our findings will require independent validation in a larger group of subjects.

**Keywords:** cannabinoid receptor, dopamine D3 receptor, premenstrual syndrome, genetic polymorphism

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**[Abstract:0219]** ***Child and adolescent mental and behavioral disorders***

# Assessment of 1572 of children with mental retardation and their psychotropic medication use

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**INTRODUCTION:** Mental retardation (MR) is a lifelong and chronic impairment which has problematic medical, social, educational and economic aspects. The combination of mental and physical disorders associated with mental retardation is higher than that of the community average. Early diagnosis and appropriate treatment are very important for increasing patients' functionality and quality of life[1]. The present study aims to examine the sociodemographic characteristics, admission complaints, the level of MR, accompanying comorbidities, the prevalence of psychotropic medication use, the medications used and the predictors of psychotropic medication in children and adolescents aged 6-18 years and diagnosed with mental retardation.

**METHODS AND MATERIALS:** In this study, hospital records of outpatient cases attending the Child Psychiatry of Ankara Pediatric Hematology Oncology Training and Research Hospital in the six-month period between June and December 2013 were screened retrospectively. Detected cases with mental retardation aged 6-18 years were evaluated in detail. In this evaluation, the sociodemographic characteristics, the level of mental retardation, the first presentation complaints, the psychiatric and medical history of the patients, the presence of comorbidity and drug use variables were examined. Psychiatric diagnoses were classified according to DSM-IV-TR. For measuring the intelligence quotient (IQ), Weschler Intelligence Scale for Children-Revised (WISC-R) and Stanford Binet Intelligence Scale were used. Thus, MR subtypes were defined according to the full-scale IQ score as the following; IQ=50-69 as mild MR; IQ=36-49 as moderate MR; unknown but presumed IQ score <70 as severity unspecified MR; IQ=21-35 as severe MR, and IQ score ≤20 as profound MR.

**Statistical Analysis:** Categorical variables were analyzed with chi-square ($\chi 2$) test. Interval variables were analyzed with t-test. The predictors of psychotropic medication use were analyzed with logistic regression analysis. In all evaluations, $p<0.05$ value was considered statistically significant.

**RESULTS:** The number of outpatients with MR in our sample was 1527 (12.8%). The mean age of cases (n=1572) was 11.3±3.3 (range 6-18 years). The sample was divided into two groups according to the age, children (6-11 years of age) and adolescents (12-18 years of age). Thus, 50.8% of the sample was formed by the children age group (n=798), the remaining were adolescents (49.2%, n=774). Mean ages of females and males were similar ($t(1570)=-1.845$, $p>0.05$). Similarly, no significant difference was detected between children and adolescents in gender terms. Males represented 60% of all subjects (n=943). Male/female ratio was almost 1.5 (M/F=1.49). Classification of MR subtypes was the following: More than half of the whole sample (57.3%) had mild MR, 15.5% of all had moderate MR, 14.8% of all had severity unspecified MR, 12.2% of all had severe MR, and 0.3% of all had profound MR. Evaluation of the patients' complaints revealed that the most common cause for presentation was school failure (37.7%). The others were the following: renewal of special education report, aggressive and/or violent behavior, speech delay or retardation, hyperactivity and/or attention deficit, objections to the special education reports arranged before, avoidant and/or anxious behavior, and other reasons. In this sample, 26.1% of all MR (n=410) were newly diagnosed cases of MR. In 3.1% of the sample (n=48), the diagnosis of mental retardation was changed to "borderline intellectual functioning (IQ=70-79) plus specific learning difficulties".

At least one psychiatric comorbidity was detected in 24.6% of all cases; most commonly found were disruptive behavior disorders (DBD; including conduct disorder (CD), attention deficit hyperactivity disorder (ADHD), and CD plus ADHD; 14.2%). The others were pervasive developmental disorders (PDD), anxiety disorders, elimination disorders, mood disorders and tic disorders. Non-psychiatric comorbidities accompanying MR were found as 49.7% of the entire sample. Amongst these, the most frequently identified one was epilepsy (21.9%), followed by cerebral palsy (CP) and speech and/or hearing impairment, respectively.

Evaluating of the relationship between MR levels and epilepsy showed that epilepsy presence in all five MR subtypes was found significant ($\chi 2=227.845$, $p<0.001$), prominently with profound MR (80%) and severe MR (61.3%). Having epilepsy in profound and/or severe MR cases was significantly higher than that of the other MR patients ($\chi 2=206,937$, $p<0.001$). The relationship between MR level and CP was also evaluated, revealing that CP prominently accompanied 80% of profound MR and 60.2% of severe MR. It was also detected that profound and/or severe MR cases display CP comorbidity significantly more than other MR patients ($\chi 2=278.320$, $p<0.001$). When the relationship between MR levels and speech and/or hearing impairment comorbidity was evaluated, it was found that speech and/or hearing impairment accompanied mostly the 12.5% severity unspecified MR and 10.6% of those with mild MR. It was determined that having speech and/or hearing impairment comorbidity in mild MR, moderate MR and unspecified MR, in favour of unspecified MR (12.5%), was significantly more common than in profound and/or severe MR cases ($\chi 2=14.117$, $p<0.001$).

Evaluation of the clinical features of the MR cases in terms of gender revealed that having any of psychiatric disorders and having pervasive developmental disorder were significantly more likely in males than in females ($\chi 2=7456$, $p=0.006$; $\chi 2=15.669$, $p<0.001$, respectively).

Psychotropic medication used in children and adolescents with MR showed that 79.6% of the sample (n=1252) had not received any kind of psychotropic medication, whilst 20.4% of all had been using at least one psychotropic drug. Of these, 16.7% (n=262) had been using one psychotropic drug and 3.7% (n=58) were using combined pharmacotherapy. When assessing the distribution of psychotropic medication use, it was observed that the most commonly used psychotropic drugs were "antipsychotics" (14.2%, n=219), the most frequently used agent being risperidone (11.5%, n=180). The second-most commonly used agents were those for ADHD treatments (5.6%, n=89), including methylphenidate (MPH; 4.6%, n=72) and atomoxetine (ATX; 1.0%, n=17). The third-most preferred agents were selective serotonin reuptake inhibitors (SSRIs; 3.8%, n=57), with fluoxetine being the most preferred substance (3.4%, n=52).

Analysis of the predictors of psychotropic medication use revealed that comorbid psychiatric disorders presence, having ADHD, having CD and having anxiety disorders were detected as predictors (p<0.001, Beta=0.029, 95%CI [0.011-0.080]; p=0.002, Beta=0.190 95%CI [0.066-0.545]; p<0.001, Beta=0.088 95% CI [0.030-0.257]; p<0.001, Beta=0.029 95%CI [0.011-0.233], respectively).

**DISCUSSION:** In this study, we examined children and adolescents with MR in terms of their clinical characteristics, psychotropic medication use and the predictors of pharmacotherapy. In a six-month period, we found that MR is 1.5 times more frequent in males than in females. All levels of mental retardation have been more frequently described in the literature in the male gender. In a study conducted in a university hospital in Turkey, it was detected that 60.3% of 209 cases diagnosed with MR were male, and 39.7% were female[2]. In another study, it was detected that 73% of 200 cases diagnosed with MR were male and 27% female[3]. In our study, about two thirds of the cases were male, which is consistent with the literature. Although there is no clear evidence, the presence of mental retardation syndrome associated with the X chromosome and boys being more sensitive to certain diseases such as neonatal sepsis could be causes of these conditions.

In the literature, it was stated that 85% of all MR cases are mild MR, 10% moderate MR, 4% severe MR, and 1% profound MR; these rates could vary according to age, socioeconomic factors and cultural structure[1]. In our study, it was found that mild MR was the most frequently found group. However, unlike in the literature, in our study it was seen that unspecified MR (14.8%) was the third-most common group. The probable explanation for this situation could be difficulties in evaluating the intelligence level of cases with hearing and/or speech disorders who constitute 9.4% of the total sample.

In a study conducted in Turkey[2] the prevalence of epilepsy in patients with mental retardation was 28.2%, similarly to the rate of 21.9% we found in our study. In the literature, it was reported that the prevalence of epilepsy is 0.7% in the normal population, 3-6% in patients with mild MR, 23% in moderate MR and 50% in severe MR[3]. In our study, it was determined that there was a significant correlation between the incidence of epilepsy and MR level. Profound and/or severe MR in patients with epilepsy were often found to have significantly higher incidence of epilepsy than that seen at other intelligence levels. It was consistent with findings of previous studies that the MR level increases along with an increase of the frequency of epilepsy[3]. Another clinical situation that was often associated with mental retardation was CP. In a study conducted with MR cases in Turkey, CP frequency seen in these cases have been reported at a rate of 14.4%[2]. The prevalence of CP in our study was found to be 17.9%, which was similar to this finding. It was reported that 10-15% of cases with MR have visual impairments and 10-15% have hearing problems[4]. Similar with these reports, in our study we found that speaking and/or hearing impairment was found in 9.4% of the cases.

Psychopathologies accompanying mental retardation are also seen at high rates in these patients because of their environmental features, as they have more exposure to adverse socioeconomic conditions, and this was linked to an increased psychopathology risk[1]. In our study, the incidence of psychiatric comorbidity was determined as 24.6%. Similar to findings of a study conducted in Turkey[3], in our study psychiatric comorbidity was significantly more frequent in mild MR than in other subtypes of MR. This may result from a high level of presence of mild MR in our sample. There is a possibility of insufficient sensitivity of tools and methods which we used in the diagnostic process, as the mental retardation level increases and difficulty in the diagnosing process or in patients who, due to severe clinical symptoms of MR, may have more limited verbal ability and more difficulty to explain their complaints.

A study conducted in Turkey reported that 79.4% of male patients with MR and 46.2% of the females have a psychiatric comorbidity[3]. Similarly, in our study, psychiatric comorbidity was found in 65.9% of males and 34.1% of females, which was statistically significant in favor of males. The most frequently identified psychiatric comorbidities in MR were reported as PDD, ADHD, anxiety disorders, mood disorders, psychotic disorders, personality disorders, conduct disorder, posttraumatic stress disorder, tic disorders and eating disorders[3]. In our study, MR comorbid diseases were found to be DBD, PDD, anxiety disorders, elimination disorders, mood disorders, and tic disorders, in order of frequency, and the comorbidity rates were generally lower than in the literature. The cross-sectional nature of our study and its being performed retrospectively may have led to this situation.

In the United States, 30-75% of all cases with MR were reported to have been prescribed psychotropic drugs[5]. In a study conducted in Turkey, 62.5% of patients with MR were found to use any psychotropic drug[3]. Psychotropic drug use was found to be 20.4% in the MR cases in our sample, and we thought that this ratio is relatively low, compared to the above-mentioned rates, due to the lower comorbidity we found. Most commonly used pharmacological agents in this area were reported as antipsychotics, benzodiazepines, lithium, antiepileptics, tricyclic antidepressants, and SSRIs[3,5]. Likewise, in our study the most commonly used psychotropic drugs were antipsychotics, followed by MPH, ATX, and SSRIs. In our sample, given that the most common comorbidity found was DBD, this may have affected MPH and ATX use rates, which were different from the literature.

**CONCLUSION:** Our study has the characteristic of a situation determination associated with cases who attended child psychiatry and were diagnosed with MR. The most important limitation of our study is that the evaluation was made retrospectively. The relatively large size of the sample is the most important advantage. There is a need for studies with more detailed information, designed as a prospective, multicenter study with a large sample size, to draw up a way of health policies related to children and adolescents with MR in Turkey. This type of studies in the future will provide a more comprehensive evaluation of cases with MR and intervention attempts which should continue lifelong from the early stages.

**Keywords:** mental retardation, children, psychotropic medication use

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**[Abstract:0224]** ***Schizophrenia and other psychotic disorders***

## Evaluation of neutrophil-lymphocyte ratio in first-episode psychosis

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**INTRODUCTION:** Schizophrenia (SCZ) is a multi-factorial mental disorder affecting approximately 1% of the world population. Recent studies on pathophysiology of schizophrenia revealed the impact of immunological and inflammatory mechanisms on disease predisposition, onset and progression.

The neutrophil–lymphocyte ratio (NLR) is a simple, inexpensive and reliable method to evaluate the extent of stress and systemic inflammation[1]. Although NLR has been extensively studied in animal studies as well as in clinical fields such as oncology, cardiovascular surgery, and cardiology, there have been only two studies published examining the relationship between NLR and neuropsychiatric diseases[2,3]. Two studies investigating the NLR in carotid endarterectomy patients and Alzheimer's disease regarded the relationship between NLR and cognitive functioning in these diseases. However, no studies have examined the relationship between psychiatric disorders and NLR. The aim of this study is to assess the relationship between first-episode psychosis and NLR and to investigate if there is a relation between NLR and severity of disease.

**METHODS:** Patients admitted to the psychiatry inpatient clinic of Konya Training and Research Hospital between January 2011 and June 2014 with the diagnosis of psychotic disorder were reviewed retrospectively. In this retrospective study, we analyzed the medical records of 3258 patients with psychotic disorder. 277 of these patients were identified as antipsychotic-naive sufferers from first-episode psychosis. We considered as "antipsychotic-naive" those patients who had not taken antipsychotic medication before admission. Patients were excluded if they met the following criteria: alcohol or substance abuse, hypertension, diabetes mellitus, heart disease, hepatic or renal failure, clinical evidence of active infection, active or chronic inflammatory or autoimmune diseases and treatment with anti-inflammatory or immunosuppressive medication. After applying the exclusion criteria, 219 FEP were excluded and 58 first-episode psychosis patients were included. Parameters including neutrophil count, lymphocyte count, hemoglobin, hematocrit, white blood cell count, Brief Psychiatric Rating Scale (BPRS) scores, and demographic data of the patients were obtained from the medical records of 58 FEP. NLR was found by dividing absolute neutrophil count by absolute lymphocyte count. NLR values of 58 patients with FEP were calculated and compared to NLR of 37 healthy controls of similar age and gender distribution. The control group consisted of healthy individuals who applied to family medicine for routine examination before marriage. The study complied with the Declaration of Helsinki, and was approved by the institutional ethics committee of Selçuk University.

**Statistical Analysis:** Statistical analyses were performed using software (SPSS 21 SPSS Inc., Chicago, IL). In this study, two group comparisons for categorical variables were assessed using Pearson's chi-square test. Normally distributed variables were compared using

the Independent T-Test, abnormally distributed variables were compared using Mann-Whitney U test. Correlation coefficients and their significance were calculated using the Spearman test. $p<0.05$ was considered as statistically significant.

**RESULTS:** There were no differences between first-episode psychosis patients and healthy controls in age and gender. Mean NLR was significantly higher in patients compared to control group (2.22±1.25 vs. 1.63±0.38, p=0.041). Neutrophil count was not different between patients and healthy control (4.03±0.70 vs. 4.20±1.48, p=0.525), but lymphocyte count was significantly lower in patients (2.56±0.55 vs. 2.19±0.77, p=0.013). The NLR was significantly higher in female patients than female healthy controls (1.61±0.36 vs 2.16±0.90 p=0.033). However, there was no significant difference between male patients and male controls (1.65±0.41 vs 2.28±1.54 p=0.437).

Red blood cell count and percentage of hematocrit and hemoglobin were significantly higher in male patients than female patients. Platelet count was significantly higher in female patients than male patients, NLR and white blood cell count were similar between male and female patients.

In the first-episode psychosis patients, NLR was not significantly correlated with severity (BPRS score) (n=58; r=0.060, p=0.655).

**DISCUSSION:** In the present study we found that NLR was higher in FEP compared to healthy controls. There was no relationship between NLR and disease severity. To our knowledge, this is the first study to evaluate NLR in FEP.

A growing body of evidence indicates relations between inflammation and immune function and risk of schizophrenia. Over 40 cytokine alterations studies examining the changes in IL-6 levels, soluble IL-2 receptor and TNF-alpha levels in schizophrenia suggest higher values in first-episode psychosis patients and relapsed patients compared to than healthy controls[4].

NLR is a simple, noninvasive marker of systemic inflammation. Semiz et al. have evaluated NLR in 156 schizophrenic patients and have found that NLR was higher in patients compared to healthy controls. They have also observed an insignificant correlation between elevated NLR levels and psychopathology severity. These results are in line with our findings[5].

Halazun et al. have found that higher NLR is associated with a three-fold increased risk of cognitive dysfunction 1 day after carotid endarterectomy. They have mentioned that systemic inflammation increases atherosclerosis and neuronal injury[3]. In line with this result, Kuyumcu et al. (2012) have evaluated NLR in 241 patients with Alzheimer's disease and found that NLR was significantly higher than in the normal cognitive function group[2]. In light of previous researches mentioning that neurodegeneration may play a role in the pathophysiology of schizophrenia, elevated NLR levels may indicate a neurodegenerative process.

The study has several limitations. First, this was a single-center study with retrospectively collected data. As a result, we could not reach all of the data from the records of patients, and we could not compare NLR levels after antipsychotic treatment. Second, we also excluded some comorbid conditions that may increase NLR levels, and there may be some other confounders that we could not measure. Third, we could not evaluate the data of other inflammatory and immune markers (i.e., C-reactive protein, sedimentation, cytokines) to verify if NLR is an independent marker in the pathogenesis of schizophrenia.

**CONCLUSION:** To the best of our knowledge, this is the first study investigating NLR levels in FEP. Our findings suggest that NLR levels are increased in drug-naive first-episode psychosis patients compared to physically and mentally healthy individuals and inflammation may play a role in the pathogenesis of schizophrenia. Further larger prospective trials are necessary to determine the relationship between NLR and schizophrenia and the effect of drugs on NLR.

**Keywords:** first episode psychosis, neutrophil-lymphocyte ratio, schizophrenia

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**[Abstract:0261]** ***Mood disorders***

# Emotional and behavioral characteristics of childhood depression

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**INTRODUCTION:** Early-onset depression could negatively influence children and adolescents in all aspects of their lives such as emotional and cognitive development, school performance and social functioning. A very first epidemiological study from Turkey revealed that the prevalence of depression in elementary school students is 2.6%, and it is approximately two times more common in girls than boys[1]. However, studies carried out in clinical settings reported higher prevalence rates and different distribution rates between sexes.
It can arguably be claimed that behavioral problems may well hide the depressive syptoms in childhood[2], and they could be difficult to notice and diagnose correctly because of various clinical presentations of depression.
This study aimed to determine the prevalence of childhood depression in a clinical setting and whether there are any differences between the behavioral and emotional problems of these children and their peers without chronic medical illnesses or psychiatric disorders.
**METHOD:**
**Subjects:** The study was carried out in the child and adolescent psychiatry department of Karadeniz Technical University, Faculty of Medicine, between the dates of March 2013 and March 2014. There were 1992 children, aged 7-12 years, who presented to our clinic for the first time between these dates. Eventually, 42 of them were diagnosed with major depressive disorder (MDD) and agreed to participate in the study. The control group consisted of 42 children, age- and-sex matched with the study group, and they were collected from other departments of our hospital; none of them had any chronic mental or physical illness.
**Procedures and Assessment Measures:** Sociodemographic characteristics of the children and their parents were recorded on a semi-structured interview form prepared by the researchers. In this study, "Child Depression Inventory (CDI)" was used as a depression screening tool and "Schedule for Affective Disorders and Schizophrenia for School Aged Children, Present and Lifetime Version (K-SADS-PL)" was used to determine MDD and comorbidities. The cut-off point of CDI is declared as 13 for clinical populations; first children completed the CDI, and if their score was 13 or over, then K-SADS-PL was administered to them. In this study, item 9 of CDI was used to identify suicidal ideation. Also, the control group was interviewed using K-SADS-PL to determine that they had no psychiatric disorder. In the end, all mothers completed the "Child Behavior Checklist for Ages 6-18 (CBCL/6-18) and scored competence and behavior problems of their children.
**RESULTS:** There were 3157 children and adolescents (1247 female, 1910 male) who presented to our outpatient clinic between the dates of the study, and 63.1% of them (n=1992) were 7-12 years of age. After completing the CDI, those who scored above 13 points were interviewed using K-SADS-PL; 48 children (2.4%) were diagnosed with MDD. However, six of these children were excluded from the study and comparison analyses were conducted with 42 (2.1%) children.
The mean age of the children was 10.1±1.3 years and 64.3% of them (n=27) were male. Mothers of depressive children often mentioned externalizing behavior problems of their children. The most common complaints were inattention (n=8; 19.0%), bad temper (n=6; 14.3%) and irritability (n=5; 11.9%). On the other hand, self-injurious behavior was detected only in the study group (n=8; 19%) and the control group members had significantly more friends ($p<0.0005$; $\chi^2=26.877$). Also, "having no friends" and "having just one friend" was observed only in the study group.
In this study, 81% of the depressive children (n=34) had comorbid diagnoses. The most frequent comorbidities were anxiety disorders (n=19; 45.2%), disruptive behavior disorders (n=12; 28.5%) and attention deficit hyperactivity disorder (n=11; 26.1%), respectively. Among the anxiety disorders, separation anxiety was the most common one (n=8; 21.4%).
In depressive children, social relations ($p=0.021$; $Z=-2.309$) and school performance ($p<0.0005$; $Z=-6.690$) scores were significantly lower than in the control group, but all emotional and behavioral problem scores were significantly higher. Internalizing and total behavior problems were significantly higher in girls, but there was no significant difference in externalizing behavior problems between the sexes. Moreover, 57.1% of the study group (n=24) had suicidal ideation and 19% (n=8) had self-injurious behavior. Children with suicidal ideation had significantly higher scores on CDI ($p=0.015$; $t=-2.552$), but there was no significant association between suicidal ideation and children's competencies, behavioral problems or sexes. Besides, self-injurious behavior was not associated with sexes, suicidal ideation or total CDI scores. But it was significantly related with children's rule-breaking behavior ($p=0.027$; $Z=-2.207$), aggresive behavior ($p=0.002$; $Z=-3.083$) and externalizing behavior scores ($p=0.001$; $Z=-3.470$).
**DISCUSSION:** In this study, the prevalence of childhood depression was estimated as 2.4%, lower than in similar studies. We used a semi-structured interview to diagnose depression, and it is thought that the difference between studies may be due to this methodological variation. Also in this study, the ratio of boys to girls diagnosed with major depression was 1.8/1. But this result would be associated with the study population, because among the attendees aged 7-12 years, there was a male dominance.

It is suggested that children tend to report their internalizing symptoms more often than caregivers or teachers, and approximately two-thirds of children diagnosed with MDD have at least one comorbid psychiatric disorder[3]. As with these studies, mothers in our study usually mentioned their children's externalizing symptoms but after interviewing the children, we diagnosed depression. Also, we found that 81% of depressive children had at least one comorbid psychiatric disorder; ADHD, seperation anxiety, oppositional defiant disorder and conduct disorder were the most frequent comorbidities.

In this study, children diagnosed with depression had fewer friends and their school and social competence scores were significantly lower than in the control group. It is reported that all factors related to the school environment, like academic performance or peer relationships, have effects on child mental health, and children who have fewer friends are more likely to experience depressive symptoms[4]. Having fewer friends or lack of friends may have caused depression in the study group or could be a result of these children's behavioral problems, because these children had significantly higher scores in both internalizing and externalizing behaviors. It is reported that children who have internalizing or externalizing behavior problems could have lower social skills and thus act out more asocial behaviors among peers. Also, in this study, internalizing behavior problems were higher in depressive girls, but there was no significant difference in externalizing behavior between the sexes. These results suggest that externalizing behavior problems could be a part of childhood depression regardless of gender differences.

Another important finding of this study was that 57.1% of the children were shown to have suicidal ideation. This ratio was found to be 71% in Brenton's study[2]. Suicidal ideation is regarded as a predictor of suicide attempts. Thus, the high rates of suicide ideation in childhood depression as shown suggest that children are at risk of suicide attempts as adolescents and should be examined carefully in this regard.

Finally, in this study self-injurious behavior was detected only in depressive children. Although a study conducted with adolescents showed that self-injurious behavior is related with suicidal ideation[5], in our study this behavior was not associated with suicidal ideation or depression severity of children. We thought that self-injurious behavior in depressive children may not always be related with depression severity. Impulsivity or high comorbidity rates of childhood depression may make additional contributions to the development of this behavior. Hence the results of this study showed that self-injurious behavior was significantly associated with rule breaking, aggressive behavior, and total externalizing behavior scores.

Although the small sample size and high comorbidity rates in the study pose limitations to generalizing these results, we suggest that findings revealed in this study could contribute to the literature.

**Keywords:** depression, child behavior, self-injurious behavior

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**[Abstract:0263]** ***ADHD***

## Are SSRIs and psychostimulants really safe in terms of genotoxicity?

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**BACKGROUNDS AND OBJECTIVE:** Attention-deficit/hyperactivity disorder (ADHD) is the most frequent psychiatric disorder in children and adolescents[2]. Depression is the most common mood disorder[4]. In the treatment of such psychiatric disorders, typically SSRI and/or methylphenidate (MPH) are used. MPH is a commonly prescribed psychostimulant in ADHD treatment[3].

El-Zein et al. have shown the genotoxic effect of a 3-month MPH treatment in 12 children[1]. In other studies, a genotoxic effect of MPH in children cannot be shown[2,3]. Additionally, in a study assessing adults, a genotoxic effect of MPH cannot be shown[3]. In the light of such information, together with a high prevalence of ADHD, increasing therapeutic usage of MPH has increased some concerns regarding its safety[5].

SSRI is widely used in the treatment of depression. In a study performed with humans, an increase in the frequency of sister chromatid exchange (SCE) via sertraline treatment has been shown. Although SSRIs are widely used in psychiatric disorders, information regarding its genotoxic effects in humans is limited[4].

In this study, we aimed to examine the effect of psychotropic drugs on early DNA damage in peripheral leucocytes by using comet analysis in adults with new depression and/or ADHD diagnoses and to evaluate their relationship with the treatment response.

**METHODS:** The research was executed at Pamukkale University Faculty of Medicine Department of Psychiatry and Physiology. Drugs and dosages to be taken by the patients were specified naturalistically.

According to DSM-4 diagnosis criteria, inclusion criteria are Depression and/or ADHD diagnosis, age between 18 and 60 and being literate.

Neurologic/chronic disease, mental retardation, concomitant psychiatric disorder and psychotropic usage for the last 2 months, as well as psychiatric disorders related to organic reasons are specified as exclusion criteria.

SCID-I or semi-structured socio-demographic question form was applied to the patients by the researcher. The patients were separated into 3 groups, depression, ADHD, and depression+ADHD. Clinical evaluation scales were performed according to the patient groups, and after the treatment, clinical evaluation scales were applied again according to the patient groups.

After taking blood samples from the patients before the treatment and in 2-month therapeutic doses during the treatment, these samples are evaluated via comet analysis in terms of genotoxicity.

**Single cell gel electrophoresis — comet assay:** 200 µl lymphocytes were placed into the centrifuge tube and 1000 µl cold PBS was added. Brakeless centrifugation was applied for 10 minutes at 200G 4˚C. 1000 µl supernatant was eliminated. 60 µl 0.5% w/v low melting point agarose (LMA) and 20 µl centrifuged cells were filled into Eppendorf vessels and placed on a lamina covered with a lamella. After storing in a refrigerator for 15 minutes, lamellas on the laminas were removed and 75 µl 0.5% w/v LMA was added at the end of the lamina and closed by unfolding another lamella. The samples was stored in the refrigerator for 15 minutes. After removing from the refrigerator, lamellas on the laminas were removed and left in the lysis solution for 2 hours. It was waited in the electrophoresis solution for 30 minutes in an electrophoresis and operated for 30 minutes at 300 ampere at 20-21 V. Laminas taken from the electrophoresis were left in the ice-cooled neutralization buffer for 5 minutes and then passed through ice-cooled distilled water. This process was repeated for 3 times. The end part of the lamina was stained with 60 µl ethidium bromide. It was left in dark for 5 minutes. Counting was done in dark environment by using a fluorescent microscope.

The possible DNA damage was evaluated by the "Comet assay IV system" software. In the damage evaluation, head length (HL), tail length (TL), head intensity (HI), tail intensity (TI), tail moment (TMo), and tail migration (TMi) parameters were used.

**Statistical Analysis:** Data was analyzed by the SPSS 21.0 package. When parametric test estimations were provided in dependent-group comparisons, significance test between two equivalents was used, and when parametric test estimations could not be provided, Wilcoxon Signed Rank Test was used. Statistical significance level (p) was accepted as 0.05.

**RESULTS:** Patients using MPH (n=25) were using 28.39 mg/day MPH on average. A significant difference was found between all the comet parameters evaluated before and after treatment ($p<0.05$).

A significant difference was found between all the comet parameters evaluated before and after treatment of the patients using MPH with less than 28mg/day (n=14, 18.5 mg/day) ($p<0.05$).

No significant difference was found between all the comet parameters evaluated before and after treatment of the patients using MPH with more than 28mg/day (n=11, 42.09mg/day) ($p>0.05$).

A significant difference was found between all the comet parameters evaluated before and after treatment of the patients using SSRI (n=21) ($p<0.05$).

No significant difference was found between all the comet parameters evaluated before and after treatment of the patients using Fluoxetine 20mg/day (n:8) ($p>0.05$).

**DISCUSSION:** According to the data of our study, MPH has shown genotoxic effect at sub-therapeutic doses. It is shown that dopamine may produce semiquinone and cause auto-oxidation in the presence of $Fe^{2+}$, which has a high neurodegenerative effect. Also, dopamine can be completely metabolized by monoamine oxidase, which produces highly reactive hydroxyl radicals. It is known that hydroxyl radicals cause DNA damage[5]. Such results raise the concern that DNA can be damaged by the free radicals that are produced during the oxidation of dopamine.

The results of our study are concordant with the study of El-Zein et al.[1]; in this study, 12 children had received a 20-54 mg/day MPH treatment for 3 months, and genotoxicity was shown in the peripheral blood lymphocytes by chromosome aberration test, sister chromatid exchange and micronucleus tests. In our study, different from the one mentioned, genotoxicity of MPH treatment is investigated by using the comet method in adult patients with a wider sample.

In the study by Walitza et al.[2], a genotoxic effect of MPH cannot be found. Reasons for the difference from these results may be that these studies have been conducted in children, while the study by Ponsa et al.[3] was conducted on only 7 adult patients, as well as effects of polymorphism differences, individual genetic predisposition, difference in method, and environmental factors.

In our study, a statistically significant correlation is found between the ASRS scale grade applied after the treatment and the drug dosage of the ADHD patients using MPH. Thus, it can be considered that as MPH dosage increases, it may cause a higher clinical response. Decrease of the genotoxicity of MPH with increasing dose can be related to the positive changes in the life conditions as a reason for a more significant clinical response to MPH at higher doses in ADHD patients. In addition, it can be considered that low cases numbers may have an effect on the results.

In a study performed in terms of genetic predisposition, it has been specified that carboxylesterase1 (CES1) enzyme has two undefined variants, which may cause hydrolytic activity loss against MPH. Also, it is specified that heterozygosity for recessive mutations in the genes responsible for DNA repair disorder may have increased sensitivity against genotoxic agents[3]. The difference in the results of our study may be related to this situation.

In our study, results may be different due to the polymorphous differences of the other study populations. Dopamine formation from rare amines such as tyramine is shown in hepatic microsomes. CYP2D6 is the only isoform that has a strong ability to convert p-tyramine and m-tyramine into dopamine. Thus CYP2D6 polymorphism may have caused the level of dopamine in the brain[2].

In our study, it is found that SSRI-group drugs have shown a genotoxic effect in humans. Bozkurt et al., in sertraline therapy for generalized anxiety disorder and depression patients, showed that the increase in SCE frequency was comparable to that in healthy controls. However, they specified that the results can be explained by psychogenic stress[4]. The results of our study are partially concordant with this information. Besides, in contrast to this study, it should be specified that not only sertraline is used in our study but also comorbidity is excluded.

In our study, while more significant genotoxicity is observed by MPH used in sub-therapeutic doses, it is observed that this effect disappeared in therapeutic doses. Our study is the widest attendant study in which genotoxicity assessment is performed according to MPH doses in adults. From this point of view, it is revealed that frequently used MPH should be used more carefully in therapeutic doses. According to the results of our study, it is found that SSRIs show genotoxic effects in humans. However, we did not observe a genotoxic effect of fluoxetine. Thus it can be concluded that frequently used SSRIs should be used more carefully.

For future research, it seems to be required that MPH and/or SSRI dose-based genotoxicity studies should be performed in adult ADHD, ADHD+Depression, and Depression patients with a wider sampling, in which the factors affecting DNA damage are considered. In those studies, measurement of the expression and activity of DNA repair enzymes and clarification of polymorphisms are also important.

**Keywords:** genotoxicity, methylphenidate, SSRI

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**[Abstract:0267]** ***Schizophrenia and other psychotic disorders***

# Evaluation of BDNF levels in untreated adolescents with first-episode psychosis

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**INTRODUCTION:** Previous studies of first-episode psychosis (FEP) have revealed widespread loss of cortical tissue. Although tissue loss occurs in all brain sites, ventricular enlargement and fronto-temporal tissue loss are less pronounced in FEP in contrast to chronic patients. These changes in tissue morphology are the first evidence for the disease. In a study involving 15 adolescent and young adult patients, those with FEP were found to have significantly lower plasma BDNF levels compared to healthy controls[1]. In untreated patients with FEP, low hippocampal volume was correlated with low BDNF levels.

The aim of the present study was to compare BDNF levels between adolescent patients with FEP and matched healthy controls. Furthermore, the present study evaluated the relationship between symptom severity and BDNF levels.

**METHOD:**

**Study Sample:** The study was conducted in the Department of Pediatric Psychiatry at Dicle University Training and Research Hospital. The study data were collected between February 2012 and February 2013. A total of 26 adolescent patients aged between 11 and 17 years who had not received prior therapy and who were diagnosed with psychosis according to the DSM 4 (acute psychosis, schizophreniform disorder) and 26 age- and gender-matched healthy adolescent control subjects aged between 11 and 17 years who did not have a medical or neurological disorder were included in the study. The parents of the patients provided informed consent for all study participants. The Non-interventional Clinical Research Ethics Committee at Dicle University Faculty of Medicine reviewed and approved the study protocol.

**Study Procedures:** Sociodemographic features of the participants were recorded and a clinical data form was completed. A structured psychiatric interview (K-SADS-PL and PANSS) was conducted with the participants. The clinical global impression (CGI) was used to evaluate disease severity. Finally, a 2 ml venous blood sample was obtained for biochemical tests.

**Forms and Scales:**

**Sociodemographic Data and Clinical Data Form:** This form contains questions regarding age, gender, education level, as well as the age, education level and occupation of the parents, consanguinity between parents, number of siblings, birth order among siblings, history of psychiatric disorder among family members and relatives, family history of alcohol/substance abuse, height and weight.

**Kiddie Schedule for Affective Disorders and Schizophrenia, Present and Lifetime version (K-SADS-PL):** The original scale was developed by Kaufman et al. This scale was adapted to the Turkish language by Gökler et al. in 2004. The K-SADS-PL is administered during an interview with the parents and children, and the final evaluation is performed using input from all data sources. The scale evaluates the presence of psychopathological conditions in children and adolescents.

**The Positive and Negative Symptom Scale (PANSS):** This scale is a semi-structured interview tool developed by Kay et al. in 1987, and the scale was evaluated for its validity and reliability by Kostakoğlu et al. in 1999. The scale consists of 30 items evaluating positive and negative symptoms and providing information about the general psychopathological condition.

**The Clinical Global Impression Scale (CGI):** The Clinical Global Impression Scale (CGI) is a standardized evaluation tool used to rate disease severity, disease course over time, and drug effects according to the clinical condition of the patient and the severity of side effects. CGI-I is rated on a 7-point scale from 1 (normal) to 7 (severe disease).

**Measurement of BDNF:** The blood samples were collected into gel tubes between 09:00 and 12:00. After withdrawal, blood samples were left at room temperature for 15 minutes to facilitate clotting. Blood samples were centrifuged at 5000rpm for six minutes. The serum was transferred to 1.5ml polypropylene tubes and stored at -80ºC for later analysis. Mature BDNF was measured using a human BDNF ELISA Kit (Hangzhou Eastbiopharm CO. LTD China). To minimize assay variance, all BDNF measurements were conducted on the same day. All experiments were performed in duplicate. The tests were performed according to the manufacturer's instructions. The optical density of each well was measured using an automated microplate reader.

**Statistical Analysis:** All statistical analysis was performed using the SPSS 15.0 software package. A p value $<0.05$ was considered statistically significant.

**RESULTS:** The mean age was 14.6±1.6 years among adolescents in the FEP group (range: 11-17 years; M/F: 11/15) and the mean age was 14.6±1.6 years in the control group (range: 11-17, M/F: 10/16). There was no significant difference between the groups in terms of age and gender, employment status of the parents, and family history of alcohol or substance abuse. Past medical history of the family members and first-degree relatives of ten patients in the FEP group was remarkable for psychiatric disorder, while there was no history of psychiatric

disorder in the control group (p=0.01). The rate of consanguineous marriages was significantly higher in the FEP group relative to the control subjects (p=0.03). There was no significant difference between the groups in terms of smoking history. The education level of the participants, the age and education level of the parents, the number of siblings, the birth order among siblings, height, weight, and BMI values are presented in Table 1.

The mean PANSS positive score was 20.6±7.4, the mean PANSS negative score was 29.0±9.9, and the mean PANSS general psychopathology score was 33.9±5.7. The mean CGI score was 4.7±0.9. The mean age at disease onset was 13.6±1.7 years. The mean duration of untreated psychosis was 14.6±15.2 months. The CGI score increased with increasing duration of untreated psychosis (r=0.48, p=0.04).

The serum BDNF concentration was significantly lower in the patient group (p=0.03). There was no significant relationship between PANSS and CGI scores and serum BDNF. There was no significant relationship between the duration of untreated psychosis and BDNF levels.

**DISCUSSION:** The most important finding of the current study is that adolescent patients with FEP had significantly lower serum BDNF levels compared to healthy controls. Our finding is consistent with reports regarding adult patients with FEP. It is widely accepted that schizophrenia is a neurodevelopmental disorder. It has been suggested that schizophrenia occurs as a result of profound synaptic and dendritic destruction in the adolescent period and the secondary development of abnormal connections. Previous studies have reported an association between decreased plasticity and neurogenesis in the hippocampus and decreased BDNF[2]. In addition, changes in serum BDNF levels reflect abnormal functioning of the dopaminergic system, which results in both positive and negative psychotic symptoms in the first episode of psychosis.

Another important finding is the absence of a significant relationship between disease symptoms, disease severity, and BDNF levels. The association between BDNF levels and positive and negative symptoms is controversial. Some studies have reported no significant correlation between BDNF levels and schizophrenia symptoms. Two studies demonstrated a negative correlation between BDNF levels and both positive and negative symptoms. Another study reported a negative correlation between serum BDNF and positive symptoms. One study found a positive correlation between BDNF levels and positive symptoms[3].

In conclusion, the present study found lower BDNF levels among adolescent patients with FEP compared to healthy controls, and there was no relationship between clinical symptoms and BDNF levels. The diagnosis of schizophrenia in patients with first-episode psychosis during the follow-up period suggests a relationship between BDNF and the pathogenesis of schizophrenia. We propose that BDNF may be an important neurobiological marker for EOS. Large-scale, multi-center follow-up studies are required in order to generalize the findings of the present study, which was the first study to be conducted in adolescent patients.

**Keywords:** BDNF, early onset schizophrenia, first-episode psychosis

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**[Abstract:0268]** ***Post-traumatic stress disorder***

## BDNF and cortisol levels in children with or without post-traumatic stress disorder after sustaining sexual abuse

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**INTRODUCTION:** Cortisol levels decrease or show no change in PTSD, although there are some exceptional cases. In the model proposed by Yehuda, PTSD was associated with increased adrenergic response and/or lack of a sufficient amount of cortisol in the circulation following trauma. In general, studies conducted on patients with PTSD have found lower BDNF levels compared to the control groups. A study of patients with PTSD and healthy controls who did not have a history of trauma found lower BDNF levels in patients with PTSD[1].

Another study compared BDNF levels between patients with or without PTSD after trauma and reported lower BDNF levels in patients with PTSD[2].

To our knowledge, there are no studies in the literature that evaluated cortisol and BDNF levels in adolescent and child victims of sexual abuse. The aim of the present study was to compare BDNF, cortisol, and ACTH levels in a special group of patients comprised of children and adolescent patients with or without PTSD after experiencing sexual assault, which is a catastrophic form of trauma.

**METHOD:**

**Study Sample:** The study was conducted in the Department of Child Psychiatry at Dicle University. The study data were collected between January 2013 and May 2013. The study included 55 children aged between 6 and 17 years, 13 of which were males and 42 were females. The patients were divided into two groups, with or without PTSD, based on the results of a structured psychiatric interview. Children who had mental retardation, history of head trauma, and those who received oral contraceptives, previous or current cortisol therapy or vitamins, and patients who had morbid obesity, chronic systemic disorders, and active infection were excluded in order to prevent interference with biochemical parameters. Two psychiatrists evaluated the patients, and parents provided informed consent in order for their children to participate in the study. Approval was obtained for the study from the Non-Interventional Clinical Research Ethics Committee at Dicle University Faculty of Medicine.

**Study Procedures:** Sociodemographic features of the participants were obtained and a clinical data form was completed. This was followed by a structured psychiatric interview (K-SADS-PL and CAPS-CA) and administration of the self-reported Children's Depression Inventory (CDI). Finally, a 2 ml venous blood sample was obtained for biochemical tests.

**Scales:**

**Affective Disorders and Schizophrenia for School Age Children-Present and Lifetime Version (K-SADS-PL):** The schedule (K-SADS-PL) was originally developed by Kaufman et al. It was adapted to the Turkish language by Gökler et al. in 2004. K-SADS-PL is administered during an interview with the parents and children, and the final evaluation is performed using input from all data sources.

**Clinician-Administered Post-Traumatic Stress Disorder Scale for Children and Adolescents (CAPS-CA):** CAPS-CA is a semi-structured interview developed to evaluate the frequency and severity of present and past PTSD in children and adolescents according to DSM-III and DSM-4 diagnostic criteria. It was adapted from the Clinician-Administered Post-Traumatic Stress Disorder Scale (CAPS) by Nader et al. in 1996. The scale evaluates 17 symptoms of post-traumatic stress disorder based on DSM-4 and eight tables related to PTSD. It was adapted to the Turkish language by Karakaya et al. in 2007.

**The Children's Depression Inventory (CDI):** The Children's Depression Inventory developed by Kovacs based on the Beck Depression scale was used in this study. However, questions specific to the childhood period such as school success and relationship with friends were added. The scale was adapted to the Turkish language by Öy and contains 27 items: Each item is scored as 0, 1, or 2 points depending on the severity of the symptom.

**Biochemical Analysis:** Blood samples were obtained in the morning between 10:00 and 12:00 am. Cortisol, ACTH, and BDNF levels were evaluated using ELISA method and ready-to-use ELISA kits.

**Statistical Analysis:** The statistical analysis was performed using SPSS 15.0 software package. A p-value below 0.05 was considered statistically significant.

**RESULTS:** The mean age was 14.16±2.62 years (range: 6-17 years) among the victims of sexual abuse. Of these victims, 27 (49%) were diagnosed with PTSD. There was no significant difference between patients with or without PTSD in terms of gender, place of living, school success, employment status of the parents, smoking, and menstrual cycle for adolescents.

Regarding the parameters related to sexual abuse, 60% (n=33) of the victims experienced sexual abuse involving penetration. Of the victims, 56% (n=31) experienced a single incident of assault and 44% (n=24) experienced multiple assaults. Of the victims, 24% (n=13) experienced sexual abuse within the family (incestuous) and 76% (n=42) experienced sexual abuse committed by non-related persons. There was no significant difference between patients with or without PTSD in terms of relationship with the abuse and presence of penetration (p=0.30 and p=0.70, respectively). However, the rate of PTSD was higher in patients who experienced multiple sexual assaults compared to the victims of a single assault ($p<0.001$).

There was no significant difference between patients with or without PTSD in terms of cortisol, ACTH, and BDNF levels. Likewise, there was no significant difference between patients with or without depression in terms of cortisol, ACTH, and BDNF levels. There were no correlations between CAPS scores and cortisol, ACTH, and BDNF levels between patients with or without PTSD.

The mean time that had elapsed since the first sexual abuse until the date of examination was 21.5±22.4 months (3-110 months). In the PTSD group, cortisol levels decreased with increasing time after trauma, and there was no significant correlation with the cortisol levels in patients without PTSD (r=-0.46, p=0.01 and r=-0.07, p=0.73, respectively). There was no correlation between time that had elapsed since trauma and BDNF levels.

**DISCUSSION:** In the current study, the presence of PTSD had no influence on cortisol and ACTH levels in children who had experienced sexual abuse, and cortisol levels decreased with increasing time after trauma in the PTSD group. The studies conducted on patients with PTSD often reported increased levels of CRH in the CSF and a decrease or no change in cortisol levels. Plasma, saliva, and urinary cortisol and plasma ACTH levels were found to be similar between patients with or without PTSD after trauma. Plasma cortisol levels decreased

in the two groups, and it was reported that cortisol levels did not predict the development of PTSD.
There are findings suggesting that low cortisol levels after exposure to trauma might have increased the risk of developing PTSD. There are also studies suggesting that no relationship between cortisol levels and the development of PTSD exists. In the present study, cortisol levels decreased as the time elapsed since the trauma increased in the PTSD group. It is therefore assumed that these individuals will have lower than normal cortisol levels in adulthood.
In the present study, presence of PTSD had no effect on BDNF levels in child victims of sexual abuse, and there was no correlation between BDNF levels and the time that had elapsed since the trauma. In general, studies conducted on patients with PTSD have found lower BDNF levels compared to the control group[1,2]. BDNF levels were compared between patients with or without PTSD after trauma, and BDNF levels were lower in patients with PTSD (2). In the study by Hauck et al., serum BDNF levels were higher in patients who experienced sexual assault in the last one year compared to the control group; however, BDNF levels did not differ significantly among those who experienced trauma beyond the last one year[3].
In conclusion, there was no significant difference between children and adolescents with or without PTSD in terms of cortisol, ACTH, and BDNF levels. However, the decrease in cortisol levels with increasing time after trauma in PTSD group points to the possible role of cortisol in the pathophysiology of the disease. Longitudinal studies on a larger sample are required in order to confirm the findings of the current study that was conducted in children and adolescent patients.
**Keywords:** BDNF, cortisol, PTSD

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**[Abstract:0271]** ***Addiction***

## Thalamic and cerebellar gray matter density reduction in synthetic cannabis users

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**INTRODUCTION:** In the last five years, substances called "Spice" in Europe, "K2" in the United States, and "Bonzai", "Jamaika", "Jamaika gold" or "Jamaika supreme" in Turkey are available and widely used, especially by young people[1].
In the present study, we investigated differences in brain regions in a group of synthetic cannabinoid users who had been abstinent for at least 7 days, in comparison healthy controls who had never used cannabis. We hypothesized that SC users would have volume reductions in the areas which have a large number of cannabinoid receptors.
**METHODS:**
**Participants:** We analyzed the medical records of patients that were treated in an addiction clinic in Istanbul between January 2013 and December 2014. The medical records of 35 patients were evaluated, and 15 were excluded due to lack of sufficient data. All participants were diagnosed as having cannabis use disorder, based on DSM-V, by two separate psychiatrists. The data derived from patient records included sociodemographic data, including sex (male/female), age, marital status, duration of education, age at first cannabis and SC use, duration of use (months), duration of problematic use of SCs (month), weekly frequency of SC use in the last year, weekly number of SC uses in the last year, and the presence of criminal records. The study was approved by the Ethics Committee of Uskudar University. All participants in the study were male and right-handed and all had complete biochemical examinations and urine toxicology tests. Twenty healthy males who fulfilled inclusion criteria and were matched in terms of age, level of education, and sociodemographic status with substance users enrolled and were grouped as controls in the study.

Participants who had another axis-I psychiatric disorder, a past or current substance use disorder other than nicotine, or neurological disorders were excluded.

Patients' depressive symptoms and anxiety symptoms were assessed by the Beck Depression Inventory (BDI) and Beck Anxiety Inventory (BAI), respectively. The psychological symptom patterns of the patients were assessed by the Symptom Checklist-90 (SCL-90).

**Structural Magnetic Resonance Image Acquisition:** Imaging was performed on a 1.5T MR scanner (Achieva, Philips Healthcare, Best, The Netherlands) with a SENSE-Head-8 coil at NPISTANBUL Neuropsychiatry Hospital, Istanbul. T1-weighted MPRAGE sequence was employed as high resolution anatomical scan (voxel size 1.25/ 1.25/ 1.2 mm; 130 slices; field of view 240 mm).

**VBM Analyses:** We examined the between-group differences in gray matter volume by using VBM. Data were processed and examined using the SPM software (Welcome Department of Imaging Neuroscience Group, London, UK; http://www.fil.ion.ucl.ac.uk/spm) and the VBM8 Toolbox (http://dbm.neuro.uni-jena.de/vbm.html) with default preprocessing parameters. Adaptive Nonlocal Means (SANLM) and a classical Markov Random Field (MRF) model were applied to the images in order to remove inhomogeneities and to improve the signal-to-noise ratio. Registration to standard MNI-space consisted of a linear affine transformation and a nonlinear deformation using high-dimensional DARTEL normalization. Subsequently, analyses were performed on segmented GM images, which were multiplied by the non-linear components derived from the normalization matrix to preserve actual GM values locally (modulated GM volumes). To check the quality of the normalization procedure, the normalized unsegmented images were visually inspected. Sample homogeneities were controlled using covariance to identify potential outliers. Lastly, the segmented and modulated images were spatially smoothed with an 8 mm full-width, half-maximum Gaussian kernel.

**Data Analyses:** The two groups were compared using the independent sample t-test, as implemented in the SPM second-level model. To account for differences in brain sizes, total intracranial volumes were entered in the model as covariates. The clusters were deemed significant if they survived FEW correction at p level of 0.05 (cluster forming threshold=20 voxels). Finally, to identify the associations between structural abnormalities and clinical scales, we conducted voxel of interest (VOI) analyses on cerebral tissues where group differences were identified. These areas were extracted using the MarsBaR toolbox and transferred to SPSS statistical software (SPSS Inc., Chicago, IL, USA) for further analysis. Pearson's correlation coefficients were computed between the extracted VOIs of the activated clusters and outcome variables.

Descriptive analyses were presented using means and standard deviations for normally-distributed variables.

**RESULTS:** The SCs group consisted of twenty males who claimed SCs as their drug of choice, had used SCs for a minimum period of one year, or currently were using SCs five or more times per week. The MR scans were acquired on day 7 after the last SC usage.

The comparison group consisted of 20 healthy males who had no history of psychopathology and use of any psychoactive drug. The sociodemographic characteristics of participants of the two study groups are presented in Table 1, and the clinical characteristics of SC users are presented in Table 2. Participants in the SCs group reported SCs as their drug of choice and did not report current use of other drugs, including alcohol. Comparing the control group with SC users, VOI analysis showed that regional gray matter density in both the left and right thalamus and left cerebellum was significantly decreased in SC users.

There was no relationship between age at first cannabis and SC use, duration of use, weekly frequency of SC use in the last year, or the weekly number of SC uses in the last year with gray matter tissue density.

**DISCUSSION:** There is a very limited literature about SCs, and according to Papanti et al., most of the available reports on SCs were limited to retrospective toxicology surveys, case reports /case series, human laboratory studies assessing potential acute toxicological effects of SCs, and interviews/surveys focusing on self-reported harm/side effects identified among SC users[3].

This is the first volumetric MRI study conducted in SC users that aimed to investigate the structure of the brain. Using VBM, we detected volume reductions in both left and right thalamus and left cerebellum in a sample of SC users, compared with the healthy control group. The thalamus functions as an information-processing and relay station; it is like a bridge for bidirectional signal flow between cortical and subcortical regions, links different cortical regions via trans-thalamic pathways, and is a point of convergence for fronto-striatal and cerebello-thalamo-cortical circuits[4]. By demonstrating that use of SCs is associated with thalamic volume loss, the current findings raise the possibility that SCs may increase the likelihood of such abnormalities.

On the other hand, cannabinoid receptors are highly expressed in the cerebellum, and deficits in cerebellar-dependent functions follow acute or chronic cannabis use in humans. These cerebellar-mediated processes are aberrant in schizophrenia and long-term heavy cannabis use, and lead to cognitive deficits that are similar to those in schizophrenia. The accumulating evidence suggests that cannabis use may lead to cognitive disturbances, psychotic symptoms, and specific regional brain alterations. Nonetheless, the effects of SC use on cerebellar structural integrity in SC users, with or without psychosis, have not been examined yet. Solowij et al. determined that cannabis use may have a relatively greater adverse effect on cerebellar white matter than schizophrenia[5]; however, we detected volume reduction in the left cerebellum in a sample of SC users, compared to a healthy control group.

It is also unclear why no differences were found in other brain regions that are known for CB1 receptor expression.

The results of the present study did not clarify if the differences between groups existed prior to the initiation of SC use, or if other variables, either not controlled for or unrecognized, contributed to the volume reduction in thalamus and cerebellum.

In conclusion, we observed a gray matter density reduction in the right and left thalamus and lower gray matter density in left cerebellum

among SC users, compared to healthy controls. Findings of this study need to be replicated with neuropsychiatric examination among both patients and controls in larger samples.

**Keywords:** cerebellum, synthetic cannabinoids, thalamus

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**[Abstract:0272]** ***Schizophrenia and other psychotic disorders***

## Evaluation of cortisol and ACTH levels in drug-naive adolescents with first-episode psychosis

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**INTRODUCTION:** Current evidence indicates the role of cortisol in psychosis; however, the relationship between psychological symptoms and cortisol is not clear. It has been reported that cortisol has an indirect effect on the pathophysiology of psychosis. Studies on untreated patients with first-episode psychosis have mostly found HPA axis hyperactivity. Brain maturation continues during adolescence and is vulnerable to stress[1]. To our knowledge, there is no study that evaluated cortisol and ACTH levels in adolescent patients with FEP. The aim of the present study was to evaluate cortisol and ACTH levels as indicators of the HPA axis activity in adolescent patients who were included in the study with a diagnosis of FEP and diagnosed with EOS after a follow-up period of six months. Furthermore, the present study evaluated the presence of a relationship between psychosis symptom severity and cortisol and ACTH levels.

**METHOD:**

**Study Sample:** The study was conducted in the Department of Child Psychiatry at Dicle University. The study data were collected between March 2013 and January 2014. A total of 23 adolescent patients aged between 11-17 years, who did not receive prior therapy and who were diagnosed with psychosis according to DSM-4 criteria, and 23 age- and gender-matched healthy adolescent controls aged between 11-17 years, who did not have a medical or neurological disorder, were included in the study. The parents of the patients provided informed consent for their voluntary participation in the study. Approval was obtained for the study from the Non-interventional Clinical Research Ethics Committee at Dicle University Faculty of Medicine.

**Study Procedures:** Sociodemographic features of the participants were obtained and a clinical data form was completed. A structured psychiatric interview (K-SADS-PL and PANSS) was conducted with the participants. The clinical global impression (CGI) scale was used to evaluate disease severity. Finally, a 2 ml venous blood sample was obtained for biochemical tests.

**Forms and Scales:**

**Sociodemographic Data and Clinical Data Form:** This form contains questions about age, gender, education level, and age, education level and occupation of the parents, consanguinity between parents, number of siblings, birth order among siblings, history of a psychiatric disorder in family members and relatives, family history of alcohol/substance abuse, height, and weight.

**Kiddie Schedule for Affective Disorders and Schizophrenia, Present and Lifetime version (K-SADS-PL):** The original scale was developed by Kaufman et al. It was adapted to the Turkish language by Gökler et al. in 2004. K-SADS-PL is administered during an interview with the parents and children, and the final evaluation is performed using input from all data sources. The scale evaluates the presence of psychopathological conditions in children and adolescents.

**The Positive and Negative Symptom Scale (PANSS):** This scale is a semi-structured interview tool developed by Kay et al. in 1987, evaluated for its validity and reliability by Kostakoğlu et al. in 1999. The scale consists of 30 items evaluating positive and negative symptoms and providing information about general status of psychopathological condition.

**The Clinical Global Impression Scale (CGI):** The Clinical Global Impression Scale is a standardized evaluation tool used to rate disease

severity, disease course over time, drug effects considering the clinical condition of the patient, and severity of side effects. CGI-I is rated on a 7-point scale from 1 (normal) to 7 (most severe patients).

**Biochemical Analysis:** The blood samples were obtained in the morning between 09:00 and 12:00. The samples were collected in gel tubes. After withdrawal, blood samples were allowed to rest for 15 minutes for clotting. Then, blood samples were centrifuged at 5000 rpm for six minutes. The sera were transferred to 1.5 ml polypropylene tubes and stored at -80°C until analysis. Cortisol and ACTH levels were evaluated using the ELISA method and ready-to-use kits.

**Statistical Analysis:** The statistical analysis was performed using SPSS 15.0 software package. A p value <0.05 was considered statistically significant.

**RESULTS:** The mean age was 14.5±1.4 years among adolescents in the FEP group (range: 8-17 years; M/F: 11/15) and 14.7±1.5 years in the control group (range: 11-17, M/F: 8/15). There was no significant difference between the groups in terms of age and gender, employment status of the parents, and family history of alcohol or substance abuse. Past medical history of the family members and first-degree relatives of seven patients (30%) in the FEP group was remarkable for psychiatric disorders, while there was no history of psychiatric disorders in the control group (p=0.02). The rate of consanguineous marriages was significantly higher in the FEP group (p=0.02). In the FEP group, the rate of consanguineous marriage in the parents was higher among male patients (p=0.045). In addition, the history of psychiatric disorders in the family members and first-degree relatives was more common among male patients, although the difference was not statistically significant (p=0.20). There was no significant difference between the groups in terms of smoking. Education level of the participants in terms of years, age of the parents, number of siblings, and BMI values are presented in Table 1.

There was no significant difference between the patients and the control group in terms of cortisol and ACTH levels. There was no significant relationship between PANSS and CGI scores and cortisol and ACTH levels. Cortisol and ACTH levels were significantly higher in male patients with FEP compared to male patients in the control group (p=0.04 and p=0.02, respectively). There was no difference in these measures in females. The data pertaining to biochemical analyzes are presented in Table 2. The clinical features of the patients in the FEP group are presented in Table 3.

**DISCUSSION:** The most important finding of the present study is the detection of higher cortisol and ACTH levels in male patients with FEP. In addition, the rate of consanguineous marriage in the parents was higher in male patients, suggesting a genetic loading. The importance of the vulnerability-stress model increases in the etiology and pathogenesis of psychosis. According to this model, predisposing biological factors increase the vulnerability of an individual to stress and predispose to the development of psychosis under distressing environmental conditions. The increase in cortisol levels has been suggested to occur before disease onset and predispose to disease development. The patients with psychosis are also known to exhibit intolerance and sensitivity to stressful stimulations. Trauma sustained in early periods of life causes hippocampal damage, and this in turn causes increased sensitivity to the development of psychosis[2].

There was no significant difference between the patients and the control group in terms of cortisol and ACTH levels. Of four studies that measured cortisol levels in the serum similar to our study, two found elevated cortisol levels in the FEP group, while the other two studies found no difference. Of seven studies that measured cortisol levels in the plasma, none found a significant difference. Cortisol levels were elevated in almost all patients above 29.5 years of age[3].

Another finding of the present study is the lack of a significant relationship between psychosis symptom severity and cortisol and ACTH levels. Almost all studies having similar design to our study have failed to demonstrate a significant relationship. However, one study reported a negative correlation between plasma cortisol level and PANSS positive score, and another study reported a positive correlation between PANSS negative score and cortisol levels.

In conclusion, although there was no significant difference between patients in the FEP group and healthy controls in terms of cortisol and ACTH levels, cortisol and ACTH levels were higher in male patients in the FEP group. In addition, the rate of consanguineous marriage was higher among the parents of patients with FEP. The increase in cortisol levels has been suggested to occur before disease onset and predispose to disease development. We consider that individuals with genetic loading regarding psychosis must be more closely monitored for the activity of the HPA axis.

**Keywords:** cortisol, first-episode psychosis, HPA axis

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**[Abstract:0273]** ***Post-traumatic stress disorder***

# Levels of cortisol and oxidative stress and DNA damage in child and adolescent victims of sexual abuse with or without post-traumatic stress disorder

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**INTRODUCTION:** Among other effects, oxidative stress also impairs normal brain functions through the inhibition of neurogenesis, altering neuronal transmission, and inducing mitochondrial dysfunction[1]. Human and animals studies demonstrated that oxidative stress is related to anxiety. In an animal model of PTSD, inflammation and oxidative stress were reported to play a critical role in the development and exacerbation of PTSD[2]. There are also studies that did not report a significant difference between patients with PTSD and the control group in terms of oxidative stress[3]. It was reported that oxidative stress could be a critical molecular linkage between the hypothalamic–pituitary–adrenal (HPA) axis dysfunction and mental disorders. It was also reported that the stress-induced increase in cortisol levels accelerates glucose metabolism and production of reactive oxygen species.

The aim of the present study is to evaluate children and adolescents who develop PTSD after experiencing sexual abuse versus those who did not develop PTSD in terms of the level of oxidative stress and DNA damage.

**METHOD:**

**Study Sample:** The study was conducted in the Department of Child Psychiatry at Dicle University. The study data were collected between July 2013 and February 2014. A total of 61 children, aged between 5 and 17 years (18 males and 43 females), participated in the study. The patients were divided into two groups, patients with PTSD and patients without PTSD, based on the results of a structured psychiatric interview. Children who achieved an intelligence score below 70 points, those with a significant neurological or medical disorder, those who received oral contraceptives, previous or current cortisol therapy, vitamins, and those with morbid obesity or active infection were excluded from the study in order to prevent interference with the biochemical parameters. The parents provided informed consent in order for their children to participate in the study. Approval was obtained for the study from the Non-interventional Clinical Researches Ethics Committee at Dicle University Faculty of Medicine.

**Scales:**

**Affective Disorders and Schizophrenia for School Age Children-Present and Lifetime Version (K-SADS-PL):** The schedule (K-SADS-PL) was originally developed by Kaufman et al. It was adapted to the Turkish language by Gökler et al. in 2004. K-SADS-PL is administered during an interview with the parents and children, and the final evaluation is performed using input from all data sources.

**Clinician-Administered Post-Traumatic Stress Disorder Scale for Children and Adolescents (CAPS-CA):** CAPS-CA is a semi-structured interview developed to evaluate the frequency and severity of present and past PTSD in children and adolescents according to DSM-III and DSM-4 diagnostic criteria. It was adapted from the Clinician-Administered Post-Traumatic Stress Disorder Scale (CAPS) by Nader et al. in 1996. The scale evaluates 17 symptoms of post-traumatic stress disorder based on DSM-4 and eight items related to PTSD. It was adapted to the Turkish language by Karakaya et al. in 2007.

**The Children's Depression Inventory (CDI):** The Children's Depression Inventory developed by Kovacs based on the Beck Depression scale was used in the study. However, questions specific to the childhood period such as school success and relationship with friends were added. The scale was adapted to the Turkish language by Öy and contains 27 items, each of which is scored as 0, 1, or 2 points depending on the severity of the symptom.

**Biochemical Analysis:** The blood samples were obtained in the morning between 10:00 and 12:00 AM. Cortisol, glutathione peroxidase (GPx), superoxide dismutase (SOD), coenzyme Q, 8-Hydroxy-2-Deoxyguanosine (8-OHdG) levels were evaluated using the ELISA method and ready-to-use ELISA kits.

**Statistical Analysis:** The statistical analysis was performed using SPSS 15.0 software package. A p value$< 0.05$ was considered statistically significant.

**RESULTS:** The mean age was 13.3±2.4 years (range: 5-17 years) among the victims of sexual abuse. Our evaluation revealed a diagnosis of PTSD in 51% (n=31) of victims. There was no significant difference between patients with or without PTSD in terms of gender, smoking status, and menstrual cycle, the latter being assessed for adolescent patients. There was also no significant difference between the groups in terms of age, age of the mother/father, and education level of the parents.

Regarding the parameters related to sexual abuse, 48% (n=29) of the victims experienced sexual abuse involving penetration. Of the victims, 46% (n=28) experienced single assault and 54% (n=33) experienced multiple assaults. 21% (n=13) of victims experienced sexual

abuse within the family (incestuous), and 79% (n=48) experienced sexual abuse committed by non-related persons. There was no significant difference between patients with or without PTSD in terms of relationship with the abuse and presence of penetration (p=0.34 and p=0.68, respectively).

There was no significant difference between the groups with or without PTSD in terms of cortisol, GPx, SOD, coenzyme Q, and 8-OHdG levels (Table 1). Likewise, there was no significant difference between the groups with or without depression in terms of cortisol, GPx, SOD, coenzyme Q, and 8-OHdG levels (p=0.43, p=0.46, p=0.38, p=0.53, and p=0.48, respectively). There was no correlation between CAPS scores and GPx, SOD, coenzyme Q, and 8-OHdG levels between patients with or without PTSD.

The mean time that elapsed since the first sexual abuse until the date of examination was 23.9±24.1 months (range: 1-115 months). In the PTSD group, cortisol levels decreased with increasing time after trauma, and there was no significant correlation with the cortisol levels in patients without PTSD (r=-0.46, p=0.01 and r=-0.07, p=0.73, respectively). Similarly, 8-OHdG levels in the PTSD group decreased with increasing time after trauma, and there was no significant correlation with 8-OHdG levels in patients without PTSD (r=-0.42, p=0.03 and r=-0.04, p=0.85, respectively).

**DISCUSSION:** In the present study, there was no significant difference between patients with or without PTSD in terms of oxidative stress and DNA damage. Furthermore, no relationship was found between the severity of the symptoms of PTSD and oxidative stress and DNA damage. In their studies, Tezcan et al. and Čeprnja et al. did not report any association between PTSD and oxidative stress[3]. However, healthy volunteers having no past history of trauma were selected as the control group in their study. In addition, the type of trauma in their study was different compared to the present study. In contrast to our findings, human and animal studies showed an association between oxidative stress and anxiety. In an animal model of PTSD, inflammation and oxidative stress were reported to play a critical role in the development and exacerbation of PTSD[2].

In the present study, cortisol and 8-OHdG levels decreased with increasing time after trauma in the PTSD group. Although we did not find any difference between the groups in terms of 8-OHdG concentrations, this finding was considered to be a reflection of the relationship between cortisol and DNA damage.

In conclusion, there was no significant difference between children and adolescents with or without PTSD after sexual abuse in terms of the level of oxidative stress and DNA damage. However, cortisol and 8-OHdG levels decreased with increasing time after trauma in the PTSD group. Although we did not find any difference between the groups in terms of 8-OHdG concentrations, this finding was considered to be a reflection of the relationship between cortisol and DNA damage. This is the first study conducted in this age group.

**Keywords:** oxidative stress, PTSD, sexual abuse

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**[Abstract:0287]** ***Anxiety, stress, and adjustment disorders***

## Dysfunctional fear of progression in DM patients and association with HbA1c level

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**INTRODUCTION:** Disease is defined as a situation resulting in physical and psychological imbalance, and this is more common among individuals with chronic diseases. People attempt to cope with the negative aspects of life caused by the disease by developing different adaptation mechanisms[1]. An important consequence of the chronic nature of the disease is that the possibility of mental, emotional, social, and psychosexual problems being experienced is higher than for diseases that are not chronic. In people with Diabetes Mellitus

(DM), depression and anxiety may be linked to hyperglycemia and increased levels of HbA1c. Scales and inventories to assess disease-specific general stress or specific characteristics of distress such as worry or FoP (fear of progression) have been developed in studies to overcome this problem[2]. In this study, we intended to research the relationship between DM and the FoP scale, a scale developed by Herschbach et al. based on patients with cancer, diabetes, and rheumatologic diseases, recommended for use by people with chronic disease and used to date on many cancer patients.

**MATERIALS AND METHODS:**

**Patients:** The sample population of the research was patients with a diagnosis of type 2 DM attending Ordu University Medical Faculty-Education and Research Hospital Diabetes clinic between 1 January and 1 June 2014. The basic inclusion criteria for the study were: no current and/or previous history of psychiatric disease or treatment, age between 18 and 80 years, voluntary participation in the study, and no physical or cognitive obstacles to being interviewed or completing the applied scales. Apart from these participants, the study scanned information in the system to include patients with HbA1c values taken within the previous 3 months. Statistical analysis classified patients into a variety of groups. According to HbA1c value, two groups were formed with HbA1c≤7 and HbA1c>7, respectively. According to BMI value, 4 groups were determined: normal, overweight, obese and morbidly obese. Three groups were classified according to age: 18-40 years, 40-60 years, and above the age of 60. Lastly, patients were grouped according to duration of disease (0-3 years, 3-5 years, 5-10 years, 10-20 years and more than 20 years). The research was completed with 151 patients who fit the criteria stated above. Information was collected with a data collection form prepared by the researchers, the hospital anxiety depression scale, Rosenberg self-esteem scale and the fear of progression questionnaire.

**Fear of Progression Questionnaire:** The Fear of Progression questionnaire (FoP-Q) was recently created by Herschbach et al. to evaluate fear of a disease advancing in patients with breast cancer, diabetes mellitus, and rheumatic diseases (2). It consists of 43 items and was developed and tested in Germany. It includes 5 subscales of affective reactions (13 items), partnership/family (7), occupation (7), loss of autonomy (7), and coping with anxiety (9). The total score can be calculated by all anxiety subscales, and there is a single total score for the coping subscale. Each item is evaluated with a five-point Likert scale (from 1 [never] to 5 [very often]). Points are given as both subscale and total points. Validity and reliability studies for Turkey have not yet been completed. The English version of the scale was translated to Turkish by Cosar et al.

**Statistical Analysis:** Descriptive statistics of all data are given as frequency, median, minimum and maximum values. As the data did not follow normal distribution, the Mann Whitney U test was used to compare two groups and the Kruskal-Wallis test was used to compare more than two groups. If a significant difference was found by the Kruskal-Wallis test ($p<0.05$), then Dunn's test was used to identify which median caused the difference. Statistical analyses were completed using SPSS software (v22, IBM Inc.). A value for $p<0.05$ was accepted as significant.

**RESULTS:** According to HbA1c of ≤7 and **>**7, the total and sub-parameters of FoP, HADS and sub-parameters, and self-esteem points were compared. Accordingly, while there was no significant difference found between the two groups in terms of total FoP points, the coping subscale in the HbA1c ≤7 group was significantly higher (p=0.0001). The HADS total points (p=0.0023) and both anxiety (p=0.0059) and depression (p=0.0001) subscale points were found to be significantly higher in the HbA1c**>**7 group compared to the HbA1c ≤7 group.

When compared in terms of gender, while there was no difference in FoP total points between the genders, the affective reaction points of women were found to be higher by a significant degree compared to the points for men ($p<0.05$). Similarly, the HADS total, anxiety and depression points for women were found to be higher by a statistically significant amount compared to men.

**DISCUSSION:** When examining the literature, no single study researching the fear of disease progression in diabetic patients was found. The relationship between these fears and blood sugar control is a topic that has not been studied to date.

The FoP of DM patients was investigated in our study based on the HbA1c levels of patients, and the FoP-Q was compared to the HADS to determine the disease-specific worries of patients. Accordingly, both HADS total points (p=0.0023) and subscales of anxiety (p=0.0059) and depression (p=0.0097) were found to be higher by a significant degree in the HbA1c >7 group compared to the HbA1c ≤7 group. While no significant difference was found between the HbA1c ≤7 and HbA1c >7 groups in terms of total FoP points and other subscale parameters, the FoP subscale of coping was found to have significantly higher levels in the HbA1c ≤7 group compared to the HbA1c >7 group. When the effect of gender on anxiety and depression is examined, though there was no difference in the total FoP points, women had affective reaction points that were significantly higher than the points for men ($p<0.05$). In a similar fashion, the HADS total and anxiety and depression points of women were found to be higher than for men at a statistically significant level.

Patients with chronic physical diseases, like cancer, rheumatic diseases and diabetes mellitus, have a high incidence of anxiety disorders. Compared with the general population, patients with diabetes mellitus had more than 6 times the rate of generalized anxiety disorders. The criteria developed to aid diagnoses of anxiety disorders are suited to the general population and may not be relevant to patients with chronic physical disease. In order to classify as a mental disorder according to the DSM-4 (or ICD-10) (3), excessive, irrational or inappropriate displays of anxiety should be present

DM is a non-contagious chronic disease beginning in middle or advanced age which creates the perception of a real threat in patients due to the disease itself, its high morbidity and mortality, and possible complications. This is different from irrational or psychiatric anxiety because the underlying fear is real and independent. As such, a specific tool is needed to assess it, and this is why the FoP-Q was

developed.

The coping scale item, separate from other subscales of the FoP-Q, inquires into whether patients can access help from various sources, such as relaxation or pleasant activities, and whether they can talk to doctors about concerns and fears (4). The high coping points obtained by patients with HbA1c ≤7 may indicate that DM patients could benefit from supportive interventions for blood glucose control. This result supports studies in the literature emphasizing the positive relationship between HbA1c levels and anxiety values (5). As a result, we believe that developing the coping skills of DM patients may indirectly provide a protective effect on blood sugar levels and thus on possible complications that may develop in the future.

Our study is the first in our country researching the fear of disease progression in DM patients. While we believe it to be an important contribution to the literature, there are some limitations. Our patient numbers are low and it is a single-center study, making it difficult to generalize our findings. This topic requires broader and multi-centered studies. Another limitation is that validity and reliability studies of the scale have not been completed in Turkey. Cosar et al. continue to work on this topic.

**CONCLUSION:** There is a positive relationship between the stress coping skills of a person and blood sugar control. The FoP-Q coping subscale points of patients with HbA1C ≤7 were higher than in the HbA1C >7 group. This shows that if the coping skills of individuals with a chronic disease like DM can be developed, if the worries of the person related to disease are reduced, this may contribute to blood sugar regulation. In chronic diseases like DM, instead of using scales based on the general population or psychiatric diseases, the use of the FoP-Q scale to identify worries related to situations that are more true to the real life of patients or that affect quality of life may be a good marker of psychiatric interventions for the clinician.

**Keywords:** diabetes mellitus, fear of progression, HbA1C

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**[Abstract:0290]** ***Schizophrenia and other psychotic disorders***

## Oxidative stress and DNA damage in drug-naive first-episode psychosis in adolescents

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**INTRODUCTION:** Oxidative stress has been implicated in the psychopathology of schizophrenia, with abnormal activity of antioxidant enzymes, decreased antioxidant levels and increased lipid peroxidation all being demonstrated in patients with schizophrenia[1]. There are, however, discrepancies between studies. Studies of adolescents with First-Episode Psychosis (FEP) showed lower total antioxidant (TAS) and glutathione (GSH) levels, and a relationship has been suggested between GDH deficiency and the loss of cortical gray matter over two years[2].

The aim of the present study is to evaluate the level of oxidative stress and the presence of DNA damage in first-episode psychosis in adolescents. Furthermore, the study investigates the presence of a relationship between the severity of psychotic symptoms and oxidative stress and DNA damage.

**METHOD:**

**Study Sample:** The study was conducted in the Department of Child Psychiatry at Dicle University, using data that was collected between February and November 2014. The study included 20 adolescent patients aged between 11 and 17 years, all of whom had been diagnosed with psychosis according to DSM-4 criteria and who had received no previous psychiatric therapy, as the patient group, and 20 age-matched healthy adolescents with no medical or neurological disorders as the control group. Patients with an intelligence score

of less than 70 points, those with marked neurological and medical problems, taking oral contraceptives, having undergone previous or current cortisol therapy or taking vitamins, those with morbid obesity, active infections or a history of substance abuse within the last 6 months were excluded from the study due to possible interference with the biochemical parameters. The parents of the patients provided informed consent for all study participants. The study was reviewed and approved by the Non-Interventional Clinical Research Ethics Committee at Dicle University, issue date 13.02.2012, number 395.

**Study Procedures:** The sociodemographic features of the participants were obtained and a clinical data form was completed. Structured psychiatric interviews were conducted with the patients (K-SADS-PL and PANSS), with the Clinical Global Impressions (CGI) scale used to evaluate disease severity. Finally, a 2 mL venous blood sample was obtained for biochemical tests.

**Kiddie Schedule for Affective Disorders and Schizophrenia, Present and Lifetime Version (K-SADS-PL):** This scale was originally developed by Kaufman et al. and was adapted into the Turkish language by Gökler et al. in 2004. K-SADS-PL is administered during an interview with the parents and the child, and the final evaluation is made using input from all data sources.

**Positive and Negative Symptom Scale (PANSS):** This is a semi-structured interview tool developed by Kay et al. in 1987, evaluated for its reliability and validity by Kostakoğlu et al. in 1999. The scale consists of 30 items evaluating positive and negative symptoms and providing information about the general status of the psychopathological condition.

**Clinical Global Impression Scale (CGI):** The Clinical Global Impression Scale is a standardized evaluation tool used to rate disease severity, disease course over time and drug effects, considering the clinical condition of the patient and the severity of side effects. CGI-I is rated on a 7-point scale from 1 (normal) to 7 (most severe patients).

**Biochemical Analysis:** The blood samples were obtained in the morning between 09:00am and 12:00 noon and were collected into gel tubes. After withdrawal, the blood samples were allowed to rest for 15 minutes to clot, after which they were centrifuged at 5000rpm for 6 minutes. The sera were transferred to 1.5 mL polypropylene tubes and stored at -80°C until the analysis. GPx, SOD, CoQ and 8-OHdG levels were evaluated using the ELISA.

**Statistical Analysis:** The statistical analysis was performed using the SPSS 15.0 software package. A p value $< 0.05$ was considered statistically significant.

**RESULTS:** The mean age was 14.5±1.6 years in the FEP group (M/F: 8/12) and 14.4±1.5 years in the control group (M/F: 8/12). There was no difference between the groups in terms of age and gender, and no difference in terms of employment status of the parents and family history of alcohol and substance abuse. Of patients in the FEP group, eight (40%) had a history of psychiatric disorders in the immediate family and first-degree relatives, while no patient in the control group had such a family history ($p<0.01$). The rate of consanguineous marriage between the parents was significantly higher in the FEP group ($p<0.01$), while there was no difference between the groups in terms of smoking status.

The mean PANSS positive score was 19.4±6.8, the mean PANSS negative score was 28.1±9.5, and the mean PANSS general psychopathology score was 31.6±5.5. The mean CGI score was 4.6±1.0, while the mean age of disease onset was 14.1±1.9 years. The mean duration of psychosis before treatment was 13.1±14.3 months.

There was no difference between the patient and the control group in terms of SOD, GPx or 8-OHdG values; and no significant relationship was identified between the PANSS and CGI scores of the patient group and the SOD, GPx, CoQ and 8-OHdG values.

**DISCUSSION:** One of the most important findings of the present study is the lack of any significant difference between patients with FEP and the healthy controls in terms of oxidative stress. Studies of both adolescent and adult patients with FEP have reported deficiencies mostly in antioxidant defense mechanisms (enzymatic, non-enzymatic) and have implicated oxidative stress in the pathophysiology of schizophrenia (particularly with regard to negative symptomatology and cognitive functioning). The study of 102 children and adolescents by Micó et al. reported a decrease in total antioxidant defense glutathione levels and an increase in GPx activity, catalase and SOD activity[2], while the study of 48 children and adolescents by Fraguas et al. found a relationship between the decrease in glutathione levels and the loss of cortical gray matter in two years[1]. The study of 105 children and adolescents by Martínez-Cengotitabengoa et al. reported lower total antioxidant and glutathione levels and a direct relationship between antioxidant defense capacity and global cognition at baseline and after a two-year follow-up period. The present study of patients with EOS found no difference in terms of oxidative stress, and therefore does not support study results that suggest a role of oxidative stress in the psychopathology of schizophrenia.

Studies of adult patients with schizophrenia reported changes in antioxidant enzyme levels, although there are discrepancies between studies. The GPx level was reported to be higher in a study of patients with first-episode schizophrenia, while another study reported lower GPx levels. The SOD level was reported to be lower in one study conducted of patients with treated and untreated schizophrenia, while another study reported higher SOD levels.

Another important finding of the present study is the lack of difference between the groups in terms of DNA damage. To the best of our knowledge, there has been no study to date evaluating DNA damage in adolescent patients with FEP, although studies of adult patients with FEP and schizophrenia have reported increased DNA damage, and this finding was interpreted as a molecular connection between schizophrenia and an accelerated aging process. An increase in 8-OHdG levels, indicating oxidative DNA damage, and telomere shortening, indicating direct DNA damage, has in the past been reported in patients with schizophrenia. This finding was considered to be an indication of the lack of oxidative DNA damage in early disease periods in patients with EOS and for an association of DNA damage

with a chronic disease course.
In conclusion, there was no difference between the patients with FEP and the control group in terms of oxidative stress and DNA damage; and furthermore, no relationship was identified between symptom severity, oxidative stress, and DNA damage. Future studies should evaluate more comprehensively the factors that contribute to the development of oxidative stress, as the present study revealed no change in the levels of oxidative stress in the early periods of disease, and there are studies that have reported higher oxidative stress in later disease stages.
**Keywords:** DNA damage, early onset schizophrenia, oxidative stress

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**[Abstract:0291]** ***Post-traumatic stress disorder***

## Examining the levels of BDNF and cortisol in children and adolescent victims of sexual abuse

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**INTRODUCTION:** Glucocorticoids act through glucocorticoid receptors (GR) found in high concentrations in the amygdala and the hippocampus. In GR-mediated molecular activation, the brain-derived neurotropic factor (BDNF)-mediated signal pathway is required for memory consolidation. BDNF expression in the central nervous system is modified by various brain traumas including stress, ischemia, epileptic seizures, and hypoglycemia. Glucocorticoids play a role in the regulation of BDNF. In the rat hippocampus, stimulation of mineralocorticoid receptors (MR) increases the level of BDNF, while stimulation of glucocorticoid receptors (GR) decreases the BDNF levels[1]. As mentioned above, trauma affects growth factors and the HPA axis. There are limited studies in the literature that have investigated the relationship between cortisol and BDNF levels in child and adolescent victims of sexual abuse. The present study compares the levels of BDNF, cortisol, and ACTH between child and adolescent victims of sexual abuse with those who have no trauma history.
**METHOD:**
**Study Sample:** The study was conducted in the Department of Child Psychiatry at Dicle University. The study included a total of 44 children (M/F: 12/32) between the ages of 8 and 17 years who had experienced child sexual abuse and 42 age- and gender-matched children (M/F: 12/30) as control group. The study data were collected between December 2011 and April 2012. Children who achieved an intelligence score below 70 points, who had significant neurological or medical disorders, who received oral contraceptives, had previous or current cortisol therapy, vitamins, and those who showed morbid obesity or active infection were excluded in order to prevent interference with the biochemical parameters. The patients were evaluated by two psychiatrists. The parents provided informed consent in order for their children to participate in the study. Approval for the study was obtained from the Non-Interventional Clinical Research Ethics Committee at Dicle University Faculty of Medicine. Sociodemographic features of the participants were obtained and a clinical data form was completed. This was followed by collection of a 2 ml venous blood sample for biochemical tests.
**Sociodemographic Data and Clinical Data Form:** This form included questions about age, gender, education level, age of the parents, number of siblings, history of psychiatric disorders or substance abuse in the relatives, height, weight, and body mass index (BMI), type of abuse, duration and frequency of abuse, relationship with the abuser, and abuse history.
**Biochemical Analysis:** The blood samples were obtained in the morning between 10:00 and 12:00 AM. Cortisol, ACTH, and BDNF levels were evaluated using the ELISA.
**Statistical Analysis:** The statistical analysis was performed using SPSS 15.0 software package. A p-value below 0.05 was considered statistically significant.
**RESULTS:** The mean age was 13.1±2.7 years (range: 8-17 years) among the victims of sexual abuse. In the control group, the mean age was 13.8±2.9 years (range: 8-17 years). The sexual abuse group consisted of 12 males and 32 females, and the control group consisted

of 12 males and 30 females. The duration of education was lower and the mean number of siblings was higher in the victims of sexual abuse and their parents compared to the control group (p=0.02, p<0.001, p<0.001, and p<0.001, respectively). There was no significant difference between the groups in terms of the history of psychiatric disease in family members or relatives and smoking status (p>0.05). There was no significant difference between the groups in terms of height, weight, and BMI (p>0.05).

Regarding the parameters related to sexual abuse, 64% (n=28) of the victims had experienced sexual abuse involving penetration. Of the victims, 52% (n=23) had experienced a single assault and 48% (n=21) multiple assaults. 23% (n=10) had experienced sexual abuse within the family (incestuous) and 77% (n=34) sexual abuse committed by non-related persons. Of all cases, 82% (n=36) were smokers and 18% (n=8) were non-smokers.

Cortisol levels were significantly higher in the sexual abuse group compared to the control group (p<0.001). Albeit statistically insignificant, ACTH levels were higher in the sexual abuse group compared to the control group (p=0.10). Consistent with these findings, the ACTH/Cortisol ratio was lower (p<0.001). BDNF levels were significantly lower in the sexual abuse group compared to the control group (p=0.04). The mean time that elapsed from the first sexual abuse until the date of examination was 22.72±21.72 months (range: 2-120 months). The evaluation of the relationship between this time span and cortisol levels revealed that cortisol levels decreased as this time interval increased (r=-0.271, p=0.03).

In the sexual abuse group, there was no relationship between the presence of penetration and cortisol, ACTH, and BDNF levels. Cortisol and BDNF levels were lower in the victims of multiple sexual assaults (p=0.03 and p=0.04, respectively). Cortisol and ACTH levels were lower in the victims of sexual abuse within the family; however, BDNF did not show a significant difference (p=0.03, p=0.049, p=0.11).

**DISCUSSION:** One of the most important findings of the present study was that high cortisol levels were observed in the sexual abuse group. Furthermore, cortisol levels decreased as time elapsed, while trauma increased. The majority of the studies conducted on child and adolescent victims of trauma were found to have elevated non-stress cortisol levels. However, a meta-analysis of retrospective studies in patients that experienced chronic stress was found them to have decreased non-stress cortisol levels. This decrease in cortisol levels over time is referred to as the "attenuation hypothesis".

The second most important finding of the present study was lower BDNF levels observed in the sexual abuse group. In human studies, BDNF levels were lower in depressed women who were survivors of childhood physical abuse. BDNF levels were also lower in bipolar patients who had a history of trauma in childhood. The inverse relationship between memory performance and childhood sexual abuse was found to be associated with apolipoprotein E gene alleles.

There are studies that implicated BDNF in the relationship between trauma and schizophrenia, bipolar disorder, PTSD, and depression[2]. In animal studies, stress was suggested to be associated with changes in the functions and structure of the hippocampus through decreased neurogenesis, increased glucocorticoids, and/or decreased BDNF. In general, studies conducted on patients with PTSD have found lower BDNF levels compared to the control group[3]. There are also studies suggesting no change or even an increase in BDNF levels.

In the sexual abuse group, the presence of penetration had no effect on cortisol and BDNF levels. However, both cortisol and BDNF levels were lower in victims that experienced multiple sexual assaults. Cortisol levels were lower in victims of sexual abuse within the family. The effects of stress on cognitive functions and psychopathological processes are related to gender, type of stress, frequency, controllability, and predictability.

In conclusion, the present study found elevated cortisol levels and decreased BDNF levels in child and adolescent victims of sexual abuse. Interestingly, cortisol levels decreased with increasing time after trauma. Furthermore, some factors related to trauma such as sexual abuse within the family and multiple assaults were found to have affected cortisol and BDNF levels. The results of the present study suggest that cortisol and BDNF could be biological molecular mediators of trauma on biological and psychological systems. While this is the first report on the effects of cortisol and BDNF-induced trauma in child and adolescent victims of sexual abuse, longitudinal studies with larger samples size are required to validate the findings of the current study.

**Keywords:** BDNF, HPA axis, sexual abuse

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**[Abstract:0306]** ***Schizophrenia and other psychotic disorders***

# Vitamin D level in schizophrenia and association with metabolic syndrome parameters

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**INTRODUCTION:** Vitamin D deficiency is a common problem in many countries. Hypovitaminosis D is more prominent in winter, in high latitudes, and in individuals with dark skin. Migrants to European countries are reported to have a higher risk of hypovitaminosis D compared with native-born people, and immigrants from Turkey have a roughly 4-fold risk of hypovitaminosis D[1]. Vitamin D deficiency is found to increase the risk of developing schizophrenia both in animal models (e.g., the litter of D vitamin-depleted female pregnant rats) or in humans[1]. A growing body of literature is related with vitamin D status and risk of brain disorders including schizophrenia or psychosis[2].

Low level of vitamin D is suspected as an important contributing factor to the development of cardiovascular diseases, hypertension, metabolic syndrome, and type 2 diabetes mellitus[3]. Although the relation between vitamin D and insulin resistance seems controversial, the Vit D deficiency is considered to be a risk factor for MetS and type 2 DM (4) and glucose intolerance[2]. Cui et al. have shown a positive correlation of vitamin D concentration and insulin sensitivity and suggested that individuals with hypovitaminosis D are at higher risk of insulin resistance and metabolic syndrome[2]. Here, for the first time, we aimed to investigate the association between Vit D3 level and insulin resistance and metabolic syndrome parameters in patients with schizophrenia.

**METHOD:**

**Participants:** This study was performed at the Department of Psychiatry of Cerrahpasa Medical School, Istanbul University. We recruited 40 patients with acute schizophrenia who had been admitted to our inpatient clinic between October 2014 and December 2014. The forty inpatients (F=24, M=16) were enrolled in the study after they met the diagnosis of schizophrenia, schizoaffective disorder, and schizophreniform disorder according to DSM IV, TR. The mean age was 41.55±16.29 years and the mean onset age of illness was 30.08±14.21 years and the mean duration of illness 11.50±9.98 years.

The clinical psychopathology in patients was assessed by Positive and Negative Syndrome Scale (PANSS). Individuals were excluded if they had a diagnosis of alcohol or substance dependence, organic mental disorder or learning disability, or a metabolic disease that may affect serum vitamin D concentrations.

After receiving patients' informed consent, 5 $cm^3$ peripheral fasting venous blood samples were taken, placed in tubes covered with aluminum foil and centrifuged at 4000 rpm for 10 min to analyze the separated serum. Hemolyzed and icteric serums were not used in this study. The total vitamin D (25-hydroxyvitamin D) values were measured by electroluminescence. A sufficient level of total vitamin D was considered >60 ng/ml; an insufficient level 30-59 ng/ml; and a deficient level was established as <29 ng/ml. The metabolic syndrome parameters were assessed according to the international diabetes federation[5]: IDF waist circumference, M>94cm / F>80cm; blood pressure, systolic ≥130 mmHg and diastolic ≥85 mmHg; HDL, M<40mg/dl and F<50mg/dl; triglycerides ≥150 mg/dl; fasting glucose, ≥110 mg/dl.

Insulin levels were measured using the Abbott C-2000i device, and glucose and lipid levels were measured using the Abbott C 8000 device. HOMA IR is calculated as: Fasting glucose X insulin / 405, and the patient was accepted as insulin-resisted if the result was >2.5.

**Statistical Analysis:** Statistical Package for the Social Sciences (SPSS) 20.0 was used for the analysis. While descriptive statistics for continuous variables were shown as mean±SD, categorical variables were expressed as number of cases (n) and %. The Mann–Whitney U test was used for nonparametric variables. The Spearman correlation test was used to determine the association between the continuous nonparametric variables. The results were evaluated for a significance level of $p<0.05$.

**RESULTS:** There were 26 patients with schizophrenia, nine patients with schizoaffective disorder and four patients with schizophreniform in the sample (n=40 in total). The mean positive symptom scale score was 16.22±4.79 points, the mean negative symptom scale score was 14.55±4.33 points, and the mean general psychopathology scale score was 26.03±6.17. There were no significant differences between patients with insulin-resistant schizophrenia and non-insulin-resistant patients between positive symptom scale (p=0.248), negative symptom scale (p=0.964) and general psychopathology scale (p=0.952).

The mean vitD3 level was 13.03±13.31nmol/L and 92.5% of patients had insufficient vitD3 (cut-off <30 nmol/L). Three patients met the criteria of metabolic syndrome and the mean metabolic syndrome parameter was 1.45±0.81. The mean HOMAIR was 2.18±1.85. The mean BMI was 27.07±6.4. The mean vitD3 level between insulin-resistant (n=11) and non-resistant (n=29) patients was insignificant (9.43±4.70 vs 14.26±15.06) p>0.05. Between insulin-resistant and non-resistant patients, differences in the mean glycose level (84.73±14.04 vs 71.90±11.97), mean HDL (46.55±12.21 vs 57.03±17.26) and mean systolic blood pressure (119.09±15.78 vs 112.41±6.89) were statistically significant ($p<0.05$). The mean vitD3 level was negatively correlated with mean BMI (r=-0.361, p=0.026), mean positive symptom score (r=-0.347, p=0.031). The mean insulin resistance index was positively correlated with BMI (r=0.337, p=0.038) and systolic blood pressure

(r=0.366, p=0.020), while it was negatively correlated with HDL (r=-0.441, p=0.004).

**CONCLUSION:** In this study, conspicuously we have found a vitamin deficiency/insufficiency prevalence of 92.5% in inpatients with schizophrenia in the acute phase. In a recently published meta-analysis, the prevalence of vitamin D deficiency in schizophrenic patients was calculated as 65.3% (95% CI 46.4%-84.2%)[6]. In a new study from Turkey (n=40), 95% of the patients with acute phase schizophrenia had vitamin D insufficiency and/or deficiency[7], while vitamin D deficiency is 2.99-fold higher in first episode psychosis than in healthy controls[8].

In the literature, vitamin D deficiency is accepted as a risk factor for MetS and type2 diabetes[4]. Vitamin D receptors are found to be expressed in pancreatic B cells and target tissues of insulin, such as hepatic, adipose, and muscle tissues[4]. Unexpectedly, we could not find an association between vit D3 level and insulin resistance, while lower vit D 3 leads to higher BMI and positive symptoms in patients with schizophrenia. Generally, there exists an inverse association between body mass index (BMI) and serum 25-hydroxyvitamin D[4], while the association between vitamin D and insulin resistance is yet controversial[9]. Interestingly, the more insulin resistance index the higher are BMI and systolic pressure and the lower the HDL level detected in patients with schizophrenia. Thus, although vit D3 and insulin resistance were not correlated in this study, both seem to be important in schizophrenia. We considered that low serum vitamin D level seems to be related with psychopathology in schizophrenia, and insulin resistance seems to be related with metabolic parameters in a distinctive way.

**Keywords:** vit D, schizophrenia, insulin resistance, metabolic syndrome

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**[Abstract:0347]** ***ADHD***

# Urinary 6-OH melatonin-sulfate levels in patients with attention deficit hyperactivity disorder

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**INTRODUCTION:** Attention deficit hyperactivity disorder (ADHD) is one of the most common neurodevelopmental disorders of childhood that affects about 5% of children and about 2.5% of the adult population.

Melatonin is synthesized from tryptophan and secreted primarily by the pineal gland. Melatonin has a major role in the entrainment of the circadian rhythm and sleep onset and increases sleep efficiency.

Sleep disorders may be encountered in children with ADHD. The circadian rhythm of pineal melatonin secretion, which is controlled by the suprachiasmatic nucleus (SCN), is reflective of the mechanisms that are involved in the control of the sleep / wake cycle. The onset of melatonin production occurs with the decrease in SCN neuron firing rate late in the day. The SCN has an active role in promoting sleep, and melatonin is the principal neurochemical agent.

There is a complex relationship between dopamine and melatonin which play a major part in the etiology of ADHD. It has been reported that melatonin increases the activity of tyrosine hydroxylase, the rate-limiting enzyme in the synthesis of catecholamines. Furthermore, it was demonstrated that the MT1 melatonin receptor Messenger Ribonucleic Acid (mRNA) expression was also present both in the cells of the nucleus caudatus, putamen and nucleus accumbens, where the D2 dopamine receptor, which is involved in the etiology of ADHD, is positive, and in the cells of the ventral tegmental area where the tyrosine hydroxylase activity is positive. For this reason, melatonin may be involved in the etiology of ADHD. This study was aimed at detecting levels of 6-hydroxymelatonin sulfate (6-OH MS), the main urinary metabolite of melatonin, in patients diagnosed with ADHD.

**METHOD:** The case group consisted of 27 children ranging from 6 to 16 years of age with no axis I additional diagnosis apart from ADHD. The control group included 28 children according to DSM-4 as demonstrated by the results of a clinical interview and K-SADS-PL-T administered by a trained interviewer. Exclusion criteria for both of the groups were set as the presence of mental retardation in the child, administration of any psychotropic drugs during the last 6 months, presence of any chronic physical disease and history of infection during the past week.

The socio-demographic data questionnaire form was completed by the researcher employing a face-to-face interviewing technique. The Conners' Parent Rating Scale Short Version was completed for the purpose of supporting the diagnosis. WISC-R was administered to cases clinically suspected of mental retardation, and the cases diagnosed with mental retardation (two cases) were excluded from the study.

**Urine Specimen Collection:** Families were handed out written instructions regarding the procedure of urine specimen collection, and the urine specimens were collected from all the children at home under parental guidance within a period of 24 hours. It was ensured that the urine specimens were collected in two separate containers, one of which was to be designated for the specimen from daytime phase from 08:00 to 21:00 and the other for the nighttime phase from 21:00 to 08:00. It was requested that the bladder should be emptied between 20:45 and 21:00 before the nighttime phase started.

**Biochemical Assessment:** Urinary concentrations of 6-OH melatonin sulfate was measured using an ELISA kit. The urinary 6-OH MS concentration (ng/ml) was multiplied by the volume of the urine in milliliters.

**RESULTS:** The average age of the case group was 9.37±2.69 (6-15) years, and that of the control group was 10.50±2.71 (7-16) years. The difference in the average age between the case group and the control group was not statistically significant (p=0.084).

The case group was divided between 14.8% girls (n=4) and 85.2% boys (n=23), while 25% of the control group were girls (n=7) and 75% boys (n=21). The difference in sex between the case group and the control group was not statistically significant (p=0.345).

An examination of the diagnosis-distribution in the case group found ADHD – Subtype Predominantly Inattentive at 22.2% (n=6), ADHD – Subtype Predominantly Hyperactive-Impulsive at 7.4% (n=2) and ADHD – Subtype Combined at 70.4% (n=19).

A comparison of the data obtained via the Conners' Parent Rating Scale – Short Version (CPRS-48) with respect to the case and control groups revealed differences among the subscales of impulsivity / hyperactivity, learning problems, oppositional defiant disorder and conduct problem, but no difference among the subscales of psychosomatic problems and anxiety.

There was no difference in 24-hour creatinine excretions between the groups, either (15.15±3.08 mg/kg and 15.07±3.58 mg/kg, respectively [p=0.690]).

The analyses performed employing MWU test yielded significantly higher nighttime levels of 6-OH MS in the case group as compared to the control group (p=0.045). The daytime 6-OH MS levels were found to be higher than in that of the control group (p=0.018). 24-hour (daytime + nighttime) 6-OH MS levels were also higher in the case group as compared to the control group (p=0.018).

**DISCUSSION:** The literature includes only few studies focusing on the relationship between ADHD and melatonin. The results of the study conducted by Molina-Carballo et al. on the effect of methylphenidate treatment in children with ADHD on serotonin and melatonin levels demonstrated, in a similar way to our study, that the nighttime urinary 6-OH melatonin sulfate levels were higher in the ADHD group than in the control group. Another study on the subject detected high nighttime urinary melatonin levels in four adults recently diagnosed with ADHD who had not received a drug treatment.

Ours is the first comprehensive study known to have researched the daytime, nighttime, and 24-hour 6-OH MS levels in ADHD.

The data obtained in our study may suggest a higher melatonin production in children with ADHD. To modulate pineal melatonin production, axons originating from SCN neurons project to the PVN of the hypothalamus where they release gamma-aminobutyric acid (GABA), and GABA has an inhibitory effect here. A study indicated that the administration of the bicuculline (BIC), an antagonist of GABA, caused the disinhibition of PVN neurons in the daytime, resulting in a stimulating effect on the melatonin synthesis from the pineal gland. In one study, the GABAergic component of ADHD was researched by using magnetic resonance spectroscopy. It was found that GABA levels in children with ADHD were significantly lower. One of the reasons for the high levels of 6-OH MS excretion in children with ADHD may be these low GABA levels in such children.

The SCN is responsible for regulating the circadian rhythm by means of a series of transcription and translation processes with positive and negative feedback effects. Clock genes such as Clock, Bmal1, Period (Per1-3) and Cryptochrome (Cry1-2) are involved in the regulation of this rhythm. The expression of Striatal Per1 requires a functional pineal gland and melatonin, its product. The rhythm of diurnal striatal Per1 mRNA and Per1 protein is observed in normal rats but not in pinealectomised rats. Another study conducted on rats, on the other hand, indicated that Per1 was involved in the regulation of rhythmic melatonin synthesis from the pineal gland and melatonin concentration increase in the shortage of Per1. Considering the data obtained from those studies which focused especially on Per1 among the clock genes together with the results of our own study, it may be presumed that a deficiency in the function of clock genes, and particularly of Per1 gene, might be a matter of relevance in children with ADHD.

It has been indicated that sleep problems are frequently encountered in children with ADHD and that chronic sleep onset insomnia is one of the basic characteristics of circadian rhythm problems. There is a close relationship between the circadian rhythm and sleep–wake cycle and the melatonin concentration. A study suggested, although hypothetically, that shorter melatonin signals might be a matter of significance in children with ADHD. There are also studies indicating that children with ADHD benefit from exogenous melatonin administration with respect to sleep disorders. When the data we obtained from our study and such information are considered cumulatively, this situation might mean that melatonin is catabolized in such children to a greater extent, although there is no data supporting this argument.

In conclusion, the higher level of 6-OH MS excretion in children with ADHD as compared to the control group suggests that melatonin synthesis or other possible conditions that affect the melatonin synthesis may be different in children with ADHD as compared to healthy children.

**Keywords:** attention deficit hyperactivity disorder, melatonin, etiology

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**[Abstract:0383]** ***Autism spectrum disorders***

# Sociodemographic characteristics of patients with adult autism spectrum disorder

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**INTRODUCTION:** The term "autism" was first mentioned by Bleuler as a sign of schizophrenia. However, Kanner used the term closer to its current conceptualization. He described "early infantile autism" characterized by an inborn "disorder of affective contact". While Kanner's descriptions of patients with Autism Spectrum Disorder (ASD) focused mainly on children, Asperger described some examples of adults with this condition.
ASD is a neurodevelopmental disorder characterized by persistent deficits in social communication and interaction and restricted, repetitive patterns of behavior, interests or activities. Brugha et al. reported ASD prevalence rates of about 1%[1].
People with ASD are more likely to be unmarried, poorly educated and economically deprived than the general population. In Turkey, there is limited data about adult ASD. In our study, we aimed to present sociodemographic characteristics of ASD patients.
**METHOD:** Medical charts of patients who presented to the psychiatry outpatient clinic at Istanbul Medical Faculty between January 2014 and January 2015 were reviewed. 44 individuals who fulfilled the criteria of ASD according to DSM-5 were detected. Parameters such as age, gender, education, working status, psychiatry comorbidities, psychotropic drug use, and IQ scores were noted. Upon rater evaluation, a rating score was derived by summing individual scores for independent living, friendships, and overall social outcomes.
**RESULTS:** 38 (86.4%) were male, 6 (13.6%) were female. Mean age was 20.8±2.3. Mean education time was 11.5±4 years. 56.8% of the patients had had special training, 38.6% of patients had had mainstream education. None of them was married. 79.5% of the patients had no specific occupation. 9.1% were part-time workers, 6.8% worked on a supported/sheltered basis, 4.5% were working full time. The comorbid psychiatric diagnosis rate was 91%. 11.3% had two or more comorbid psychiatric disorders. In decreasing order, the diagnoses were Mental Retardation (43.2%), Attention Deficit and Hyperactivity Disorder (20.4%), and Anxiety Disorder (9%). 91% of patients were using psychotropic agents, mostly antipsychotic drugs (65.9%). Based on the data of friendship relations, 27.3% of patients were rated as having a relationship with at least one other person in their age group, 25% of patients were rated as having no friends, 22.7% of patients were rated as having some acquaintances with whom they might talk or share activities, but these were generally within arranged social groups, 20.5% of patients were rated as having healthy relationships. 38.6% of patients still lived at home but with considerable independence, 6.8% of patients lived by themselves with only limited support. 22.7% of patients were rated as having a 'good' outcome, i.e., they were working with some support, could organize their own activities. 11.4% of patients had a 'very good' outcome, i.e., they were in paid employment, had some friends and a high level of independence.
**DISCUSSION:** ASD represents one of the most common neurodevelopmental disorders and can cause significant lifetime disabilities. The prevalence of ASD tends to remain stable, so those diagnosed with ASD during childhood are likely to suffer the disorder in adulthood. Nevertheless, the clinical characteristics may vary over time. Stereotyped movements and language problems, especially in subjects with a normal IQ, tend to decrease in severity and pervasiveness with age. On the other hand, obsessive-compulsive features (complex rituals, repetitiveness, and compulsions) often become the prominent aspect of the clinical picture. Impulsive behaviors, self-injuring and peculiarity of interests remain stable over time[2].
With respect to social abilities, the literature quite uniformly reports that both expressive and receptive languages tend to improve with age. In addition, difficulties with fundamental social skills may decrease as children grow older; similarly, poor eye contact and reduced responsiveness and conflicts with peers are mitigated in adults. The most typical social manifestations of the autistic spectrum disorder in adults include dull intonation, repetitiveness on limited topics with difficulties in shifting attention between different subjects, deficits in discriminating emotional nuances and in communicating with others, poor sympathetic abilities, and a high tendency towards systematization of relationships[2,3].
Although the outcome of ASD in adulthood was extremely poor in studies conducted pre-2000, the prospects for patients have improved in the last 2 decades. Fewer adults were continuing to live with their parents, and a much smaller number compared to previous studies was in any form of hospital. Nevertheless, the mean percentage of patients having a good-very good outcome remains below 20%. The rate of patients who were in some form of work or educational programs remained relatively low[4].
It has been evident that intellectual disability is one of the determining prognostic factors for ASD patients, with very few people with a childhood IQ below 75 living independently as adults. Early language development is another crucial factor. Thus most people who do well as adults have usually developed at least some useful speech by the age of 5 years. There also appears to be an association between the severity of early autistic symptomatology (severity of repetitive and stereotyped behaviors, level of impairment in the social domain, overall symptom severity) and later outcome. Mental health and medical problems also tend to have a negative impact on outcome. Although little is known about the effect of educational programs, appropriate educational programs may have a positive impact in later life[4,5].
Psychiatric comorbidity in adult ASD is highly frequent and may represent the main reason for high rates of psychotropic drug use.
Different classes of psychotropic drugs have been suggested for specific dimensions of ASD. The majority of data are focused on second-

generation antipsychotics in children and adolescents, with a supposed efficacy on some core dimensions of ASD as well as on the management of several comorbidities. Psychopharmacological treatment is essential for the management of some behavioral problems and comorbidities[2].
Risperidone and aripiprazole are the drugs that have been studied most and have been shown to be effective in reducing psychotic symptoms (irritability; repetitive, aggressive, and impulsive behavior) and in improving some aspects of sociability in controlled clinical trials. They can also be useful in the management of the manic phases of Bipolar Disorder (BD)[5].
Mood stabilizers are preferable as maintenance treatment in comorbid ASD-BD, although there is a substantial lack of studies in this area. Several observations suggest the efficacy and safety of anticonvulsants, particularly valproate and lithium. The use of antidepressants, both tricyclics and selective serotonin reuptake inhibitors should be considered in the presence of comorbid anxiety disorders[5].
The category of ASD includes heterogeneous entities, in terms of both specific clinical manifestations and psychiatric comorbidities. The progression of ASD from childhood to adulthood is influenced by the severity of the clinical picture, gender, onset of neurological disorders, such as epilepsy during adolescence, and by psychiatric comorbidity. Due the heterogeneity of clinical manifestations and the poor knowledge of specific childhood disorders, adult psychiatrists too often underdiagnose ASD, classifying these patients as affected by mental retardation, schizophrenia, or other psychotic disorders[2].
Long-term prospective investigations are needed in order to provide more extensive and appropriate supported living and employment schemes.
**Keywords:** autism, adult, sociodemographic

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**[Abstract:0405]** ***ADHD***

## Compliance with methylphenidate treatment and drug abuse of adults with attention deficit hyperactivity disorder (ADHD)

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**INTRODUCTION:** Attention deficit hyperactivity disorder (ADHD) is a neuropsychiatric disorder characterized by symptoms of inattention with or without evidence of impulsivity/hyperactivity. In 80% of the children with ADHD, symptoms persist through adolescence and adulthood[1].
Compliance with treatment is an important factor for the outcome and patients' health. When related literature is revised, it is seen that compliance with treatment in ADHD is studied in children[2]. It is also important to mention that, though stimulants are highly effective as first line pharmacotherapies for ADHD, they pose a risk for abuse[3].
Patients with ADHD have a high risk for substance abuse. It was found that adults with ADHD had significantly higher rates of drug as well as comorbid drug and alcohol use disorders than non-ADHD adults[4].
There are many studies conducted in order to determine comorbid diagnoses with ADHD. According to one study, adults with ADHD, compared with adults without ADHD, had significantly more current Axis I disorders[5].
The purpose of the present study is to determine the prescribed methylphenidate use routines of adult patients diagnosed with ADHD. How strictly these patients follow the prescribed doses and timings will be evaluated in order to see their compliance with methylphenidate treatment. The study also aims to understand the prevalence of comorbid conditions and drug abuse of these patients.
**METHOD/PROCEDURE:** 42 out-patients followed at the ADHD treatment program in the Istanbul Medical Faculty Hospital Psychiatry Department were enrolled in the study. Before confidential semi-structured face to face interviews, participants were informed and

consent provided. After completing a socio-demographic form, participants were asked to provide information about the details of their disorder, their medicines for ADHD and details of other existing diagnosed disorders if any. Details like type of medication, age of patient at the time of their first diagnose of ADHD, and drug use periods were investigated. Patients were asked whether they use the ADHD medicine differently from their prescription in terms of either the dosage or the timing. Participants also provided information about their lifetime use of various illicit and licit drugs including tobacco, cannabis, inhalants, synthetic cannabinoids, heroin, cocaine, amphetamines, hallucinogens, any type of medicine in order to experience intoxicating effects and any other drug not already mentioned.

Patients over 18 years of age who had been prescribed methylphenidate for ADHD for at least 3 months and volunteered to participate were included in this study.

**RESULTS:** A total of 42 patients diagnosed with ADHD participated in the study, 11 (26.2%) female and 31 (73.3%) male. The mean age of the participants was 22.45 years±5.1 (range 18-43). 39 (92.9%) of the participants were single and 3 (7.2%) were either married or engaged. 4 (9.5%) of the participants were secondary school graduates, 21 (50%) of them were high school graduates, 16 (38,1%) had graduated from either vocational school or undergraduate program, and 1 (2.4%) had a higher education degree. 52.2% (n=22) of the participants were students and 2 of these students had part-time jobs; 11 (26.2%) participants were employed and 9 (21.4%) were neither students nor employed.

Of the participants, 18 (42.9%) had been diagnosed with ADHD at the age of 12 or younger, 6 (14.3%) had been diagnosed between the ages 13-17 and 18 (42.9%) had been diagnosed at the age of 18 or over. Participants were also asked to report the main ADHD feature as 'only attention', 'only hyperactivity/impulsivity' and 'both attention and hyperactivity/impulsivity'.

26 (61.9%) of the participants did not have any additional diagnosis whereas 16 (38.1%) had at least one additional diagnosis. 3 of these 16 participants had 2 comorbid diagnoses (in all three cases, the third comorbid disorder was a depressive disorder). The distribution of the comorbidities: Depressive disorders (n=6), Obsessive Compulsive Disorder (n=3), Anxiety Disorders (n=2), Mild MR(n=2), Borderline PD (n=2), Tic Disorders (n=1), Conversion (n=1), Conduct Disorder (n=1) and Dyslexia (n=1).

36 (84%) of the participants had taken their medication on their own whereas 7 (16%) of them had taken them under somebody else's supervision. 15 (35.7%) of the participants reported using the medicine differently (in timing) than prescribed; the distribution being as follows: 4 (9.5%) were 'not using it on the weekends', 4 (9.5%) were 'using it periodically', 11 (11.9%) were ' using it only as needed' and 2 (4.8%) were 'frequently missing doses'. 16 (61.9%) reported changing the doses when taking the medicines they were prescribed: 4 (9.5%) were 'using more than the doctor's prescription', 1 (2.4%) was 'using less than the doctor's prescription' and 11 (26.2%) were using 'as much and frequently as they feel necessary'. 14 out of the 15 participants who tended to use their medicine differently (in timing) than prescribed were among those who took their medication on their own; whereas only 1 participant who used the medicine differently (in timing) than prescribed was taking it under someone else's supervision. From a different point of view, 14 (32.6%) of the 36 participants who had taken their medication on their own were prone to use medicine differently than their prescriptions, and this constitutes 33.3% of the total participants.

11 (26.1%) of the participants reported using illicit/licit drugs (to experience intoxication effects) at least once in their lifetime. 6 participants used only one type of illicit/licit drugs whereas the remaining 5 used more than one type of illicit/licit drugs. The distribution of the drugs: Cannabis (n=10), Synthetic Cannabinoids (n=2), Cocaine (n=1), Amphetamines (n=1), Hallucinogens (n=1), Licit drugs for intoxication purposes (n=3).

**DISCUSSION:** Compliance with treatment is an important factor for the outcome and patients' health. The present study intended to determine the compliance with methylphenidate treatment in adults with ADHD. The results suggest that the participants with ADHD tend not to use their medications properly, especially the ones who take their medications independently. 15 participants were not following their prescription schedule and 14 of these participants were among those who were taking their medicines independently. Similarly, 16 participants tended to change the dose of their medication based on their needs. It is thought that there is a high possibility of increase in compliance of medication treatment when the patient is supervised or given the prescribed dose of medicine by someone else.

When symptoms are taken into consideration, adults with ADHD report mostly 'attention' problems, followed by combined type; and least reported is 'hyperactivity/ impulsivity' with the ratios 47.6%, 42.9% and 9.5%, respectively. Similarly findings of another study show that patients in the predominantly hyperactive/impulsive group represent a small rate among the total number of participants[5]. There is a high possibility that the hyperactivity/impulsivity problems common in childhood ADHD tend to fade, while in adults, inattention problems arise or stand out over time.

Lifetime substance use was high in the sample group. Our findings show that ADHD patients are a non-negligible risk group for lifetime substance use with the ratio of 11 (26.1%).

A 38.1% comorbidity rate seems lower than the previous reports in the literature. Depression was the most common comorbid diagnosis, and this finding was compatible with the literature.

The main limitation of the present study was its reliance on self-report as the primary method of assessment. Although prescribed doses and medications were cross-checked from patient files, it was not feasible to cross-check the use of illicit drugs or drifts from the prescribed methylphenidate using routines that the participants reported. It is possible that participants underreported the frequency of drug use or compliance of treatment due to the socially undesirable nature of these behaviors.

The scope of the present study will be enlarged in a subsequent study as data collection continues with new incoming patients.

**Keywords:** attention deficit hyperactivity disorder, methylphenidate, substance abuse

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**[Abstract:0422]** ***Neuroimaging in psychiatry***

# Neural correlates of impulsive aggressive behavior in subjects with a history of alcohol dependence

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**INTRODUCTION:** Aggression is one of most enduring, complex, and problematic forms of human social interaction. The consequences of human aggression exact a substantial toll on public health and criminal justice systems, communities, and individuals. Epidemiological and experimental data show that chronic alcohol dependence is related to an increased risk for assault and aggressive behavior. By some estimates, as much as 50% of all violent crimes, and greater than 60% of intimate partner violence, involve alcohol. A review of the neurobiology of personality disorders concluded that impulsive aggression was characterized by abnormal functioning in amygdala, OFC, DLPFC, and anterior cingulate cortex (ACC)[4].

In the present study, we employed a well-validated laboratory task the Point Subtraction Aggression Paradigm (PSAP; 1) that was adapted for use during fMRI. The PSAP allows for control and manipulation of independent variables, including the frequency of provocation. The timing and frequency of experimental events can be precisely controlled, allowing for examination of neural activity when individuals are provoked and during bouts of aggressive behavior. Based on previous work in the neurobiology of aggression and brain imaging studies of alcohol-dependent subjects, we hypothesized that compared to control subjects alcohol-dependent subjects would demonstrate (a) more aggressive responding on the PSAP; (b) reduced BOLD activation in frontal cortex (notably, OFC) and the limbic system (reflecting diminished activation of emotional regulatory circuitry); and (c) greater ROI BOLD activation in amygdala following provocation and during aggressive responding.

**METHODS:**

**Subjects:** This study was approved by the local IRB (at UTHSC Houston) and in accordance with the Declaration of Helsinki. Participants were recruited through local classified newspaper advertisements. Exclusionary criteria included (a) current or past medical problems (e.g. seizures, diabetes, high blood pressure, renal or cardiovascular disease), (b) current use of any medications, (c) current illicit drug use or alcohol use (measured by daily urinalysis and breath alcohol testing), and (d) current of past history of an Axis I mood or psychotic disorder, as determined by the Structured Clinical Interview for the DSM-4 (SCID-I, version 2.0, First et al., 1996). All subjects with past alcohol dependence met DSM-4 criteria for alcohol dependence within the past 24 months, and were in early full remission, early partial remission, or sustained full remission.

At intake, subjects read and signed an informed consent document. Subjects were provided information about urine drug testing, breath alcohol testing, psychiatric evaluation, experimental procedures and compensation. After consent, subjects provided urine samples for drug screen analysis using a one-step drug screen test card (Innovacon, Inc.), which tested for cocaine, stimulants, opiates, benzodiazepines and marijuana. Temperature monitoring and creatinine level determinations were used to detect attempts to alter urine samples. Subjects also provided breath alcohol samples using an AlcoSensor III (Intoximeters, Inc.), which required subjects to expire air for 10 seconds to measure alcohol content. No differences were observed in subject demographics, including gender [Fisher's exact=0.41, ns]; age [t (24)=1.29, ns]; education level [t (24)=0.51, ns]; number of smokers [6 in each group]; level of tobacco use [Mann-Whitney U, z=0.78, ns]; Shipley scale cognitive aptitude (Zachary, 1986) [t (24)=0.75, ns]; or lifetime use of other drugs [Fisher's exact=0.24, ns]. Demographic information on the two groups is provided in Table 1.

Subjects came to the lab for 3 days. They provided breath and urine samples each day upon arrival. Subjects were removed from the study

if they provided two consecutive alcohol positive breath or drug-positive urine samples. Two subjects were excluded from the study for consecutive positive THC samples. All other subjects were free of illicit drugs and alcohol on all testing days. On the first test day, subjects were instructed on the PSAP and completed 3 practice PSAP sessions in a mock-scanner (Philips) to familiarize them with the protocol, habituate them with the scanner environment and stabilize aggressive responding.

**Behavioral Assessments:** Subjects performed a version of the Point Subtraction Aggression Paradigm (PSAP, 2), a well-validated laboratory measure of human aggression that was adapted for fMRI. The paradigm utilized a computer-simulated social interaction in which subjects were paired with a fictitious other person, as established by instructional deception. Before the first test session, subjects were shown a diagram of the computer monitor and response panel and were read instructions. There was no use of terms such as aggression, game, competition, or anything that might indicate the behavior of interest. During the task, subjects had two response options available, labeled A or B on the computer screen. The money-earning option (A) added $2.00 to the subject's earnings counter (shown near the top of the screen) after a fixed response ratio of 40 responses was completed. The aggressive option (B) ostensibly subtracted $2.00 from the "other" person, at no gain to the subject, after a fixed ratio of 10 responses. Throughout the task, subjects were periodically provoked via $2.00 subtractions from their earnings, and instructed that when the "other" person chose the B option s/he kept the $2.00 subtraction (providing an ostensible reason for subtractions). No provocations occurred when the counter was at $0. All provocations occurred at randomly scheduled intervals that occurred on average every 90 sec, and were scheduled only during bouts of pressing on the A (monetary) option; this allowed independent assessment of neural activation patterns (a) during provocation prior to the initiation of aggressive responding, and (b) during aggressive responding. Switching to option B (aggressive) was only permitted after the completion of a ratio. However, there were no restrictions on the initiation of consecutive A ratios or B ratios.

**fMRI Protocol:** All subjects underwent scanning on a Philips 3.0 T Intera system with SENSE head coil (Philips Medical Systems, Best, Netherlands). Spin-echo Echo Planar Imaging (EPI) fMRI with a pulse sequence sensitive to BOLD effect at 3.0 T was utilized to eliminate signal dropout in the medial orbitofrontal region, a key region of interest. The fMRI images were acquired in the transverse plane using single shot spin-echo EPI with SENSE acceleration factor of 2.0, repetition time (TR) of 2200 ms, echo time (TE) of 75 ms, flip angle of 90 degree, number of slices=22, in-plane resolution of 3.75 mm x 3.75 mm, slice thickness of 3.75 mm; gap between slices 1.25 mm, 290 whole brain dynamic volumes per run Transverse plane acquisition, and a run duration of 10 min 38 s. Each subject completed 3 runs in separated by approximately 5 minutes. A high-resolution T-1 weighted 3D-MPRAGE structural scan (0.94 mm x 0.94 mm x 0.94 mm) was acquired for co-registration with the fMRI scans. Statistical analysis of the fMRI data was conducted using SPM8. Statistical analyses utilized SPM8 Random Effects models, with two-tailed corrected cluster-level $p<0.05$.

**RESULTS AND DISCUSSION:** Here we utilized the PSAP with fMRI to better understand the neural correlates of reactive aggression in individuals with past alcohol dependence. Alcohol-dependent subjects produced more aggressive responses per provocation than control subjects, but also made significantly more monetary responses. Rates of monetary earnings and subtractions were similar even though alcohol-dependent subjects made more overall responses on both the monetary and aggressive options. This could reflect diminished inhibitory control over responding, greater problems organizing patterned motor movements, poor adherence to instructional control, or some combination thereof.

Analysis of BOLD activation during aggressive responding and following provocation revealed between-group differences cortically in postcentral gyrus, middle frontal gyrus, and precentral gyrus, and subcortically in the basal ganglia (primarily dorsal striatum). In all regions, subjects with past alcohol dependence showed less activation than controls. Broadly, these regions most well established functions include visual motor processing, and planning and coordinating complex movements. Chronic alcohol use may disrupt activation of the collective emotional/inhibitory circuitry and manifest as a general inhibitory control deficit .

When all 26 subjects were combined across groups and aggressive responding (B_response) was regressed on the contrast of post-provocation to non-provocation responding (PA), we observed one statistically significant positive regression slope located in a contiguous cluster comprising the fusiform gyrus, parahippocampal gyrus, and postcentral gyrus. These regions are most well established in subserving sensorimotor functions, including visual and tactile information processing and coordination of motor movements.

Multiple clusters were observed in the significant negative regression slopes. These multiple clusters involved orbitofrontal cortex, prefrontal cortex, and caudate and putamen. The negative relationships suggest that aggressive behavior on the PSAP was related to decreased activation in these regions. The present data suggest that the dorsal striatum may play a role in modulating response to aversive stimuli. More broadly, current theories propose that it is the interconnected network between the limbic, OFC, and DLPFC regions that primarily subserve the processing of emotional and goal driven behavior, and that damage or dysfunction in this network results in problems with the regulation of emotion and subsequent difficulties with response inhibition, decision making, and aggressive behavior[5].

**Keywords:** aggression, alcohol dependence, fMRI

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**[Abstract:0447]** ***Mood disorders***

# Implications of childhood trauma on deliberate self-harm in patients with major depression

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**INTRODUCTION:** Stress experienced in the first year of life is an important risk factor for the emergence and continuation of psychiatric disorders. Psychological effects of adverse experiences in childhood continue for a long time. The frequency and severity of traumatic experiences increases the diversity and prevalence of the psychopathology. Especially major depression, posttraumatic stress disorder, attention-deficit /hyperactivity disorder, borderline and antisocial personality disorder, alcohol/substance abuse, panic disorder, generalized anxiety disorder, bipolar disorder and schizophrenia are also seen more frequently in patients with a history of childhood maltreatment. As well as in the formation of many psychiatric disorders, traumatic experiences in the first year of life, have an important role in the emergence of major depression. Sexual abuse in childhood and deprivation of parents' attention are associated with adult depression. Early-life trauma has also been found to influence the clinical manifestations of depression. Lower improvement and recovery rates, longer periods of depression, more chronic course of illness, and earlier onset of depressive symptoms were also found in depressed patients with a history of childhood trauma. The relationship between deliberate self-harm and childhood maltreatment has also been demonstrated to be significant in many different studies. Deliberate self-harm was significantly greater in preschool children, adolescents, and adults who experienced traumas in early life than in the control group. Some studies which used severity and frequency assessment scales revealed a dose-response relationship between trauma and deliberate self-harm. The aim of our study is to evaluate childhood traumatic experiences which can be found in the etiology of major depression and the impact of these experiences on deliberate self-harm behavior and to develop different ideas for the treatment of the disease in the context of the literature on patients suffering from major depression.
**METHODS:** One hundred and six patients who presented with depressive symptoms to RTEU Training and Research Hospital psychiatry clinic between the dates of September 2012 and June 2013, aged between 18-60 years and with adequate education, diagnosed with major depression according to DSM-IV-TR diagnostic criteria, who had not received any psychiatric treatment for the last 6 months, were included into this study. Before starting the study, approval from Recep Tayyip Erdogan University School of Medicine Clinical Research Ethics Committee has been obtained. Illiterate patients or those younger than 18 years or older than 65, sufferers from significant diseases which are outside the scope of the study (cancer, diabetes, liver failure, renal failure, hypertension, endocrine disorders, etc.), persons with mental retardation, severe psychotic disorder and organic mental disorders, post-traumatic stress disorder, or a history of alcohol and drug addiction were excluded from the study. The sociodemografic and clinical data form, Hamilton Depression Scale (HAM-D), the short form of the Childhood Trauma Scale (CTQ-28), and deliberate self-harm inventory SCID-I were applied to the patients. All patients were given the required information and gave written consent.
**RESULTS:** Of the patients recruited into this study, 86 (81.1%) were female and 20 (18.9%) were male. The minimum age was 18, the maximum age 60. The average age of all patients was 33.37+11.1, while the average age of women was 32.19+11.00 and the average age of men 38.45+10.3. Regarding the educational status, the majority of the study group members were primary school graduates with 33%, followed by 22.6% and 21.7% of secondary and high school graduates. 65.1% of participants were married, while 21% were single. Regarding their working status, 42 (39.6%) of participants were housewives; followed by 20 (18.9%) and 18 (17%) being unemployed and self-employed or in dependent employment (civil servants, workers), respectively. Five participants were retired, while three participants were students. 55.7% of respondents had lived in the city.72 of participants had a prior history of psychiatric disorder. 68.9% of patients included in the study had traumatic experiences: 56.6% childhood emotional abuse, 37.7% childhood physical abuse, 34% childhood sexual abuse, 53.8% childhood emotional neglect and 44.3% childhood physical neglect were found. 49.1% of participants were observed to have used at least one deliberate self-harm behavior. Participants indicated that the preferred self-harm method they used was self-poisoning by drugs (overdosing). The most common self-harm method in women was self-poisoning by drugs, followed by self-cutting.

Men told that the most common self-harm method they used was hitting their head. When comparing deliberate self-harm and childhood maltreatment, 84.6% of the deliberate self-harm group reported childhood maltreatment, while 53.7% of the other group reported childhood maltreatment, and a statistically significant difference was found (p=0.001). 75 % of the deliberate self-harm group and 38.9% of the other group reported emotional abuse, and a statistically significant difference was found (p<0.001). 61.5% of the deliberate self-harm group and 14.8% of the other group reported physical abuse, and a statistically significant difference was obtained (p<0.001). When exploring under the angle of sexual abuse, 55.8% of the deliberate self-harm group and 13% of the other group reported sexual abuse, and a statistically significant difference was found (p<0.001). When assessing deliberate self-harm behavior and emotional neglect, 67.3% of the deliberate self-harm group and 40.7% of the other group reported emotional neglect, and the difference between these groups was statistically significant (p=0.011). While 57.7% of the deliberate self-harm group had suffered physical neglect, 31.5% of the other group had observed physical neglect, and a statistically significant difference was obtained (p=0.012).When evaluating deliberate self-harm behavior motivations, the desire to get rid of sadness and depression ranks first with 71.1%, followed by the wish to die with 69.2% and request to stop the feeling of helplessness with 65.4%, respectively. The least reported deliberate self-harm motivations were to scare others, with 3.8%, and to draw others' attention, with 7.8%, respectively. While at least 1 and at most 16 motivations were reported, the average number of motivations was 6.96 and the median score was 6.

**CONCLUSION:** High levels of childhood trauma in patients with major depression were identified in this study. In addition, deliberate self-harm behavior was seen to be significantly more common in the presence of childhood maltreatment with all of the subscales in patients with major depression. The presence of CTE (childhood traumatic experiences) in patients with major depression is important for the clinical course, management and treatment of the disorder. Therefore it is important emphasizing preventive mental health services; training the community and primary caregiver who is responsible for maintaining the child; creating better parent-child relationships; ensuring the protection of the child before exposure to trauma; making a detailed follow-up and evaluation of the child if he or she was exposed to trauma; continuing the follow-up both during childhood and adulthood in terms of mental health; evaluating the CTE groups as a separate group and to establish supportive interviews and new therapeutic approaches for these groups;

**Keywords:** childhood trauma, deliberate self-harm, major depression

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**[Abstract:0472]** ***Schizophrenia and other psychotic disorders***

## Comparing facial emotion recognition ability in smoker and non-smoker patients with schizophrenia

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**INTRODUCTION:** Schizophrenia patients have social cognition deficits as compared with normal individuals in the following key domains identified by the National Institute of Mental Health (NIMH) Consensus Committee: Emotion Perception and Processing, Social Perception and Knowledge, Attributional Bias, and Theory of Mind. Many recent studies demonstrated that patients with schizophrenia have impairments in a wide range of social cognitive abilities, including recognizing emotions from facial expressions, mentalizing, and social decision-making[1]. It is understood that these impairments are structural features of schizophrenia associated with specific symptoms and significantly affect cognitive patients' functioning.

Emotions are processes mostly reflected in the facial expressions. Perception and recognition of facial emotional expressions is one of the basic social-cognitive skills for people to guide social functioning and behavior. Interpersonal relationship, conflict and social agreement

are extensions of this basic function. In patients with schizophrenia, problems in the capture of social hints and the perception of emotions in people's faces are associated with impaired social functioning[2]. It is thought that important clinical schizophrenia-specific outcomes (social withdrawal, development of delusions, connection with cognitive processes) may be determined by identifying difficulties in the recognition skills of facial expressions and emotions in schizophrenic disorders.

It is well known that the frequency of cigarette smoking in schizophrenic patients is higher than in the normal population and the cessation of smoking is more difficult for these individuals. Also, in numerous studies, it has been demonstrated that nicotine administration or smoking provide beneficial effects with neurocognitive deficits, in particular attention and memory in patients with schizophrenia. However, there is no sufficient data assessing the effects of nicotine on social cognition in the literature yet.

The objective of the present study was to investigate whether there are differences in social cognitive functions of smoker and non-smoker patients with schizophrenia by evaluating their facial emotion recognition ability. Considering the previous studies revealing the efficacy of nicotine on cognitive functioning in general, we expected that non-smoker schizophrenia patients would perform worse in facial emotion recognition than the smoker group.

**METHODS:**

**Participants:** The study group consisted of 58 smokers (18 female, 40 male; mean age: 35.32±8.26; education level: 9.36±3.12 years) and 40 non-smokers (18 female, 22 male; mean age: 35.17±7.35; education level: 9.00±2.99 years) patients diagnosed with schizophrenia (SCZ). The total of 98 volunteers were in a follow-up program at Sakarya University Education and Research Hospital (35 outpatients and 23 inpatients with SCZ smokers; 28 outpatients and 12 inpatients with SCZ non-smokers).

**Assessment:** Both groups were evaluated by using the Positive and Negative Syndrome Scale (PANSS) which is a well-known semi-structured interview assessing a wide range of symptoms in schizophrenia. The test includes 'positive', 'negative' and 'general psychopathology' symptom sub-scales.

All participants were administered the Facial Emotion Recognition Test which included 56 photos of four males and four females with six facial emotions (happy, sad, fearful, angry, surprised, disgusted) and neutral facial expression from Ekman & Friesen's series "Pictures of Facial Affect". At first, the test had a trial section which was composed of the first seven photos that included each emotional facial expression (i.e., angry, sad, happy, neutral, fearful, disgusted and surprised). Then, 49 mixed photos were used for the data analyses in the study. In these 56 photos, numbers of expressions were equal for each emotions. In addition, reaction time to each facial pictures was also recorded.

In addition, the Fagerstrom Test for Nicotine Dependence (FTND) was used for scoring the smoker participants.

**Statistical Analyses:** Data were analyzed with the Statistical Package for Social Sciences for Windows (SPSS) version 18.00. Demographic information was analyzed through descriptive statistics. For the analyses of abnormally distributed data, the Mann Whitney U test was used and for normally distributed data, the Independent Sample T test was used for the comparisons. A p value <0.05 was accepted as statistically significant.

**RESULTS:** There were no statistically significant differences between groups on mean of ages (35.32±8.26 vs 35.17± 7.35 and p=0.925), distribution of gender, average education period (9.36±3.12 vs 9.00±2.99 years and p=0.568), and duration of illness (11.42±7.23 vs 12.15±6.91 years and p=0.545). SCZ smokers' mean duration of smoking was 17.55±8.19 years and mean FTND score was 4.84±2.49.

PANSS total score was 68.67±16.64 in the smoker group and 73.97±16.59 in the non-smoker group, in terms of PANSS total scores, a statistically significant difference was not found (p>0.05). Besides, there was no significant difference between groups on 'positive' and 'general psychopathology' symptom sub-scales, while 'negative' symptom sub-scale score was significantly higher in SCZ non-smokers than SCZ smokers.

We found that, according to the Facial Emotion Recognition Test, SCZ smokers performed significantly better than SCZ non-smokers in recognizing facial emotions of happy, sad, angry, surprised, disgusted (p<0.05 for each). But there was no significant difference between groups in recognizing the emotion of fearful. In addition, when evaluating the groups in terms of reaction time for each emotion while recognizing them, it was observed that SCZ smokers replied in significantly less time to each facial emotions except for fearful as compared to SCZ non-smokers (p<0.05).

**DISCUSSION:** In the current study, we aimed to investigate the effects of nicotine on facial emotion recognition ability in smoker and non-smoker SCZ patients. As a result, statistically significant group differences were found in favor of SCZ smokers for both the accuracy rate of answers to facial emotion recognition and reaction time for emotions. In other words, this study suggests that smoking may contribute to recognize the facial emotions, i.e., social perception and social cognition, in patients suffering from schizophrenia. The results received were in line with our expectations. Also, we found that 'negative' symptom sub-scale score was significantly higher in SCZ non-smokers than in SCZ smokers, consistent with the previous studies.

There is evidence for an explanation as to how nicotine affects cognitive functions in schizophrenia: decreased levels of alfa7-neuronal nicotinic acetylcholine receptor (a7-nAChR) in the hippocampus and the frontal cortex of schizophrenic patients – the accepted hypothesis is that a7-nAChR has a role in the pathophysiology of cognitive deficits in schizophrenia, and smoking alleviates cognitive deficits in these patients.

Besides, there is no direct evidence to explain the impacts of nicotine on social cognition in patients with schizophrenia. A few studies have suggested that the processing of facial expressions may be altered by cholinergic enhancement[3]. Functional magnetic resonance

imaging (fMRI) studies have shown that nicotine administration induces a dose-dependent increase in neuronal activity in a distributed system of brain regions, including the nucleus accumbens, amygdala, cingulate and prefrontal cortex. According to the imaging studies, amygdala, superior temporal gyrus and fusiform gyrus come to the fore among brain regions related to face and emotion recognition[4]. While the amygdala is related to both face and emotion recognitions, it has been found that the superior temporal gyrus is more sensitive in recognizing emotions and the fusiform gyrus is more sensitive in recognizing the faces. In addition, it is indicated that the amygdala has an indirect connection with the dorsolateral prefrontal cortex working memory-related brain region. In other studies, it is suggested that the impairments in face and emotion recognition are associated with amygdala volume loss, amygdala damage, and hippocampus volume loss. In light of this knowledge, it can be thought that nicotine contributes to positive effects on social cognition by inducing neuronal activity in the amygdala, hippocampus and dorsolateral prefrontal cortex.

In the literature, although the connection between social cognition and neurocognition has not yet been exactly clarified, the general impression is that they are related but separate constructs. In addition, previously demonstrated more clearly positive effects of nicotine on neurocognitive processes such as working memory, speed of processing and attention were shown to be moderate and relatively consistent relationships with the social-cognitive processes of emotion perception, social perception and theory of mind. In this context, it is emphasized that normal neuro-cognitive function is necessary but not sufficient for good social cognition performance[5].

The present study shows that nicotine may facilitate social cognitive processes in patients with schizophrenia. However, it is not clear why social cognition is better in SCZ smokers, whether it is due to a positive contribution of nicotine to overall cognitive functions or a separate healing mechanism of nicotine on social cognition. Thus, this topic can be an interesting focus of future research in schizophrenia, and more studies are needed to clarify the link between domains of social cognition and nicotine administration/use in schizophrenic patients.

**Keywords:** schizophrenia, smoking, social cognitions

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**[Abstract:0475]** ***ADHD***

## Utilization of the d-CPT test in differentiation of attention deficit-hyperactivity disorder and anxiety disorders in children

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**INTRODUCTION:** ADHD diagnosis is established by clinical interviews, collateral information, and rating scales, rendering the diagnostic process prone to informant and evaluator bias. Consequently, there has been much interest in developing an objective diagnostic tool for ADHD. The utilization of continuous performance tests (CPT) paradigms thus became an attractive research area.

These tests involve execution of a predetermined reaction to target and non-target stimuli. Failure to execute the response to target stimuli is called an "omission error" and reacting to non-target stimuli is called "commission error". Omission errors may be linked to problems with attention[1], and some subtypes of commission errors may be associated with "inadequate control", or impulsivity[2]. Studies report that children with ADHD demonstrated higher rates of omission errors than unaffected peers. Although the clinical utility of these tests has been controversial, a large meta-analysis revealed that children with ADHD made significantly more errors of omission and commission than normal children[3]. These errors are significantly corrected by psychostimulant medications[3]. Studies also highlight the effectiveness of incorporating distractors (auditory, visual and combined) in CPT to better distinguish ADHD from non-ADHD children.

It is postulated that the presence of anxiety may partially inhibit the impulsivity and response inhibition deficits seen in ADHD; however, it

may exacerbate working memory and other cognitive deficits. There is limited information about continuous test performance of subjects with non-ADHD psychiatric conditions. One study comparing adult ADHD patients, adult anxiety-disordered patients, and normal adults using CPT found that the ADHD group demonstrated higher response inhibition performance deficits compared to both control group and anxiety disorders[4]. To our knowledge, there are no studies that compare CPT measures of children with ADHD and Anxiety Disorders. The aim of this study was first to explore whether children with ADHD would differ from children with Anxiety Disorders in rates of omission errors, commission errors, and reaction times. Assuming that there would be a difference, we hypothesized that subjects with anxiety disorders would also not be affected by distractors as much as ADHD subjects are. Thirdly, we wanted to show if medical treatment of ADHD would close the gap between subject groups.

**METHODS:**

**Participants:** 50 subjects were enrolled in the study; 2 subjects refused to complete the test after agreeing and starting the test (1 subject with ADHD refused due to "boredom", and 1 subject with Anxiety Disorder refused due to a preexisting headache). Data from 48 subjects were collected (38 male,). The sample included 30 subjects with a primary diagnosis of ADHD (inattentive, hyperactive/impulsive or combined presentation) and 18 subjects with Anxiety Disorders (Generalized Anxiety Disorder, Social Anxiety Disorder, Separation Anxiety Disorder, Panic Disorder). Most common comorbid conditions were Disruptive Behavioral, Learning and Tic Disorders for the ADHD group and OCD for the anxiety group. Medicated patients with ADHD (56%) were on varying doses of methylphenidate (%76) or atomoxetine (%24). Medicated patients with Anxiety Disorders were mostly on fluoxetine or sertraline.

**Design:** The study was conducted between December 2014 and February 2015 at two different child psychiatry clinics in Istanbul. All patients who received a diagnosis of ADHD or Anxiety Disorders were asked to volunteer for participation in the study. Diagnoses were established according to DSM 5 criteria by a child and adolescent psychiatrist supported by rating scales. Written informed consent from the parents and verbal assent from the subjects were obtained.

**Test Paradigm:** Subjects were given MOXO d-CPT test[5] on a desktop computer with a 23-inch screen by a clinical psychologist. Standardized instructions were given to all subjects prior to starting the paradigm, and psychologists were blinded to patients' diagnostic information prior to testing. The test takes 15 minutes, and participants are asked to respond to target stimuli pressing the space bar on the keyboard, while the target and non-target stimuli are presented without distractors, with visual distractors, with auditory distractors, and with combined auditory and visual distractors. The MOXO test measures omission errors as attention index and commission errors as impulsivity index. The test also measures reaction times (timing index) and hyperactivity index, which measures responding to non-target stimuli more than once or executing undesired behavior (pressing a different key than the one asked).

**Statistical Analyses:** Differences between independent samples were analyzed by non-parametric Mann-Whitney U test.

**RESULTS:** The distribution of data did not differ significantly across gender. The results revealed significant differences between subjects with ADHD and Anxiety Disorders in omission errors, timing and hyperactivity indices but not for impulsivity index when visual distractors are added to the task. ($p<0.01$, $p=0.03$, $p<0.01$ and $p=0.065$, respectively).

When results from omission and commission ratings were combined, differences between ADHD and Anxiety groups were statistically significant for no distractor, visual, and combined distractor conditions ($p=0.01$, $p=0.02$, $p=0.04$, respectively), but not for auditory distractor condition ($p=0.09$).

When subjects with ADHD were compared among each other according to medication use, significant differences were found in domains of attention indices except for combined stimuli condition ($p=0.02$, $p<0.01$, $p=0.02$ and $p=0.08$ respectively). The rate of commission errors was not significantly different between groups.

Comparison of subjects who are not on medication for ADHD and subjects with anxiety disorders yielded powerfully significant results for attention, timing, impulsivity and hyperactivity indices ($p=0.01$, $p=0.04$, $p=0.05$, $p=0.01$). When results were compared across distractor conditions, groups also differed significantly (no distractor; $p<0.01$, visual distractor; $p<0.01$, auditory distractor; $p=0.01$, combined distractor $p=0.01$). The differences between reaction times at the beginning and the end of the study was also statistically significant between medicated and non-medicated ADHD subjects ($p=0.04$).

Interestingly, when subjects on medication for ADHD and subjects with anxiety disorders were compared, the results did not differ significantly except for the hyperactivity index total score ($p=0.03$).

**DISCUSSION:** This study investigated effects of environmental distractors on attention and impulsivity in children with ADHD and Anxiety Disorders. Our results show that children with ADHD commit more omission errors than anxious counterparts when presented with no distractors, visual distractors and visual and auditory combined distractors. There were no statistical differences between groups when presented with auditory stimuli. Our results are in line with previous research which showed that visual distractors are better differentiators than auditory ones. The differences were similar when reaction times were measured.

ADHD subjects engaged in more commission errors than anxiety disordered patients; however, this difference was not evident when presented with distracting stimuli. It was previously argued that commission errors are linked to ADHD symptoms in the impulsivity domain; however, other research showed that these are related to ADHD symptoms in general and cannot only be seen as an index of impulsivity. We suggest that presentation of visual and auditory stimuli may further trigger anxiety symptoms (especially self-doubt, perfectionistic views, hyper-vigilance) and may lead to more commission errors in subjects with Anxiety Disorders, thus closing the gap

between ADHD and anxiety-disordered children.

The strong inter-group difference in the hyperactivity index may suggest that ADHD individuals are more prone to rule-breaking than anxious counterparts. Hyperactivity index, by showing execution of hitting an alternative key on keyboard, or hitting the desired key multiple times may be seen as a measure of engaging in unwanted behavior. This is in line with our clinical observation that ADHD subjects were getting easily bored and did engage in behaviors to mock the test and the clinician due to boredom or fatigue. This index may be seen as an index of similar behavior in the classroom and home; engaging in seemingly unsolicited behavior, such as limit-testing, although not universally disruptive. Our results suggest that ADHD medications are helpful with attention (including reaction time) and impulsivity symptoms, but not with the hyperactivity index. It can be argued that the hyperactivity index of this test may be measuring these "limit-testing" behaviors rather than true hyperactivity, which is expected to show strong clinical response to ADHD treatment.

In summary, children with ADHD and Anxiety Disorders had significant differences in the d-CPT test, especially when presented with concurrent visual distractor stimuli, proving our hypothesis. ADHD medications have a clear effect in correcting these differences and closing the gap between groups. Errors of omission are more closely linked to "pure ADHD" symptoms than commission errors, which may tap into symptoms that may also be present in Anxiety Disorders. Hyperactivity index of d-CPT may be measuring a tendency to "go against the norm", or limit-testing behavior instead of true hyperactivity.

This study has several limitations such as small number of participants (especially when broken down into subgroups) and voluntary participation, which may affect generalizability of the results. The results should be confirmed with larger samples.

**Keywords:** ADHD, anxiety disorders, children, distractors

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**[Abstract:0483]** ***Anxiety, stress, and adjustment disorders***

## Vitamin D deficiency in depressive, anxiety and adjustment disorder

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**INTRODUCTION:** Depression and anxiety are associated with significant disability, mortality, and health care costs. Depressive disorder, anxiety disorder and adjustment disorder are mostly diagnosed in outpatient clinic. Although the development of depression and anxiety are a complex and multifactorial process, there is evidence that dysfunctions in various endocrine axes may be independent risk factors in the development of depression and anxiety. The importance of the vitamin D endocrine system in relation to bone health has been recognized, but recent findings suggests that vitamin D may have neurological functions. The function of vitamin D in the brain is not completely understood, but the vitamin D receptor is found in many areas of the brain, including the cingulate cortex and hippocampus, which have been implicated in the pathophysiology of depression[1].

Low levels of vitamin D have been associated with development of cardiovascular disease, hypertension, neurodegenerative disease, diabetes, metabolic syndrome, and cancer. Low levels of vitamin D either at birth or during postnatal periods have been indirectly implicated in a number of developmental brain disorders such as multiple sclerosis, autism, and schizophrenia[1]. Several studies have investigated the relationship between depression and vitamin D, but with conflicting results. Some of them have found an association between low levels of serum 25-(OH)D and depressive symptoms[2,3], whereas other studies have found no associations[4,5]. Low serum 25-hydroxyvitamin D (25(OH)D and elevated PTH levels have been linked with various psychiatric disorders including depression, eating disorder and schizophrenia. Lee et al. found that among community-dwelling middle aged and older European men depression severity was associated with lower 25(OH)D levels[3].

In this study, we have measured serum 25(OH)D levels in patients who had been diagnosed with anxiety, depressive and adjustment disorder to assess if low level of vitamin D was associated with quality of life, severity of depression, and anxiety symptoms.

**METHOD:** The study population consisted of 63 outpatients aged between 18 and 60 years with a diagnosis of major depressive disorder, adjustment disorder and anxiety disorder without PTSD (Posttraumatic stress disorder) and OCD (Obsessive–compulsive disorder) based on DSM5 criteria, who were followed at the outpatient unit of the Psychiatry Clinic of Şişli Hamidiye Etfal Research and Teaching Hospital between October and December 2014. Patients were evaluated with Structured Clinical Interview for DSM-4 (SCID-I), sociodemographic form, Beck Depression Inventory (BDI), Beck Anxiety Inventory (BAI) and 36-Item Short Form Health Survey (SF-36). Substance abuse, pregnancy, lactation, significant medical or neurological disorder, psychotic and bipolar disorders were excluded. Hemogram, folate, vitamin B12 and thyroid function tests and vitamin D levels were measured in order to discern general medical illness. Vitamin D deficiency is defined with 25(OH)D below 20 ng/ml, and vitamin D insufficiency is defined with a 25(OH)D of 21–29 ng/ml; levels of 30ng/ml or above are normal. The data was analyzed using SPSS version 20.0. All data were first analyzed for normality of distribution using the Kolmogorov–Smirnov test of normality. When comparing differences between groups, the Mann–Whitney nonparametric test was used for non-normally distributed continuous variables and unpaired t test was used for normally distributed variables. The one-way ANOVA was used to compare three or more unmatched groups. Correlation analysis was performed by Pearson or Spearman correlation test. One-sample t-test is used to test whether the average of a sample differs significantly from a population mean. Results were considered statistically significant at $p<0.05$.

**RESULTS:** In our population, 82.5% (n=52) of the patients were female, 17.5% (n=11) were male. The average age was found 31.5±10.2. 46% (n=29) of the patients were single, 41.3 % (n=26) were married, 7.9% (n=5) were divorced and 4.8% (n=3) were widowed. The mean duration of education was 9.5±3.9 years. 41.3% (n=26) of the patients were employed, 46% (n=29) were unemployed and 12.7% were students. Only 19% (n=12) of the patients had a physical illness. 81% (n=51) of the patients did not use medication. 46% (n=29) were current smokers, 22.2% (n=14) were diagnosed with adjustment disorder, 60.3% (n=38) of the patients were diagnosed with major depressive disorder and 17.5% (n=11) with anxiety disorder. Of the participants, 15.9% (n=10) had a mild depression episode, 31.7% (n=20 a moderate depression and 52.4% (n=33) had a severe depression according to BDI. The blood tests were normal except vitamin D levels. The means of BDI, BAI scores and vitamin D levels were, respectively, 24.2±8.2, 26.6±14.1, and 13.2±7.1. 98.5% (n=62) of the patients had low vitamin D levels defined as less than 30ng/mL. The quality of life was determined significantly lower in eight sections of SF-36 (vitality, physical functioning, bodily pain, general health perceptions, emotional role functioning, physical role functioning, social role functioning, mental health) compared to Turkish reference data. Physical, social, emotional, and physical role functioning were found significantly higher in men than in women (p=0.004, p=0.016, p=0.032, p=0.092, respectively). No association was found between vitamin D levels and severity of depression and anxiety scale and all domains of SF-36 scale. There were no significant differences in vitamin D levels among the three diagnoses.

**DISCUSSION:** In the present study, we have found that 98.5% of the patients had low vitamin D levels; 81% of the patients had vitamin D levels below the sufficient range. This finding showed that prevalence of vitamin D deficiency is higher in our population than in recent study[3]. Vitamin D levels also vary seasonally, with low values during the winter months because of the reduced sun light. In our population, vitamin D levels may be affected because the present study was conducted during October and December. We did not find an association between vitamin D levels and severity of depression and anxiety scale. Recently, several studies have investigated the possible link between depression and vitamin D levels. Inconsistent with our findings, Hoogendijk et al. reported that among community-dwelling older people depression status and severity was associated with lower 25(OH)D levels[2]. Similar to our findings, Pan et al. reported no association between depressive symptoms and 25(OH)D levels in middle-aged and elderly Chinese[4].These apparently conflicting results may be due to the fact that these studies were either small in sample size or conducted in specific populations such as fibromyalgia, Alzheimer's disease, secondary hyperparathyroidism.

It is well known that major depression and depressive symptoms have an impairing effect on health-related quality of life. Depression has a significant effect on perceived physical functioning and bodily pain, and even on general health perceptions. Similarly, we found that all domains of Sf-36 were lower in our population than Turkish reference data.

In the present study, there were no significant differences in vitamin D levels between major depressive disorder, adjustment disorder, and anxiety disorder. Scheneider et al. found that although 25(OH)D levels were significantly lower in people with schizophrenia, alcohol addiction, or major depression than in controls, there were no differences in 25(OH)D levels between the three diagnoses[5].

In conclusion, this study has determined low levels of vitamin D in patients, although there were no associations between vitamin D levels and severity of depressive symptoms. Additionally, healthy controls are needed to compare with patients for vitamin D levels. Further studies are required to investigate whether vitamin D supplementation has an effect on treatment and prevention of depression.

**Keywords:** major depressive disorder, vitamin D, anxiety

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**[Abstract:0485]** ***Anxiety, stress, and adjustment disorders***

# Anxiety levels and parental bonding in recurrent aphthous stomatitis patients

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**INTRODUCTION:** Recent epidemiological and longitudinal studies indicate that attachment relationships may be a significant predictor of physical health in adulthood[1]. Empirical studies have found that insecure attachment orientations are associated with higher physical and psychological symptom reporting both in non-clinical and clinical samples[2]. Recurrent aphthous stomatitis (RAS) is one of the most common oral mucosal diseases. It is diagnosed clinically with painful, recurrent, yellowish white or grey, single or multiple, round or oval ulcers with erythematous margins, mainly confined to non–keratinized oral mucosa. Despite its worldwide occurrence and the extensive amount of research that has been devoted to the subject, the etiology of the disease is not well understood. Psychological-emotional factors are considered as one of the major predisposing factors. We hypothesized that RAS patients' physical status would be negatively associated with scores on adult attachment. As far as we know, this is the first study to compare the parental bonding of the RAS patients with healthy controls, also taking into consideration their state of anxiety and depression.
**METHODS:** The study subjects were recruited from the Ear, Nose and Throat (ENT) Department of Kahramanmaraş City State Hospital. All of the study subjects signed an informed consent form according to the Helsinki II Declaration, obtained from the Ethical Committee of the University of Kahramanmaraş, Turkey, prior to the launch of the study. All the patients and the individuals of the control group were aged 18 or above, ensuring that they could understand and score the questionnaires correctly. Included in this study were 34 patients with RAS who were not undergoing any psychiatric and medical treatment, as well as 34 age- and gender-matched healthy individuals as the control group. Both the experimental and the control groups were resident in the same geographic area and had the same socioeconomic status. Patients were evaluated with sociodemographic form, Beck Depression Inventory, State-Trait Anxiety Inventory-State form (STAI-S), State-Trait Anxiety Inventory-Trait form (STAI-T), Short Form of Inventory of Parent and Peer Attachment (IPPA-Armsden ve Greenberg 1987) which was developed by Raja, McGee & Stanton (1992). The IPPA short form is composed of "trust", "communication" and "alienation" factors, and each one of them contain 4 sub-items which were completed for mother and father separately. Anxiety levels were measured using Spielberger's STAI (1983), which evaluates both trait anxiety as a general aspect of personality (STAI-T) and state anxiety as a response to a specific situation (STAI-S). The sensitivity of the STAI-S and STAI-T scale to general stress has been shown consistently in research of emotional reactions. STAI is unique in its measurement of anxiety independently of depression and includes 40 questions for the assessment of both trait anxiety (20 questions) and state anxiety (20 questions). Each item is scored on a four-point scale, with response categories varying according to the nature of the question. For both levels, the range of values falls between 20 and 80, with a high score indicating a higher level of anxiety. Beck Depression Inventory is in common use as a self-report scale to assess the severity of depression. The BDI was developed to determine the type and the degree of depression based on symptoms and takes the form of a questionnaire containing 21 items rating emotional, cognitive, motivational and physiological symptoms, among others. The data were analyzed using SPSS version 20.0. All data were first analyzed for normality of distribution using the Kolmogorov–Smirnov test of normality. When comparing differences between groups, unpaired t test was used for normally distributed variables. Correlation analysis was performed by Pearson or Spearman correlation test. Results were considered statistically significant at $p<0.05$.
**RESULTS:** The mean age of the patient group was 35.68±13.5. 53% (n=18) were women, 47% (n=16) were men. STAI-S scores were significantly higher in the RAS patients when compared to the healthy controls (p=0.023). In contrast, the scores of STAI-T of the patients did not significantly differ from the control group. Patients with a Beck-D score of higher than 16 were regarded as depressive. Accordingly, 35.2% (n=12) of the patient group were depressive and 64.7% (n=22) were not. There was no significant difference between the patients

and the control groups according to depressive state. On the other hand, depressive patients had significantly higher scores in STAI-S (p=0.046) and lower scores in the factors of alienation from father (p=0.011) and trust in father (p=0.002) in IPPA when compared to the non-depressive patients with RAS. There was no relationship between the sub-items and total scores of IPPA and STAI-S or STAI-T scores.
**DISCUSSION:** The definitive etiology and pathogenesis of RAU is still unclear, although several factors are generally considered as essential in the development of RAU, such as nutrition, drugs, food hypersensitivity, hormones, infections, trauma, tobacco, and psychological stress[3]. A correlation between psychological status and RAU has commonly been reported. For instance, Albanidou-Farmaki et al. came up with findings similar to our research, claiming that anxiety as both a trait and state could play a role in patients with RAU, reporting significant differences between patients with RAU and controls. Soto-Araya et al. reported that anxiety and stress were significantly connected with RAU, unlike depression. Cohen also found a high incidence of RAU in patients under stressful situations.
According to our study, STAI-S scores were significantly higher in the RAS patients when compared to the healthy controls, similar to the mentioned literature. But there was no significant difference between the patients and the control groups according to the depressive state.
In this study, we could not find any difference between the patients and the control group according to their parental bonding. Our findings reveal that the patients with RAS showed higher levels of state anxiety than the healthy controls, confirming the findings of the previous studies[4,5]. State anxiety, alienation from father and trust in father sub-items were significantly worse in RAS patients with comorbid depression than the patients without depression. Future research is needed to clarify whether depression comorbidity is the result or cause of these factors.
**Keywords:** anxiety, psychological bonding, recurrent aphthous stomatitis

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**[Abstract:0494]** ***Mood disorders***

## The effect of personality traits on functionality in patients with bipolar disorder

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**INTRODUCTION:** Bipolar disorder, in its classic description, is a serious psychiatric disease characterized by depressive, manic or hypomanic stages that involves a high risk of mortality and morbidity in almost every aspect of functionality. In the past, the prevalence of the disease was assumed to be around 1% of the population, but nowadays it is estimated at 5% when we consider it as a spectrum disorder. It is a very important health issue leading to serious social and economic consequences. In every patient, the form and timing of the onset, progress, and response to the treatment differ, and these differences have been assumed to be effected by multi-dimensional, not fully understood processes, causing uncertainty, which leads us to the conclusion that it might me more appropriate to accept the disease as a heterogeneous spectrum disorder rather than a homogenous disease as in the classical description. It is thought that patients are totally normal between episodes or with minimal symptom levels, but this view is changing dramatically towards an opinion that it is actually a more continuous disease than it seemed before. In the past, it was thought that functionality loss (which was related to disorders like schizophrenia and depression back then) have not been seen in euthymic stages, but this idea has been changing rapidly for the last 30 years with studies about the disorder. Today, it is consistently reported that functionality impairment is a continuous problem that can be seen even in the euthymic stages. The degree of functionality impair is hard to determine in bipolar disorder due to its nature. Other than its unpredictable natural course, aspects like comorbid substance abuse, personality traits, low premorbid functionality levels, psychotic symptoms, drug side effects, and the number, severity, and onset of previous episodes are also parts of the reasons of this difficulties.

**METHODS:** In this study, we included 80 bipolar disorder-diagnosed patients who applied to Rize Education and Research Hospital, Psychiatry Clinic between the dates of 01.02.2013 and 01.01.2014 and had the capability of accomplishing the interviews and questionnaires, matching study inclusion criteria and having therapeutic levels of mood stabilizer drug blood levels. Before the study, an approval from Recep Tayyip Erdogan University School of Medicine Clinical Research Ethics Committee had been received. All patients had been informed and signed a written approval form. Patients having an active episode, psychosis, dementia, mental retardations, Parkinson disease, degenerative diseases or neurologic diseases like multiple sclerosis, Systemic Lupus Erythematosus, chronic renal diseases or any other chronic physical diseases were excluded. Remission phase is defined as not having active episodes for at least 3 months. We applied inventories such as Young Mania Rating Scale, Hamilton Depression Rating Scale, Eysenck Personality Questionnaire, Bipolar Disorder Functionality scale (BDFS), SCID I and SCID II.

**RESULTS:** Out of 80 patients included in the study, 57 (71.3%) were women and 23 (28.7%) men. Their age was in the range of 18-74 and the average age was 40.51+14.2. The average age for women was 40.91+13.75, for men 39.52+15.74. 38 of them were in the age range 18-36, 30 between 37 and 56 and 12 of them were 56 and above. 25% of the patients were university graduates. Most of the patients were housewives (52.5%) and 93.8% of them had health insurance. 50% of them were married and 68.75% of them were living with their family. When we analyzed the sample regarding socio-economic levels, we found that 16 of them belonged to the lower class, 38 were lower midle class, 26 were upper middle class. There was no patient who defined himself as a member of the upper class. 51 (63.8%) of them lived in cities, 23 (28.8%) in towns and 6 (7.55%) in villages. After psychiatric evaluations by psychometric questionnaires, 67 (83.75%) of the patients were diagnosed as bipolar disorder type I and 13 (16.25%) diagnosed as bipolar type 2. The average illness time was 13.8+9.1 years; in women 14.63±9.4, in men 11.87±8.2. Onset age was 26.28±4.1 for women and 27.65±3.9 for men. Average manic episode number was 3.7+5.8, depressive episodes were 4.5+7.7, mixed episodes were 1.2+2.1 and hypomanic were 1.1+4.1. There was no significant statistical difference between those. When we evaluated the long-term course of the disease, we found that there was complete or almost complete functionality in 38 (47.5%) patients, significant functionality loss in 36 (45%) and very poor functionality in 6 (7.5%). By gender, 31.3% of women have complete or almost complete functionality, 32.5% of them have impaired functionality and 7.5% have bad functionality. For men, those numbers were 16.3% for complete functionality and, 12.5% for impaired functionality. When we analyze the course between the episodes, 34 (42.5%) of them were symptom-free, 27 (33.8%) of them had light symptoms, 14 (17.5%) had moderate symptoms and 3 (3.8%) of them had severe symptoms chronically. 31 (38.8%) of them showed seasonal changes. 11 (13.8%) had a rapid cycling history and 40 (50%) of them had a psychotic symptoms history. As the result of the Eysenck Personality Questionnaire - revised short version, average points of sub-scales have been found as 3.14+.3 for the neuroticism subscale, 1.84+1.6 for the extraversion subscale, and 1.59+1.2 for the psychoticism subscale. The average point BDFS for men was 101.65±15.6, average point BDFS for women was 93.35±18.2 (p= 0.6). For the Bipolar 1 disorder-diagnosed group, the average point was 97.91±17.7, for Bipolar 2 it was 84.54±14.7 (p= 0.01). In our study, the lowest scores for BDFS subscales were "taking initiative", "fulfilling potential" and "introversion". The highest average subscale points are for "joining social activities", "participating in house works", "daily activities" and "hobbies". We found a significant but weak negative correlation between psychoticism and functionality. There was no significant relationship between the other Eysenck Personality Questionnaire subscales with functionality.

**CONCLUSION:** In our study, when we evaluate the long-term course of the disorder, it is found that 36 (45%) patients have partly impaired functionality and 6 (7.5%) have poor functionality. In the study, BDFC subscale points are lowest in the taking initiative, fulfilling potential and introversion sections. The highest scores were in the social activities, daily activities and hobbies sections. The only subscale that showed a significant relationship with functionality was psychoticism. In our sample, it seems that the higher the psychoticism subscale points get, the lower functionality scores become. In bipolar disorder, it is important to determine the functionality of patients. In this context, more research about the determining role of personality traits is required.

**Keywords:** Personality traits, bipolar disorder, functionality

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**[Abstract:0501]** ***Neuroimaging in psychiatry***

# Effects of smoking on gray matter volume reductions in major depressive disorder

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**INTRODUCTION:** Major depressive disorder (MDD) is a potentially debilitating psychiatric disorder characterized by feelings of guilt, anhedonia, and sadness, and may involve dysfunction in cognition, sleep, appetite, and energy. In particular, magnetic resonance imaging (MRI) has been widely applied to identify the key brain regions implicated in the pathophysiology of MDD. Several meta-analyses of region-of-interest and voxel-based morphometry structural MRI studies in MDD have been reported, providing evidence of volume reductions in the hippocampus, amygdala, orbitofrontal cortex (OFC), anterior cingulate cortex (ACC) as well as caudate and putamen[1]. However, there have been a number of non-replications and contrasting results across studies. A number of explanations for the great variability in findings have been proposed including age of the sample examined, medication status, illness severity, sex, and age of MDD onset.

One important confounding variable may be smoking behavior, since smoking has been associated with a range of mental disorders including schizophrenia, anxiety disorders and depression. Studies in healthy controls have found associations between cigarette smoking and a variety of adverse central nervous system effects, such as global brain atrophy, and structural abnormalities in prefrontal regions as well as reduced gray matter (GM) volumes in the anterior cingulate, occipital and temporal cortices including the parahippocampal structures and hippocampal substructures[2]. Thus, smoking status might impact gray matter volumes in studies with psychiatric populations. In line with this, a recent study found that a proportion of the volume reduction seen in the hippocampus and dorsolateral prefrontal cortex in schizophrenia is associated with smoking rather than with the diagnosis of schizophrenia[2]. To the best of our knowledge, there is no study that has specifically evaluated the underlying brain structural changes that may mediate the impact of smoking status in MDD.

The purpose of this study is to evaluate the effect of smoking status on gray matter volumes in MDD patients. As most previous studies found smaller gray-matter volumes in smokers than nonsmokers, we hypothesized that MDD participants who smoke cigarettes would exhibit lower gray-matter volume in ACC, OFC and subcortical structures compared with non-smoker MDD patients.

**METHODS:**

**Participants:** Forty MDD participants (20 smokers and 20 non-smokers) were recruited from outpatients at the Department of Psychiatry, Bozyaka Education and Research Hospital. All MDD participants were diagnosed by two trained psychiatrists individually using the Structured Clinical Interview for DSM-4 and met the following inclusion criteria: fulfilling DSM-4 criteria for major depressive disorder; aged 18 to 65; no comorbid other Axis I psychiatric disorders; currently experiencing an episode of depression with a score of at least 20 on the 17-item Hamilton Depression Rating Scale (HDRS-17) and medication-free for at least 2 months.

Exclusion criteria for all participants were: less than 18 years of age; any MRI contraindications; pregnancy; history of head injury or neurological disorder and any concomitant medical disorder. All participants were right-handed, underwent baseline clinical assessment and MRI scan within 48 hours of initial contact. Nicotine dependence levels were assessed with the Fagerström Test for Nicotine Dependence (FTND). All participants gave written informed consent to participate in the study. The study was approved by local research and ethics committees.

**Image Data Acquisition:** All MRI scans were performed on a 1.5T Achieva MR imager (Philips Medical Systems, Eindhoven, Netherlands) with a standard quadrature head coil. All subjects were scanned with a 3D T1-weighted turbo gradient echo sequence with SENSE using the following parameters: coronal orientation, matrix 256 x 256, 1 x 1 $mm^2$ in-plane resolution, slice thickness 1 mm, TE/TR=5.6/12ms, flip angle $\alpha$=19°.

**Statistical Analysis:** Demographic and clinical characteristics were analyzed using an independent-samples t-test with significance set at $p<0.05$. If data did not meet the assumptions required to perform parametric analysis, the non-parametric Mann–Whitney U-test was performed.

For the MRI data, the structural data was analyzed with FSL-VBM[3] (http://fsl.fmrib.ox.ac.uk/fsl/fslwiki/FSLVBM), an optimized VBM protocol carried out with FSL tools. Briefly, structural images were skull-stripped and then tissue-segmented into gray matter, white matter, and CSF. The resulting gray matter partial volume images were aligned to MNI152 standard space using an affine followed by a nonlinear registration with the Image Registration Toolkit. The resulting images were averaged to create a study-specific template, to which the native gray matter images were then non-linearly re-registered. The registered partial volume-segmented images were modulated (to correct for local expansion or contraction) by the Jacobian of the warp field and smoothed with an isotropic Gaussian kernel with

FWHM=7mm. The Harvard–Oxford Cortical and Subcortical Structural Atlases implemented in FSL were used to create masks for our regions of interest (ROIs): the left and right hippocampus, left and right amygdala, left and right caudate, left and right putamen, ACC and OFC. Probability range was set to 50 % for all 10 structures. Finally, to compare groups, a voxel-wise general linear model was applied using permutation-based (5000 permutations) non-parametric testing, correcting for multiple comparisons across space. First, volumes were compared in our ROIs, using the created masks. Second, an exploratory whole-brain analysis was done, using the gray matter image from the study-specific template to investigate whether any not predicted differences existed between groups.

**RESULTS:**

**Demographic and Clinical Characteristics:** We did not find any significant differences in age, years of education, number of depressive episodes, age at first episode, duration of current depressive episode, HDRS-17 scores and body mass index scores between the groups.

**VBM Results:** The VBM ROI analyses showed that left hippocampus (p= 0.009), right caudate (p= 0.015), left amygdala (p= 0.020) and right amygdala (p= 0.024) volumes were smaller in smokers with MDD compared to non-smokers with MDD. We found no group differences for the volumes in the ROIs for the right hippocampus, left caudate, left and right putamen, ACC and orbitofrontal cortex.

The exploratory whole-brain analysis did not reveal any gray matter volume differences between smokers with MDD and non-smokers with MDD.

**DISCUSSION:** To our knowledge, this is the first study to specifically examine the impact of smoking status on gray matter volumes in patients with MDD. We hypothesized that differences in smoking behavior in MDD might explain the variability of GM volume reductions reported in the literature. We found that compared to non-smoker MDD patients, smoker MDD patients showed significantly lower volumes in the left hippocampus, right and left amygdala and the right caudate. It is important to consider that the two patient groups did not differ in their disease severity.

The results of our study are in line with previous investigations in healthy controls suggesting that smoking may impact GM volumes of hippocampus, amygdala and caudate[4]; however, other studies have found more widespread differences in the cortex between smokers and non-smokers[5]. Discrepancies may be attributable to the small sample sizes or to the differential patterns of smoking behavior assessed across studies. One possible interpretation of our results is that volume differences in the hippocampus, amygdala and caudate in smoker MDD patients vs. non-smoker MDD patients may be more related to adverse effects of cigarette smoke or to an interaction between smoking and a primary pathological process that affects neurons of the hippocampus and other brain regions. Also, the possibility that MDD patients who smoke carry genetic variants that increase the susceptibility for MDD and addictive behavior cannot be excluded. Due to the cross-sectional design of our study, we were not able to measure causal relationships. Thus, it is conceivable that MDD patients with more pronounced structural brain changes are more prone to smoking.

Our findings need to be viewed in light of some limitations. Firstly, the study sample is small and the findings need to be replicated in other populations and in a larger sample. Secondly, this is a cross-sectional study and the longitudinal follow-up of these subjects would proffer further insights into the complex interaction between smoking status, illness factors and changes in brain gray matter volumes. A third limitation is the lack of a control group, and at this time we are reporting preliminary results based on only 40 patients, 20 in each group.

In conclusion, our preliminary data suggest that volumetric reductions previously reported in MDD may be partially attributable to smoking, especially in subcortical structures. Therefore, we recommend an assessment of smoking status in future MRI studies in samples including psychiatric patients.

**Keywords:** depression, gray matter volume, smoking

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**[Abstract:0525]** ***Genetic psychiatry***

# Hypomethylation of BDNF gene promoter in bipolar disorder patients

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**INTRODUCTION:** Bipolar disorder-1 (BD-1) is a mood disorder characterized with recurrent manic or mixed episodes, and the lifetime (and 12-month) prevalence estimate is 1%. The biological basis of the disease is still not very clear. It is known that genetic and environmental factors are involved in the pathogenesis of the disease. Family, twin and adoption studies provide strong evidence for the importance of genetic etiology of bipolar disorder. There could not be determined a major disease-associated locus because of the occurrence of bipolar disorder in interaction with multiple genes and environmental factors. All these data suggest that the genetics of bipolar disorder is very complex. Epigenetics has an important role in gene and environment interactions. This means environmental factors such as nutrition, maternal care and behavior, hormones and drugs, the early life experiences, and environmental agents in early development stages influence the gene expressions through epigenetic mechanisms[1]. Brain Derived Neurotrophic Factor (BDNF) is a neurotrophin that regulates synaptic transmission and plasticity, and it has a role in proliferation, differentiation, survival and death of neuronal and non-neuronal cells[2]. BDNF may also play a role in the pathophysiology of bipolar disorder. We hypothesized that there is a defect in DNA methylation mechanisms, and the BDNF gene is affected by these processes in bipolar disorder patients. Therefore, in order to test our hypothesis we aimed to investigate the DNA methylation status of two regions in the BDNF gene in patients with bipolar disorder.

**MATERIALS AND METHODS:** The study included 100 BD patients (Bipolar depression: 18, Mania: 33, Euthymic: 49; aged 30.8±9.3 years, 56 male and 44 female) with bipolar disorder and 59 healthy controls (aged 30.0±6.3 years, 29 male and 30 female). DNA was extracted from blood samples by using the salt-chloroform method. Determination of the methylation pattern of CpG islands was based on the principle that bisulfite treatment of DNA would result in conversion of unmethylated cytocine residues into uracil, whereas methylated cytocine residues would remain unmodified. Methylation-specific PCR was performed with primers specific for either methylated or unmethylated DNA.

**RESULTS:** In this study we found that there was a hypomethylation in BDNF gene promoter 1 in bipolar disorder patients compared to healthy controls ($p<0.001$). The comparisons of the methylated or un-methylated status for each area according to the study groups are presented in Table 1. When patients were analyzed according to their attack type, there was a hypomethylation in BDNF gene promoter 1 in patients in depressive or manic episodes compared to healthy controls and euthymic episode ($p=0.011$). However, BDNF gene promoter 2 was hypermethylated in patients in euthymic episode compared to healthy controls ($p=0.010$).

**CONCLUSION:** DNA methylation plays a role in neuronal cell survival and maturation; balance of the methylation level is important for neuronal survival, and hypomethylation causes abnormalities in neuronal function. Although it is not clear, it has been mentioned that DNA hypomethylation may cause cell death by apoptosis. A normal level of DNA methylation is required for controlling genomic expressions. An animal study found that DNA hypomethylation is associated with genomic instability which may lead to cancer development. Cancer studies show that DNA hypomethylation caused chromosomal instability, abnormal gene expression, and loss of imprinting. Considering these data, it can be thought that DNA hypomethylation may cause diseases by affecting gene functions such as genomic instability and cell survival and maturation, and even through apoptosis. It is found that the methylation status is correlated with antidepressant treatment, and it is suggested that the methylation status is not associated with only the disease itself but can also be associated with pharmacological treatment[3]. Another study showed that antidepressants are associated with increased methylation, and mood stabilizers are associated with decreased methylation[4]. The methylation status was found lower in patients who received valproate or lithium. But the methylation status is higher in patients with antidepressant treatment compared to antidepressant and mood stabilizer combined (4). In addition to antidepressants and mood stabilizers, it is shown that antipsychotics have effects on DNA methylation. Except haloperidol and olanzapine, sulpirid ans clozapin have demethylation effects on rats[5]. As seen from these data, antidepressants, mood stabilizers, and antipsychotics influence DNA methylation levels. However, it is not exactly known how these drugs affect the methylation status. The effects of gene methylation on treatment and clinical symptoms are unclear, too. It is thought that DNA methylation levels of related genes in bipolar disorder are involved in the etiopathogenesis of the disease. The level of methylation status of other candidate genes in relation with clinical disease should be investigated. Regulating DNA methylation may be a new therapeutic target for treatment of the disease.

**Keywords:** DNA methylation, hypomethylation, BDNF gene, bipolar disorder

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**[Abstract:0535]** ***Research methods in psychiatry***

## Eyes tell the psychopathology: preliminary findings

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**OBJECTIVE:** A number of studies on eye movement dysfunction in patients with psychiatric disease have been published. Glutamatergic neurotransmission mediated by the NMDA receptor is involved in the pathophysiology of schizophrenia and some neurological diseases[1]. The frontal-thalamic-cerebellar circuit has been implicated in eye movements. The presence of eye-tracking abnormalities among schizophrenia patients and their biological correlates has been reported by numerous investigators examining smooth-pursuit and saccadic eye-movement measures, as well as measures of motion perception[2]. An association between eye-tracking abnormalities and NMDA receptor antagonism is important because it indicates which neurophysiological mechanisms are related to eye-tracking abnormalities. There is strong evidence that eye-tracking abnormalities are related to genetic risk for schizophrenia[3]; thus, a relationship between eye tracking and NMDA antagonism may also help us understand the biological underpinnings of disease vulnerability. On the other hand, the behavioral and pharmacological effects of the noncompetitive N-methyl-D-aspartate (NMDA) receptor antagonist ketamine have been used to study important aspects of psychotomimetic action in humans. Several lines of evidence support the use of ketamine as a pharmacological model of schizophrenia. Schizophrenia patients administered subanesthetic doses of ketamine experience a brief exacerbation of positive, cognitive, and possibly negative symptoms. Ketamine also appears to provoke psychotic symptoms specific to a patient's disease history. Imaging studies have shown that ketamine changes the neuronal activity in areas thought to be involved in the pathophysiology of schizophrenia, including the medial frontal and anterior cingulate cortex, the hippocampus, and the cerebellum. Other studies have shown that ketamine causes schizophrenia-like positive, negative, and cognitive symptoms in normal healthy volunteers including deficits in sensory processing and eye-tracking performance. The non-competitive N-methyl-D-aspartate receptor antagonist ketamine leads to transient psychosis-like symptoms and impairments in oculomotor performance in healthy volunteers.
In the literature, as far as we know, all studies have been conducted with specific tools (infrared oculography etc.) and special units for saccadic eye movements. In our study, we aimed to investigate the relationship between vertical eye position (VEP) and psychopathology via a scale designed by us.
**METHOD:** Patients with the diagnosis of a psychiatric disorder (n=228) and control subjects (n=340) were included into the study. All subjects gave written informed consent in accordance with guidelines from the institutional review board of the GATA Haydarpasa Training Hospital. Subjects underwent a medical history, a physical examination, and laboratory tests, including a drug screen. A scale designed for measurement of the distance between eye limbus and palpebrae called as VEP was applied.
**RESULTS:** There was a statistically significant difference in terms of VEP scores between patients with the diagnosis of psychotic disorders (other than paranoid psychosis), depressive disorders, antisocial personality disorder, and controls ($p<0.001$). There was no difference in patients with diagnosis of anxiety disorders and paranoid psychosis.
**CONCLUSIONS:** These results suggest that VEP abnormalities may be related with psychopathology. Evidence from neuroimaging and microstimulation studies suggests that cerebellar circuitry is involved in integrating and coordinating smooth-pursuit and saccadic eye-movement information from the frontal cortex via a frontal-thalamic-cerebellar circuit. It has been argued that abnormalities in this circuit may underlie schizophrenia-related eye-tracking abnormalities. NMDA receptors are present on cells throughout the cortex, including the frontal/prefrontal cortex and the cerebellum, where they could play a functional role in eye-tracking abnormalities. In contrast, NMDA antagonism by ketamine is known to decrease neuronal activity in the cerebellum potently, an action that can explain the observed deficits in pursuit initiation[3] and pursuit maintenance as well as increases in disruptive leading saccades during smooth pursuit. Several investigators have noted

functional cerebellar abnormalities in patients with schizophrenia[4]. Thus, it is possible that some of the eye-tracking deficits associated with schizophrenia risk seen during ketamine challenge are mediated by shared cerebellar pathophysiology. Glutamate is the major excitatory neurotransmitter of the Central Nervous System (CNS), and it is crucially needed for numerous key neuronal functions. Yet, excess glutamate causes massive neuronal death and brain damage by excitotoxicity—detrimental over-activation of glutamate receptors. Glutamate-mediated excitotoxicity is the main pathological process taking place in many types of acute and chronic CNS diseases and injuries.

Successful attenuation of ketamine-induced deteriorations has been described for typical and atypical antipsychotics such as haloperidol, clozapine and olanzapine, and anti-epileptics such as lamotrigine, a glutamate agonist. Phencyclidine was also found related with vertical nystagmus. Risperidone treatment has previously been shown to improve antisaccade performance in schizophrenia patients after switching from typical antipsychotics to risperidone and in antipsychotic-naive first-episode patients.

With regard to smooth pursuit performance, no beneficial effects of risperidone on ketamine-induced smooth pursuit eye movements (SPEM) deficits were found. Some studies have investigated the effects of antipsychotics on SPEM in first-episode and chronic schizophrenia patients[3]. No treatment effect on predictive pursuit in first-episode patients but a worsening in SPEM performance in antipsychotic-treated, chronic schizophrenia patients compared with non-treated chronic patients has been observed. Hence patients' pursuit performance deficits seem to persist despite pharmacological treatment, possibly even representing cumulative adverse effects of typical and atypical antipsychotics on the pursuit system.

A neural circuitry involving the cerebellum has been proposed to have a central role in integrating and coordinating SPEM and saccadic information. It could be argued that NMDA receptor blockage in areas involved in frontal-thalamic-cerebellar circuits such as frontal eye fields, thalamus, and cerebellum would be likely to cause disruption in SPEM. We suggest that VEP is also responsible for the same mechanism. An involvement of a glutamatergic imbalance in cortical-subcortical-cerebellar circuits underlying the integrative theory of cognitive dysmetria may be assumed[5].

In conclusion, we suggest VEP as a physical examination sign for psychiatric disorders. Our findings are preliminary and should be investigated by further studies. Increased glutamatergic activity is associated with many psychiatric disorders as well as VEP in the brain; therefore, VEP may be used as a practical physical examination sign and may be helpful in diagnosis. Further studies are needed in order to show if VEP is an indicator of parental proneness or can be used as a phenotype. It should be examined more deeply if VEP's item can be used as endophenotype, genetic transition, connection with prognostic or disease susceptibility and response to treatment.

**Keywords:** eye sign, psychopathology, endophenotype

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**[Abstract:0548]** ***Genetic psychiatry***

## No association between DNA methylation in BDNF gene and schizophrenia patients in Turkish population

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**INTRODUCTION:** Schizophrenia is a multifactorial disorder. Genetic and environmental factors are involved in the etiology of schizophrenia. Although genetic factors are risk factors for schizophrenia, it is assumed that some environmental factors are required for the manifestation

of disease[1]. Epigenetic mechanisms regulate gene functions without causing change in the nucleotide sequence of DNA. These regulations are reversible; the most commonly studied epigenetic mechanisms are DNA methylation and histone modification[2]. DNA methylation and epigenetic mechanisms are associated with psychiatric disorders such as depression, psychotic disorders, post-traumatic stress disorder, autism, eating disorders, and substance dependence[3]. Epigenetics has an important role in gene and environment interactions. This means environmental factors influence the genomic expressions through epigenetic mechanisms. DNA methylation is caused by coupling of a methyl group to CpG sites with the DNA methyltransferase enzyme. A normal level of DNA methylation is required for controlling genomic expressions. Brain Derived Neurotropic Factor (BDNF) is a neurotrophin that regulates synaptic transmission and plasticity, and it has a role in proliferation, differentiation, survival and death of neuronal and non-neuronal cells. It has been suggested that BDNF may play a role in the pathophysiology of schizophrenia. Genetic studies show an association between BDNF and schizophrenia. In this study we aimed to investigate the DNA methylation status of the BDNF gene in patients with schizophrenia.

**METHODS:** The study included 49 patients (aged 35.31±10.35 years, 33 male and 16 female) with schizophrenia and 65 unrelated healthy controls (aged 35.18±9.05 years, 46 male and 19 female). Volunteers in the control group had no personal or familial history of schizophrenia. Individuals with known major health problems, diabetes and malignancies were excluded from the study. Patients were diagnosed with schizophrenia according to the 4$^{th}$ edition of the Diagnostic and Statistical Manual for Mental Disorders (DSM-IV). The severity of schizophrenia symptoms in the patients was evaluated using the Positive and Negative Syndrome Scale (PANSS) and the Clinical Global Impression severity scale (CGI-S). DNA was extracted from blood samples by using salt-chloroform method. Determination of methylation pattern of CpG islands was based on the principle that bisulfite treatment of DNA would result in conversion of unmethylated cytosine residues into uracil, whereas methylated cytosine residues would remain unmodified. Methylation-specific PCR was performed with primers specific for either methylated or unmethylated DNA. The primers were designed for 2 different CpG islands in the BDNF promoter. 100 ng DNA samples were treated with EpiMark Bisulfite Conversion Kit (Catalog No: E3318, New England Biolabs), in accordance with the manufacturer's standard instructions. The collected data were analyzed using the SPSS version 18.0 (SPSS Inc., Chicago, IL, USA). Both descriptive and analytical statistics were used. Chi-square/Fisher's Exact test was used to compare categorical variables. To compare the continuous variables, t test was used.

**RESULTS:** The mean ages and the gender distribution of the study groups were similar. There were no significant differences in the methylated or un-methylated status for each area between schizophrenia patients and controls (Table 1). When patients were compared with clinical parameters such as duration of the illness, CGI-S, PANSS scores, BMI, and methylated or un-methylated status for each areas, we did not find any significant difference ($p>0.05$).

**DISCUSSION:** This study found no difference in methylation status of two regions of the BNDF gene between schizophrenia patients and healthy controls. Although the methylation status of some other genes has been studied in schizophrenia patients, there are limited studies about the methylation status of the BNDF gene in schizophrenia patients. However, in one study BDNF gene methylation status and BDNF gene expression were investigated in schizophrenia patients; BDNF gene methylation was found lower, BDNF gene expression higher in schizophrenia patients compared to controls. The methylation status of some genes other than BDNF has been studied in schizophrenia patients, e.g., MB-COMT and RELN. One study found hypomethylation in the MB-COMT gene and increased transcript levels of MB-COMT in schizophrenia patients. In that study, it is suggested that MB-COMT hypomethylation is a major risk factor for schizophrenia. Another study shows hypermethylation of the RELN promoter. But in contrast to these other studies, it shows that there is no difference in methylation status of COMT and RELN genes in schizophrenia patients compared to healthy controls[4]. As far as we can understand from these studies, data on DNA methylation status in patients with schizophrenia are conflicting. However, there must be an association with DNA methylation and schizophrenia according to our hypothesis, and again the methylation status must be different in schizophrenia patients compared to controls. Bu our findings do not support our hypothesis. As mentioned above, there are inconsistent results in methylation studies. Several other factors such as patients' received antipsychotics or analyzing methylation in blood may affect the methylation status. In a study which examined the effect of antipsychotics on DNA methylation, it is found that clozapine and quetiapine reduced DNA methylation, but there are no similar effects of haloperidol and risperidone on the DNA methylation status. Another study in animals shows that clozapine reduced BDNF methylation and increased social interaction[5]. The authors are aware of some limitations of this study. First, we analyzed DNA methylation in peripheral blood, which does not reflect directly the central nervous system. Second, this is a naturalistic and cross-sectional study and patients were continuing their medication. Therefore, antipsychotics received may have affected the methylation status. DNA methylation is a dynamic and reversible process, and many other environmental factors also affect methylation. For these reasons, examining the methylation status and protein levels of the BDNF gene in certain intervals throughout the treatment period in the same patients may be more worthwhile. In conclusion, there were no differences in BDNF gene methylation status between schizophrenia patients and healthy controls. Further studies are necessary with more patients, and the limitations referred in this paper should be considered.

**Keywords:** DNA methylation, BDNF gene, schizophrenia

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**[Abstract:0549]** ***Genetic psychiatry***

# Cannabinoid receptor 1 (CNR1) gene polymorphisms in schizophrenia patients: Rs6454674 polymorphism is associated with disease severity

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**INTRODUCTION:** It is considered that schizophrenia is caused by a combination of multiple elements, such as genetic, biological, environmental, and psychological factors. According to this view, people may have a genetic predisposition for schizophrenia, but the disease may not emerge if some other factors are not added. Among these factors are birth complications that can cause mutagenesis or a change in gene expression, biological factors such as nutrition, and to a lesser extent certain environmental impacts including psychological factors. The endocannabinoid system contributes to the regulation of memory, cognition, emotion, and stress. In addition, it contributes to a spectrum of personality traits in normal individuals and a susceptibility to mood disorders. Endogenous cannabinoids have been found to be higher in the cerebrospinal fluid of schizophrenic patients[1]. It has been reported that endocannabinoids cause GABAergic inhibition and dopaminergic increase in the mesolimbic and nigro-striatal systems, which play a role in the neurobiology of schizophrenia[2]. There are limited studies about CNR-1 gene polymorphism in schizophrenia. In this study, we investigate cannabinoid receptor 1 (CNR1) gene polymorphisms in schizophrenia patients.
**METHODS:** CNR1 gene polymorphisms were studied in 66 schizophrenia patients and 65 healthy controls. To obtain genomic DNA, proteinase K digestion and salt-chloroform method were used. Clinical Global Impression severity scale (CGI-S) and Positive and Negative Syndrome Scale (PANSS) were administered for evaluating the severity of schizophrenia symptoms. CNR1 gene polymorphism has been determined by using polymerase-chain- reactions (PCR), Restriction Fragment Length Polymorphism (RFLP), and SSCP (Single Strand Conformation Polymorphism) methods for the Rs6454674, Rs806368, and Rs1049353 sites.
**RESULTS:** There was no difference in CNR 1 gene polymorphisms between schizophrenia patients and control groups (Rs6454674 T/G; p=0.973, Rs806368 T/C; p=0.349, Rs1049353 A/G; p=1). CGI-S, PANSS total, PANSS positive, PANSS negative and PANSS general psychopathology scores were significantly lower in schizophrenia patients with RS6454674 polymorphism than non-polymorphism.
**CONCLUSION:** Various theories have been proposed to explain the relationship between cannabis use and schizophrenia. It has been suggested that patients with schizophrenia use cannabis for self-medication, or that psychosis arises as a result of the use of cannabis, or that there are genetic and biological similarities between schizophrenia and cannabis use disorder. Considering this data, it is hypothesized that the endocannabinoid system (ECS) has a role in schizophrenia. In accordance with this hypothesis, endocannabinoid levels were studied in cerebrospinal fluid (CSF) and blood of schizophrenia patients. These studies show increased cannabinoid levels in CSF and blood of schizophrenia patients, and it is suggested that ECS alterations take a part in the pathophysiology of schizophrenia. Nevertheless, genetic studies have not shown this relationship conclusively. CNR genes are studied with various methods in schizophrenia. But results are conflicting and do not support clearly the relation between ECS and schizophrenia[3]. However, the result clarified that use of cannabis is a risk factor for onset of schizophrenia especially in vulnerably people[4]. We also found that there were no differences in CNR1 gene polymorphisms between schizophrenia patients and healthy controls. Our finding is consistent with previous studies which did not find any relationship between CNR1 gene polymorphisms and schizophrenia[5]. In conclusion, the results suggested that there may be an association between CNR1 gene polymorphisms and clinical symptoms and disease severity in schizophrenia patients.
**Keywords:** endocannabinoid system, cannabinoid receptor 1, gene polymorphism, schizophrenia

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**[Abstract:0592]** ***Addiction***

## The effect of synthetic cannabinoids on P-wave dispersion: an observational study

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**INTRODUCTION:** Synthetic cannabinoids (SC) were first marketed as legal cannabis alternatives in Europe in the early 2000s. Consumption of SC has become widespread, despite law enforcement and regulatory control measures. The consumption of products containing SC may lead to serious adverse effects[1]. Psychiatric disorders may lead to an increased risk of cardiovascular disease (CVD). Previous studies have shown that P-wave dispersion (PD) is associated with increased risk of CVD[2]. PD is also associated with psychiatric disorders including hypochondriasis, depression and panic disorder[3,4]. The aim of the study is to investigate the effect of SC on PD in patients with SC consumption.

**MATERIALS AND METHODS:**

**Study Population:** The study population included 53 patients with SC consumption whose use of SC was admitted personally and/or detected in urine screening tests in Erenkoy Mental and Neurological Diseases Training and Research Hospital. Socio-demographic data was collected by using a questionnaire. Physical examination findings, medical history data, and resting 12-lead electrocardiograms (ECG) were obtained from the entire study population. PD was measured through 12-lead ECG obtained during patient admission. Patients with underlying cardiac conditions, abnormal ECG findings, or taking antidepressants or other medication that might interfere with ECG results were excluded. After exclusion criteria, the remaining 40 patients with SC consumption were included in the study. The control group consisted of 20 healthy age- and sex-matched volunteers. The study was approved by the local ethics committee and written informed consent was taken from all participants.

**Addiction Profile Index (BAPI):** The severity of addiction was determined by using addiction profile index (BAPI score). Total BAPI score was calculated as described previously[5]. BAPI has been validated by Ogel et al. in 2012. The cut-off point of the BAPI score was 10.7. BAPI score <12 was defined as low level of addiction, BAPI score 12-14 as moderate and BAPI score >14 as high level of addiction.

**Electrocardiographic Measurements:** Following a resting period of 20 minutes, 12-lead ECG was recorded at supine position at a paper speed of 50 mm/s and an amplitude of 20 mm/mV by using a Nikon Kohden ECG device (Japan). The onset of the P-wave was defined as the point of first downward departure from the top of the baseline for negative waves. The return to the baseline of the bottom of trace was considered to be the end of the P wave. The difference between the maximum and minimum P wave duration was calculated from any derivation of the 12-lead ECG and was defined as the PD (Pd=Pmaximum-Pminimum).

**Statistical Analysis:** Statistical analyses were performed using SPSS 20.0 statistical software package. Continuous data were expressed as mean±standard deviation while categorical data were presented as number and percentage of patients. Chi-square and Fisher's Exact test were used for comparison of categorical variables while student-t test or Mann-Whitney U test were used to compare parametric and nonparametric continuous variables, respectively. Correlation analysis was performed by Spearman's correlation test. Linear regression analyses were performed to determine the predictors of BAPI score. A value of $p<0.05$ was considered statistically significant.

**RESULTS:** The study population consisted of 40 patients with SC consumption and 20 age- and sex-matched healthy controls (26.9±7.3 years versus 26.2±6.4 years and 39 male versus 19 male, p=0.687, 0.611, respectively). The majority of patients was single (30 single versus 10 married) and graduated from primary school (35 patients). Mean duration of patients' SC consumption was 1.8±0.7 years. All patients completed BAPI scale for evaluation of addiction level. Mean BAPI score of study population was 13.8±2.8. Our study population had a moderate level of addiction according to BAPI score. Biochemical measurements were in normal range in the study population.

Heart rate was similar between the two groups (71.2±12.9 vs. 71.7±8.9, p=0.889). Patients with SC consumption had significantly higher

PD value than controls (41.2±13.8 ms versus 32.3±7.6, p=0.002). Correlation analysis revealed that BAPI score was significantly correlated with PD value (r=0.528, p=0.003). Linear regression analysis was performed to determine the predictors of BAPI score in patients with SC consumption. Among PD value, age and heart rate that were included in the linear regression model, PD value was shown to be significantly and independently affecting BAPI score (Beta: 0.477, t= 2.783, p=0.010).

**DISCUSSION:** Patients with SC consumption had significantly higher PD values than controls. BAPI score was significantly correlated with PD value. PD was an independent predictor of BAPI score. Our results demonstrated that SC consumption may lead to increased risk of CVD through increased PD. To the best of our knowledge, this is the first study to evaluate the effect of SC on PD in patients with SC consumption. Nowadays, there is an increased interest in consumption of SC in Turkey. Due to its ready accessibility and lower price compared to other cannabinoids, the usage of SC, especially the usage of bonsai, has been increasing among the young population. In accordance with the literature, the mean age of patients with SC consumption in our study population was 26.9±7.3 years. Due to its widespread usage, a lot of cases have attended to emergency clinics with a variety of symptoms ranging from dizziness to cardiac arrest. Therefore, clinicians should pay more attention to evaluating these patients in emergency clinics. Timely diagnosis and early treatment of those patients may save their lives. Although routine urine and blood samples are required for differential diagnosis, they are not sufficient for a diagnosis of SC consumption. Therefore, detailed medical history and more attention to environmental factors are important methods for an accurate diagnosis. Although all laboratory parameters were in the normal range for our study population, detailed medical history revealed the usage of SC by patients. Experimental research suggests that there is a strong relationship between psychiatric disorders and CVD. Due to increased risk of CVD, numerous clinical studies have been performed to this day. Therefore, we proposed a possible effect of SC on ECG parameters and designed the present study accordingly.

The 12-lead ECG is a common method for evaluation of CVD. As it is cheaper and more available than other diagnostic methods, clinicians firstly use it for the differential diagnosis of CVD. Previous studies have shown that PD is a non-invasive electrocardiographic marker that can be used to determine the increased risk of atrial fibrillation. Increased PD has been reported in several clinical settings such as coronary artery disease, hypertension, chronic renal disease, mitral stenosis, hypertrophic cardiomyopathy, and depression. Although there are several pathways leading to a prolongation of PD, the main mechanism of PD in these patients is thought to be based on structural and electrophysiological changes in the atrial myocardium. In our study, we found that patients with SC consumption have significantly higher PD than healthy controls. The PD value was also correlated with BASI score in these patients. Therefore, our results demonstrated that SC may lead to increased risk of CVD trough prolongation of the PD.

**Study Limitations:** There are several limitations for our study, such as small sample size. Therefore, large-scale studies should validate our results. Our study was designed cross-sectional. We did not follow up the patients prospectively. Therefore, we have no prognostic data for those patients. It would be better if we followed up the patients and documented new onset CVD in patients with SC consumption who have prolonged PD. The usage of the SC should be validated by novel urine tests. Further large-scale prospective studies are needed to validate our preliminary results.

**CONCLUSIONS:** Patients with SC consumption have higher PD values than healthy controls. The PD value was correlated with BASI score. PD was also independent predictor of BASI score in those patients. Our results demonstrated that SC consumption may lead to increased risk of CVD through prolonged PD. A simple and cheap ECG may help the clinician to assess cardiovascular risk in patients with SC consumption.

**Keywords:** cardiovascular risk, P-wave dispersion, synthetic cannabinoid

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**[Abstract:0625]** ***Geriatric psychiatry***

# Socio-demographic characteristics and disability in patients with dementia

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**Abstract**: Dementia is a neuropsychiatric syndrome that is deteriorating with age. Social and occupational functionality of dementia patients are usually impaired significantly. In this study, we analyzed 65 dementia patients. We found that 90.8% of people with dementia did not use any drugs. Disability ratios of dementia types were mild 26.2%, mild to moderate 20%, moderate 29.2%, severe 9.2%, and unspecified 15.4%. Dementia is an insidious and progressive syndrome which causes the loss of cognitive ability.

**INTRODUCTION:** Dementia is a neuropsychiatric syndrome that is deteriorating with age. A study found that people with dementia represent 5% of the population older than 65 years and 40% of those older than 85 years[1]. Dementia may damage mental functions and result in behavioral problems, conducing to a lower quality of life. According to the authorized institutions in Turkey, disability rates of patients with dementia should be classified according to their functionality. These rates defined as follows: mild 25%, mild to moderate 50%, moderate 70%, severe dementia 90%[2].

The aim of our study was to investigate individuals older than 65 years regarding sociodemographic characteristics and dementia, seen at the medical board of Dicle University in the years 2013 and 2014, Further, we evaluated whether they were using drugs for dementia and the rates of disability.

**MATERIALS AND METHODS:** We analyzed 402 subjects older than 65 years who applied to the medical board in Dicle medical faculty in the years 2013 and 2014. Subsequently, researchers investigated the medical records of Dicle University hospital for the diagnosis of dementia, retrospectively. Eventually, we found that 65 of the 402 persons were diagnosed with dementia. These patients were compared in terms of the age, gender, ratio of disability, use of pharmacologic agents and severity of disability.

**RESULTS:** We found 55% (n=36) males and 45% (n=29) females in all dementia patients (n=65). These patients had a mean age of 80.1years, but non dementia patients (n=337) had a mean age of 72.1years. Also, 64.6% (n=42) of dementia patients were evaluated as severely disabled. Six (9.2%) of 65 dementia patients used pharmacologic agents for the symptoms of dementia. Four of 6 patients among the severely disabled used acetylcholinesterase inhibitors such as donepezil, one of 6 patients used N-methyl-D-aspartate (NMDA) receptor blockers such as memantine, and one more patient was using donepezil plus memantine. Disability ratio of the dementia patients were mild 26.2% (n=17), mild to moderate 20% (n=13), moderate 29.2% (n=19), severe 9.2% (n=6) and unspecified 15.4% (n=10).

**DISCUSSION:** Dementia is a neuropsychiatric disorder characterized by insidious and progressive features. It may become more frequent with age. In our study, we found that the mean age of dementia patients was higher than the age of those not diagnosed with dementia. In dementia, neural structures in the central nervous system are damaged, affecting various cognitive domains. For this reason, activities of life as well as social and occupational functionality of dementia patients is significantly damaged[3]. At the medical board of Dicle University, 64.6% of all dementia patients were found to meet the criteria for disability. These patients ultimately lose the ability to perform daily tasks. For this reason, these patients cannot continue to lead their lives independently.

Dementia also affects family caregivers. Given the progressive and terminal nature of dementia, the patients and their caregivers cannot distinguish between senility and cognitive impairments. Unfortunately, we found that 90.8% of people with dementia did not use any drugs for their complaints.

**CONCLUSION:** Dementia is an insidious and progressive syndrome causing the loss of cognitive ability. It may get worse with age. Therefore, all geriatric patients should be evaluated by the physicians with regard to dementia, even if they are consulting for reasons other than dementia. It should be kept in mind that patients admitted with complaints of aging must be examined by the physicians for dementia to prevent the progression of disease and reduce the loss of ability.

We conclude that dementia is associated with many impairments for the quality of life and possibly results in severe disability.

**Keywords:** dementia, disability, anti-dementia drug use

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**[Abstract:0652]** ***Schizophrenia and other psychotic disorders***

# The prevalence of metabolic syndrome in outpatients with severe mental illness in antipsychotic monotherapy or polypharmacy

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**INTRODUCTION:** People with severe mental illness (SMI) have significantly higher levels of morbidity, mortality and shorter life expectancy compared to the general population. The shortened lifespan is mostly due to preventable cardiovascular disease (CVD)[1].
Metabolic syndrome (MetS) is increasingly recognized as a major cause of CVD, both in the general population and in people with SMI[1,4]. SMI itself may increase genetic CVD risk factors. But many other factors contribute to the morbidity and mortality in these patients[1,5].
Although there are many studies on the treatment of patients with schizophrenia and other SMI, studies about prevalence and characteristics of antipsychotic polypharmacy and its metabolic outcomes are limited in Turkey. The aim of this study was to examine the prevalence of metabolic syndrome and related factors in outpatients with SMI who were in antipsychotic monotherapy or polypharmacy. Further, we aimed to compare the practices of polypharmacy and monotherapy in terms of the rationale and compatibility of the treatment and to examine the relation between antipsychotic polypharmacy and MetS.
**METHODS:** This study included 290 patients with SMI between 18 and 65 years of age who were followed at KTU Psychiatry Department Schizophrenia-Bipolar Disorder outpatient clinic. Data of patients who were diagnosed with schizophrenia, schizoaffective disorder or bipolar disorder according to DSM-IV-TR between January 2007 and December 2014 were screened. Data were obtained from clinical records in the charts and electronic medical records. The data for patients who were on antipsychotic monotherapy or polypharmacy with effective doses of antipsychotic drugs for at least 8 weeks and whose complete metabolic data was fully recorded for the same time period were taken into the study. MetS was diagnosed according to NCEP ATP III (National Cholesterol Education Program Adult Treatment Panel) definition.
**RESULTS:** The mean age of the 290 patients included in this study was 39.8±11.2 years, 57.6% were male and 42.4% were female. 183 patients (63.1%) were diagnosed with schizophrenia, 85 patients (29.3%) were diagnosed with bipolar disorder and 22 patients (7.6%) were diagnosed with schizoaffective disorder.
93 patients (32.1%) were receiving antipsychotic polypharmacy. Combinations of two second-generation antipsychotics were most common (n=73, 78.5%), followed by combinations of a first- with a second-generation antipsychotic (n=19, 20.4%). There was no significant difference between monotherapy and polypharmacy groups in terms of MetS prevalence (n=62, 31.5%, n=31, 33.3, p=0.751 respectively).
Patients with a diagnosis of schizoaffective disorder were receiving the highest number of psychotropic drugs (3.13±1.16). Schizoaffective disorder patients were followed by bipolar disorder patients (2.84±1.09) and schizophrenia (2.30±1.07) in terms of co-prescribed psychotropic drugs. In this regard, patients with schizoaffective disorder differ significantly from those with bipolar disorder and schizophrenia (p=0.000). However, the number of total psychotropic drugs did not indicate a significant difference between patients with or without MetS (2.53±1.20 vs. 2.51±1.09, p=0.932).
Overall MetS prevalence was 32.1% (n=93) according to ATP-III. The prevalence of MetS was higher among women, but this difference was not significant statistically (n=123, 35% vs. n=167 29.9%, p=0.365). High triglyceride level, increased waist circumference, and low HDL were frequent among the patients (54.8%, 58.3% and 46.9%, respectively). The high frequency of positive triglyceride criteria in males (60.5% vs. 47.2%, p=0.024) and waist circumference criteria in females (75.6% vs. 45.5%, p=0.000) were remarkable.
The prevalence of MetS increased significantly with age (p=0.002). Also we found that mean age is significantly different between patients with or without MetS (42.97±9.57 vs. 38.31±11.49, p=0.000).
Frequency of smokers was higher in patients with MetS but the difference was not significant statistically (50.5% vs. 48.2%, p=0.713).
The prevalence of MetS was 30.6% in schizophrenia patients, 36.4% in schizoaffective disorder patients, and 34.1% in bipolar disorder patients according to ATP III. The differences in MetS prevalence between diagnostic categories were not significant (p=0.767). When schizophrenia and schizoaffective disorder were combined into a category termed ''schizophrenia spectrum disorders'', the prevalence of MetS in this combined group was 31.2% (n=64). However, the difference in MetS prevalence between this combined group and bipolar disorder still was not significant (p=0.63).
We conducted logistic regression analysis to examine the relevance of variables for the presence of MetS. For the multivariate analyses, we entered into the model all variables that possibly determinant for metabolic syndrome. However, in logistic regression analysis, MetS was significantly associated with higher BMI (r2: 0.121, p<0.01).
**CONCLUSION:** Depending on MetS criteria used, gender, ethnicity, country, age groups, and antipsychotic treatment, percentages vary considerably[1,4,5]. In this cross-sectional retrospective study of outpatients with SMI who were on antipsychotic monotherapy or polypharmacy, the prevalence of MetS was 32.1% according to ATP III. This was similar to the previous studies from Turkey and other

countries. Women were more likely to be diagnosed with MetS, which is consistent with recent studies.

In a large adult population sample representing all geographical regions of Turkey, Sanisoglu and associates reported MetS prevalence across the country as 17.9% and specifically in the Black Sea region as 14.2% according to IDF (International Diabetes Federation)[3]. Yazıcı et al. have reported the prevalence of MetS as 34.2% in a Turkish cohort. In another study from Turkey, it was found that MetS prevalence according to IDF criteria was 32% among chronic inpatients hospitalized in the regional mental health hospital[2].

While several studies found MetS to be more common in older patients, fewer studies reported no age differences[2,3,4]. In the present study, the prevalence of MetS increased with age significantly. Similarly, in a study conducted in our country (METSAR), it was reported that MetS incidence increased with age in the adult population (20 years and over).

The mean BMI was significantly higher in patients with MetS. Kato et al. (2004) posited that the relationship between MetS and central obesity was stronger than the relationship between MetS and obesity (as determined by BMI)[5]. In the present study, increased waist circumference was the most common MetS criterion, and females were significantly more likely to meet this criterion. This finding was consistent with the recent literature about MetS. This suggest that waist circumference is an important criterion for monitoring patients.

We did not find any difference in terms of duration of illness or number of exacerbations and hospitalizations between patients with and without MetS. Smoking was not different between SMI patients with or without MetS in the recent studies. This was consistent with our results.

In our study, there was no significant difference between monotherapy and polypharmacy groups in terms of MetS prevalence. Correl and associates found MetS prevalence 34.4% in a monotherapy group and 50% in a polypharmacy group in patients with schizophrenia. In our study, consistent with prior studies (Cerit et al. 2008, Gulec, Oyekcin 2009, Songur et al. 2012), there was no significant difference between monotherapy and polypharmacy groups in terms of MetS prevalence.

It is known that atypical antipsychotics can trigger weight gain and related metabolic changes; however, in the present study there was no relationship between the type of drugs used and MetS diagnoses, which is similar to what was reported by Kato et al. (2004), Heiskanen et al. (2003) , Sarısoy et al. (2013) and Cerit et al. (2008).

It has been repeatedly found in recent studies that people with SMI exhibit a higher MetS prevalence than their peers in the general population across the world[1,4,5]. Our finding supports that information. It is found that higher BMI is a powerful predictor of MetS and the prevalence of MetS increased with age significantly. Moreover, in logistic regression analyses, metabolic syndrome was significantly associated with higher BMI.

We could not compare antipsychotic subgroups in terms of MetS prevalence due to the sample heterogeneity and small number of cases. Further research is needed to determine the metabolic effects of specific antipsychotic combinations, duration of treatment and individual dosage used in polypharmacy.

In conclusion, our results confirm previous reports that patients with SMI are most likely to receive antipsychotic polypharmacy and MetS is highly prevalent among patients treated with SMI. We are not able to generalize our findings to the general population. But it is important that our findings have shown similar findings to those of recent studies conducted in the Black Sea region which have shown that MetS prevalence is higher in SMI patients compared to the general population (Sanisoglu et al. 2006, Boke et al. 200, Sarisoy et al. 2013). This might be caused by certain characteristics shared by the specific population in the Black Sea region such as genetic features, dietary habits or other variables that are related with MetS in this particular region of Turkey.

Finally, we have not found any significant effects of antipsychotic medication (such as monotherapy, polypharmacy, same-class/multiclass polypharmacy, typical/atypical, high-risk medication like clozapine, olanzapine and others) on metabolic syndrome. In order to determine the complex effects of not only antipsychotic but also other psychotropic drugs on metabolic syndrome, further studies with control groups and medicine sub-groups being distributed homogeneously are needed. However, in the light of our results, we believe we can hypothesize that in the patients with SMI, there are many more factors that determine the risk of metabolic syndrome besides antipsychotic medication, and most of those have not been elucidated yet.

**Keywords:** antipsychotic monotherapy, antipsychotic polypharmacy, metabolic syndrome, severe mental illness

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**[Abstract:0655]** ***Anxiety, stress, and adjustment disorders***

# Investigation of specific familial transmission characteristics in social phobia

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**INTRODUCTION:** Environmental, specifically familial behaviors and parenting styles are particularly significant in the development of social phobia (SP). The development of anxiety in children seems especially affected by parental behaviors, genetic inheritance, prevention of social initiative, and role modeling[1]. Retrospective studies have described parents of SP patients as people with limited socialization and isolated, with disconnected relationships. In addition to parental behaviors, an increased parental anxiety level is another variable related to SP. Parents who show anxiety disorders like SP, agoraphobia, and panic disorder are at greater risk to have children with anxiety disorders like SP. On the other hand, published studies also reported that these symptoms as not related specifically to SP but to all kinds of anxiety disorders and identified no differences in parenting styles in families of patients diagnosed with SP[2].

Early childhood adverse experiences have also been commonly observed among the developmental risk factors for SP. Experiences that increase risk for SP include parental psychopathology, conflicts within the family, divorce, emotional, physical, and sexual abuse, loss of a parent, and early separation from parents. These risk factors increase not only the likelihood of SP but are also implicated in the development of other types of psychopathology.

Our study examines the developmental effects of parenting style, parental anxiety levels, and childhood adverse life events in the manifestation of various modes of SP. We compared patients diagnosed with SP and their parents with a control group and their parents.

**METHODOLOGY:**

**Sample:** The research sample consisted of 60 (n=60) individuals aged between 14 and 24 years diagnosed and treated at S.B. Ankara Dışkapı Y.B.E.A.H. Psychiatry Outpatient Clinic Adolescence Unit. The control group consisted of 30 (n=30) healthy individuals between 14 and 24 years of age who volunteered to be part of the study. In both groups, parents who agreed to participate in the study were included (SP parents n=45; control parents, n=30). This study utilized the data from a master's thesis titled "Parental child rearing attitude in social anxiety development". All participants in the study provided informed consent, and approval was obtained from the local ethical board.

**METHOD:** The SCID-1 was administered to all patients who were admitted to the clinic as well as to all controls, and a sociodemographic questionnaire was given to the parents for family interview. Liebowitz's Social Anxiety Scale (LSAS) was used to evaluate the severity of social anxiety experiences and avoidance behaviors. The Parent Attitude Research Instrument (PARI) was completed separately by all participants in order to evaluate perceived parenting attitudes for all. The subjects were requested to complete the forms with attention to their own parenting practices and family experiences. Because of parent loss, separation or divorce, failure to contact, and lack of time, only 45 parents in the SP group were able to participate in the study. All parents of the healthy control group were also evaluated using the PARI and the LSAS.

**Scales:** The Parent Attitude Research Instrument was developed in 1958 by Schaefer and Bell. Children complete a 1-4 Likert-type scale to evaluate the scale's reliability and validity. The subjects complete scales rating child rearing attitudes using 5 subscales. Over-Protective Mothering (Factor 1) particularly shows mothers' over-protectiveness and interference. Democratic behaviors and definitions of equality (Factor 2) show supportiveness and participatory relationships. Mothers' refusal of the housewife role (Factor 3) shows tension and anger in parents, especially the mothers' relationship with the children. Husband and wife incompatibility (Factor 4) shows the effects of conflict between the spouses on child rearing attitudes. Harsh Discipline (Factor 5) describes punishing, harsh mothers' and fathers' attitudes.

The Liebowitz Social Anxiety Scale was developed in 1985 by Liebowitz, and the validity and reliability of the Turkish version has been demonstrated by Dilbaz. This is an inventory developed to measure levels of social anxiety and is constructed with two subscales: anxiety and avoidance.

**Statistical Analysis:** The SPSS 15 package was used to complete the Statistical Analysis. Data were analyzed using statistical methods that compared the patient and control groups and the male and female groups using single direction variation analysis, and risk factor effects were evaluated using a multi-linear regression analysis. The significance factor for results was found to be $p<0.05$.

**RESULTS:** The SP and control groups were compared with regard to their age, gender, SES status, educational levels, professions and other variables and no significant statistical differences found. Also no other statistically significant sociodemographic factors were identified between the parents of those diagnosed with SP and the control group, with the exception of the mothers' educational levels ($\chi^2=14.02$, $p<0.05$). Early childhood adverse life events were reported significantly higher in the SP group, reaching 20% against the controls at 1.1% incidence of early childhood adverse life experiences ($\chi^2=8,540$, $p<0,05$). When compared according to rates of separation anxiety, the SP group showed a 28.3% rate and the control group a rate of 13.3% ($\chi^2=2,52$, $p=0,91$).

The scores of patients' parents on the Liebowitz anxiety and avoidance subscales were significantly higher than the controls'. According

to results of the univariate variation analysis of 2 (patients and controls) X 2(males and females), PARI subscale scores showed significant group difference in the over-protective mothering group; adolescents from the SP group showed higher scores on the protective mother scales than controls ($F(3.256)= 3.05$; $p<0.03$). Gender differences were not found between the groups.

When we analyzed the parents' experiences, PARI subscales showed significant differences for PARI1 (over-protective mothers) subscale, for mothers ($F(3.163)= 2.73$, $p<0.05$) and for fathers ($F(3.256)= 3.05$, $p<0.03$). They were significantly higher than those of the control group's mothers and fathers. Also, a significant gender difference was found for fathers ($F(1, 377)= 7.27$; $p<0.009$); the fathers of both the SP and control groups scored significantly higher for girls on the PARI1 over-protective mothering scales. No significant differences were identified with relation to the other subscales.

**DISCUSSION:** This study aimed to consider the roles of variables like family parenting styles, parents' levels of anxiety, avoidance behaviors, and childhood adverse events in individual risk for the development of SP. For those diagnosed with this disorder, rates of parental divorce, separation and death of a parent were found higher than in the control group. In the literature, some studies showed a relationship between incidence of this kind of traumatic experience and the development of this disorder while others did not.

The results of this study showed that the mothers and fathers of those diagnosed with SP showed higher levels of anxiety and avoidance behaviors in social situations than controls. Studies examining the genetic inheritance for SP show a concordance for monozygotic twins of 24% and for dizygotic twins of 15%; for close relatives, the frequency of the disorder is also 15%. The high levels found for social anxiety and avoidance behaviors among the parents of our patient group are in agreement with Bandura's model, suggesting that children's anxious thinking and avoidant behaviors are socially learned. Stemberger's study described patients' parents as having limited social relationships and being avoidant. Bruch et al. suggest in their study that patients took parental behavior assessed as socially anxious as a model and thus learned the disorder. It is also possible that when parents limit children's initiative, discourage alternative behaviors for initiative, or abuse them, the way may be paved for the development of the disorder. Studies in the literature show a relationship between parental attitudes toward initiative and encouragement of initiative, and the development of SP[3].

Another important finding of this study was that the patient group scored higher on the over-protective parent style (PARI 1) scale in comparison with the control group. In the literature, when parenting approaches have been examined retrospectively, SP patients' parents have generally been described as over-protective, rejecting, or neglectful[4].

This study was limited in the range of anxiety disorders that it examined and was cross-sectional. We would recommend studies considering other anxiety disorders and with a longitudinal design that examine the reciprocal parent-child relationships in this area.

In conclusion, we determined that when compared with a control group, SP is related to specific family characteristics like parental anxiety levels, avoidance levels and parental attitudes. In future studies, larger sample sizes and groups drawn from broader diagnostic categories would be useful. Prospective, qualitative studies will help to determine the etiological factors that contribute to the development of SP.

**Keywords:** developmental model, parental child rearing attitude, social phobia

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**[Abstract:0693]** ***Tic disorders***

## Antipsychotics use in children with tic disorders: a cross-sectional study

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**INTRODUCTION:** Tics are involuntary movements seen commonly and widespread in the childhood period as motor or vocal involuntary muscle contractions which show a sudden, rapid, intermittent, recurrent, non-rhythmic, stereotyped nature. Many patients with tic disorders do not need to receive any medication because their tics are mild, transient, and without causing any social or functional impairment. In some patients, however, social isolation and stigmatization, a decrease in academic performance, and low self-esteem

levels stemming mainly from the tics could cause social and functional deterioration. In these situations interventions would be necessary to treat the tics.

Management of tic disorders is one of the most problematic issues in child psychiatry discipline. There is no standard treatment protocol for the tics. Psychoeducation, family interventions, behavioral approaches and pharmacotherapy could be used individually or in combination for the treatment. Pharmacotherapy uses two groups of agents: antipsychotics and non-antipsychotics. Most psychotherapeutic agents in this field are antipsychotics. This study aimed to evaluate the children aged 3-18 years with tic disorders retrospectively in a cross-sectional study.

**METHODS AND MATERIALS:**

**Sample:** Over a one year period, records of children and adolescents admitted by our child psychiatry outpatient clinics were retrospectively evaluated and data of those diagnosed with tic disorders according to the DSM-IV-TR were examined in detail. Clinical features, comorbid psychiatric disorders, and medications used were noted.

**Statistical Analysis:** For data analysis, SPSS for Windows of 17.0 (Statistical Package for Social Sciences, Version 17.0, Chicago: SPSS Inc., 2008) statistical software package was used. Categorical variables were analyzed with chi-square ($\chi 2$) test. Predictors of medication use were analyzed with logistic regression analysis. $p<0.05$ was accepted as statistically significant.

**RESULTS:** Data of 92 children diagnosed with tic disorders were collected. Mean age of sample was 10.7 (±3.1) (3-18 years). Males were 79.3% (n=73) and females were 20.7% (n=19). According to the age groups, children (3-11 years of age) represented 63.0% (n=58) and adolescents (12 years of age and above) 37.0% (n=34). According to the DSM-IV-TR tic disorders classification, 46.7% (n=43) of all children had 'tic disorder not otherwise specified (NOS)', 23.9% (n=22) of them had 'Tourette Syndrome', 20.7% (n=19) of all had 'chronic tic disorder with single or multiple motor tics' and 8.7% (n=8) had 'transient tic disorder consisting of multiple motor and/or phonic tics'. There was a significant correlation between being male and having any of tic disorders compared to females ($\chi 2=10.620$, $p=0.014$), while values were found similar between children and adolescents ($\chi 2=5.574$, $p=0.134$).

At least one psychiatric disorder was found in 43.5% (n=40) of children with tic disorders. These comorbidities were the following: 25.0% of them had attention deficit hyperactivity disorder (ADHD), 9.8% of all had anxiety disorders (outside of obsessive compulsive disorder (OCD)), 7.6% of all had specific learning disorder (SLD), 5.4% of all had mental retardation (MR) and 4.3% of all had OCD.

There was no difference between sexes in terms of having any comorbid psychiatric disorder ($\chi 2=1.380$, $p=0.303$). Comorbidity distribution between the age groups (children versus adolescents) was also similar ($\chi 2=0.933$, $p=0.334$).

At least one pharmacotherapeutic agent use was found in 45.7% (n=42) of all children with tic disorders, whereas 54.3% (n=50) of the children were not using any psychotropic agents. The most prominent agent group being used was antipsychotics (31.5%, n=29), which included the following: aripiprazole (15.2%, n=14), risperidone (13.0%, n=12), and haloperidol (3.3%, n=3). The other medications used were atomoxetine (ATX; 9.8%, n=9), methylphenidate (MPH; 6.5%, n=6), and selective serotonin reuptake inhibitors (SSRIs; 6.5%, n=6). Significantly higher medication use in children with tic disorders was found if they had any comorbid psychiatric disorders ($\chi 2=24.567$, $p<0.001$).

Predictors of any psychotropic medication were the following: having Tourette Syndrome ($p=0.001$, Beta=0.082, 95%CI [0.018-0.380]) and the presence of comorbid psychiatric disorders ($p=0.003$, Beta=0.057, 95%CI [0.009-0.374]). In this cross-sectional sampling, the only predictor for antipsychotic medication use was having Tourette Syndrome ($p=0.009$, Beta=0.177 95%CI [0.048-0.650]).

**DISCUSSION:** Tic disorders are neuropsychiatric disorders starting in the childhood period which have an unclear etiology and heterogenic manifestations. In this study, antipsychotic agents used in children with tic disorders were evaluated in a clinical sample with a cross-sectional study design. Several studies reported that comorbidities in tic disorders are frequently seen, and the most common of them are ADHD, OCD, SLD, and anxiety disorders. In our samples, OCD frequency was found lower than in the literature. Lower OCD rates found in this study might result from the relatively limited size of our sample.

It has been reported that atypical antipsychotic agents are more frequently chosen drugs for treating tic disorders than other psychotropic agents. In our study, aripiprazole and risperidone were found the most used agents to treat tics, consistent with the literature. The reason may be that these two atypical antipsychotic drugs are very well-known as safe to use during childhood with lower adverse-effect profiles. It might also be possible that a lack of alpha-2 agonists in our country for the treatment of tics could lead to an increase of using antipsychotic drugs.

ADHD comorbidity in tic disorders was reported as seen at a rate of 20-90%. In our study, every one out of four children with tic disorders also had an ADHD diagnosis, which is consistent with the literature. This could also explain the rate of agents (17%) that are used for ADHD treatment such as MPH and ATX. Using SSRIs would be associated with the presence of comorbid anxiety disorders and OCD.

Half the sample did not use any psychotropic agents. This is consistent with any treatment guidelines for tics, explaining that psychosocial interventions were used at the first stage of developing tics in these patients.

TS has more severe clinical manifestation on account of its chronic nature and presence of emotional and behavioral problems accompanying it. As one of the predictors of using psychotropic medication, having TS could very well associate with its clinical presentation. Comorbid situations in tic disorders are known to increase the deterioration of the functioning. For this reason, it is no surprise to find that another predictor of using pharmacotherapy was the presence of any psychiatric comorbidity. It is, however, very

noticeable that although comorbidity presence and having TS were found as predictors of using drugs in tic disorders, comorbidity was not found as the predictor of using antipsychotic drugs. This could be explained as firstly chosen drugs were the primary treatment option (MPH, ATX, and SSRIs) of the accompanying disorders to the tics instead of the antipsychotics.

All in all, for an optimum treatment of tic disorders, comorbid situations accompanying tics are also be considered. Management of tic disorders should be comprehensive, including education, behavioral approaches and psychopharmacotherapy.

**CONCLUSION:** This is a descriptive study of children with tic disorders, and findings point out Tourette Syndrome and having another psychiatric disorder are prominent elements for the use of psychotropic medication.

Generally our results are consistent with the literature. Generalization of all results is not possible, though, because of its small sample and its cross-sectional nature. There is a need to study in this fields with prospectively planned, multi-center research with and larger samples to evaluate tic disorders and antipsychotics use.

**Keywords:** Tic disorders, children, antipsychotics

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**[Abstract:0695]** ***Biological psychiatry and neuroscience***

## Arterial stiffness measurements in patients using atypical antipsychotics

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**OBJECTIVE:** Patients with serious mental illnesses such as schizophrenia and bipolar disorder have a 25- to 30-year shorter life span, and the main reason of increased risks of morbidity and mortality is cardiovascular disease (CVD) and stroke compared to the general population[1-2]. Epidemiologic investigations suggest that these patients have an increased prevalence of cardiometabolic risk factors, such as overweight and obesity, dyslipidemia, diabetes, hypertension, and smoking. Treatment with second-generation (atypical) antipsychotic medication can also be associated with adverse metabolic effects. Some of them are associated with substantial weight gain and adverse metabolic effects, while others have less prominent effects on these aspects. Arterial stiffness has been identified as an independent risk factor for atherosclerosis and cardiovascular disease. Several indices have been developed to characterize arterial stiffness, of which pulse wave velocity (PWV) is the most recognized and established index[3], because it is very evidential and measurable by commercially available devices. The parameter of real spreading of the pulse wave in the arterial system is pulse wave velocity (PWV) or pulse transit time (PTT), related according to PWV=L / PTT. L is the longitudinal distance of two points between which the velocity is measured. The PWV and PTT increase as large arteries stiffen with age or disease processes.

In this paper we examine the vascular indices as PWV, PTT (Pulse Transit Time) in patients with schizophrenia and bipolar disorder who widely use antipsychotics that are known to be associated with adverse weight and metabolic effects.

**MATERIAL AND METHODS:** Patients with diagnosis of schizophrenia or bipolar disorder judged to be clinically stable on treatment with oral quetiapine (QUET n=16), risperidone (RISP n=13), olanzapine (OLZ n=15) and aripiprazole (ARP n=13) for at least 6 months and controls (n=40) were recruited into the study. Mean upper limb vascular indices (PWV, PTT), pulse rate, SDB (systolic blood pressure), and DBP (diastolic blood pressure) were compared by Independent sample test in all patients and medicine groups and were also compared to the control group. The pulse waves were recorded via a pulse oximeter transducer using the Neuro-MEP-Micro (v.2009) electromyography device (Neurosoft Medical diagnostic equipment, Ivanovo, Russia), in supine resting condition. The distance between the sternal notch and the index finger pulp was measured in meters. The upper limb pulse wave velocity was calculated by dividing

distance by pulse transit time.

**RESULTS:** The subjects in the psychiatric disorders group had a mixture of diagnoses as follows: schizophrenia (n=18) and bipolar disorder (n=39).The differences between the age and gender compositions of the patient and control groups were not significant (p>0.05). Most of the patients' (n=50) FRS score were in Group 1, 4 of them were in group 2, and 1 of them was in group[3]. Pulse rate, SBP, DBP, and PWV were higher, RRI (R-R Interval) was lower in the all patient group than in controls (p≤0.05). Pulse rate was higher in drug groups except ARP group, HDL cholesterol and SBP were higher in RISP group, total cholesterol was higher in QUET group, DBP was higher in all drug groups. PWV was higher in all medication groups but statistically significant in QUET and OLZ groups. (p≤ 0.05).

**CONCLUSIONS:** The presence of psychiatric diagnoses and use of atypical antipsychotic drugs is associated with changed vascular indices. Measuring arterial stiffness using the PWV values is a noninvasive, cheap and easy-to-apply clinical approach to determine early vascular changes in this group of patients and may be an important surrogate marker to assess subclinical atherosclerosis and the worsening of arteriosclerosis during treatment in psychiatric patients.

**Keywords:** atypical antipsychotics, pulse wave velocity, pulse transit time, arterial stiffness, atherosclerosis

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**[Abstract:0716]** ***Autism spectrum disorders***

## Reassesment of pervasive developmental disorder-not otherwise specified outcome according to DSM-5 diagnostical criteria

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**OBJECTIVE:** Autism Spectrum Disorders (ASD) are developmental disorders characterized by deficits in social relating, communication impairments, and the presence of restricted interests and stereotyped behaviors[1]. While they are classified as "Pervasive Developmental Disorders (PDD)" in DSM-4-TR, DSM-5 defined a single category "Autism Spectrum Disorder". With this change, the concern that some cases will remain outside of the diagnosis has been an important research topic. Certain studies indicate that that only 60-63% of individuals who were diagnosed as PDD with DSM-4-TR are diagnosed as ASD when reevaluated with DSM-5[2,3]. In this study, we investigate cases under 6 years of age diagnosed as PDD-NOS with DSM-4-TR to establish if they receive a diagnosis of ASD with DSM-5. If a patient is not diagnosed with ASD, we investigate whether the patient is diagnosed with Social Communication Disorder (SCD), which is a new diagnosis introduced with DSM-5.

**METHOD:** Patients between the ages of 0 and 6 diagnosed with PDD-NOS by Ege University Disabled Health Committee in 2010-2011 have been enrolled. Kiddie-Schedule for Affective Disorders and Schizophrenia (K-SADS) was administered for each participant in the study. All participants were diagnostically reevaluated by a questionnaire form which examines ASD and Social Communication Disorder diagnosis criteria based on DSM-5. Children Autism Rating Scale (CARS) was administered for every participant in the study and Aberrant Behavior Checklist (ABC) was completed by their parents.

**RESULTS:** Parents of 28 of the 150 patients diagnosed by the committee accepted to participate in the study voluntarily. Patients in this study were 23 boys and 5 girls. The mean age of the children at the time of first diagnosis was 3.79 years (SD=1.22) and their current mean age was 8.18 years (SD=1.80). As a result of reevaluation, while 18 patients (64.3%) were diagnosed as ASD according to DSM5, 10 of them (35.7%) were not. According to DSM-5, the mean CARS scores of diagnosed and undiagnosed children were found as 30.47 (SD=6.64) and 20.20 (SD=3.21), respectively. CARS score was significantly correlated with diagnosis of ASD according to DSM5 (p<0.001). Likewise, according to DSM-5, the mean ABC scores of diagnosed group and undiagnosed group were found as 40 (SD=24.42) and 11.50 (SD=9.22), respectively, and ABC score was significantly correlated with the diagnosis (p=0.002).

CARS score was significantly correlated with the severity of ASD diagnosis according to DSM-5 (p=0.027). However, ABC score was not correlated with the severity of ASD diagnosis according to DSM-5 (p=0.370).
Comorbid psychiatric disorders according to K-SADS in the ASD-diagnosed group were found as ADHD in 6 children, depression in 1 child, conduct disorder in 1 child, enuresis in 2 children, encopresis in 1 child, and tic disorder in 1 child. Only in 1 child, ADHD was found as a comorbidity in the undiagnosed group.
**CONCLUSION:** In spite of the limited sample size of our study, it was observed that 64.3% of patients met criteria for ASD based on DSM-5 at re-evaluation after 4 years from the first diagnosis. None of the cases which were not diagnosed as ASD met the criteria of Social Communication Disorder, which is a new diagnosis in DSM-5; however, this result might be related to the limited size of our sample. Psychiatric disorders were found more common in the ASD-diagnosed group. In this study, we observed that there was a statistically significant correlation between ASD diagnosis based on DSM-5 and CARS and ABC scores. The results of our study and the present literature were found to be consistent. We consider that it would be convenient to support these findings with other studies in Turkey with an increasing sample size.
**Keywords:** autism spectrum disorder, diagnosis, DSM-5

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**[Abstract:0794]** ***Biological psychiatry and neuroscience***

## Cortical gray matter variations in young women at high risk for familial depression and their depressed mothers with (positive) family history

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**INTRODUCTION:** Major depressive disorder (MDD) is one of the most prevalent psychiatric disorders, which leads to significant social and economic burden across the world. One way to increase knowledge about pathophysiology is to understand how the pre-disease state processes to the disease state. The pre-disease state can be best studied in the high-risk populations who have higher chance of proceeding to disease. First degree relatives especially the offspring of patients are accepted as high-risk groups. Researchers were able to observe structural and functional abnormalities in the high-risk groups. Miskowiak et al observed increased anterior cingulate and dorsomedial prefrontal cortexes, pre-supplementary motor area with parietooccipital areas activation to happy or fearful faces in healthy twins with a co-twin history of depression[1]. On the other hand, Chen et al reported reduced hippocampal volume in girls of depressed mothers[2]. The primary aim of this study was to investigate the cortical grey matter volume alterations in young women who were at risk for familial depression. The secondary aim was to perceive if those alterations were parallel with their MDD diagnosed mothers.
**METHOD:**
**Subjects:** After approval by the Ethics Committee of Ege University and the recruitment via Internet advertisements and by invitation from the hospital database between 2009-2013, we screened 53 pairs of depressed mothers with their daughters. Among these pairs,

24 women with the diagnosis of MDD with recurrent episodes (mean age: 46.2±3.9 years) and their healthy daughters (the high-risk for familial depression group; HRFD) aged between 18-26 (mean age: 22.3±2.1 years) were included. The recurrent MDD diagnoses weremconfirmed by Structured Clinical Interview for DSM-4 (SCID). iInclusion criteria for the MDD mothers were; being free from clinically significant depression (Hamilton Depression Rating Scale (HAM-D)<16), having no other axis I diagnoses, having at least one healthy daughter with no history of depression between the ages 18-25, having a first-degree relative with an MDD diagnosis, having no history of psychotic symptoms. Patients with chronic medical illness and those who had relatives with bipolar disorder or schizophrenia were excluded. The control group was composed of age similar 24 healthy mothers (mean age: 47.3±5.6 years) who had healthy daughters of similar ages (mean age: 22.1±2.1 years) to the high-risk group. The healthy daughters of the control group constituted the low-risk for familial depression group (LRFD). Exclusion criteria for control groups were; any current or past psychiatric disorder confirmed with SCID, having any first-degree relative diagnosed with major depression, bipolar disorder or schizophrenia, having a chronic medical illness, having significant childhood trauma (e.g. sexual or physical abuse).

Mothers and daughters gave their written informed consent after receiving a full explanation of the study's purpose and procedures. Mothers in the MDD group continued their ongoing treatment and no treatment modification was done for this study. Depressive symptoms were assessed by HAM-D and Beck Depression rating scales on the same week for MRI scan.

**MRI Acquisition:** 3D T1 weighted, sagittal, magnetization prepared rapid gradient echo (MPRAGE) scans of the head, 2D T2 weighted axial, Turbo Spin Echo (TSE) scans of the whole brain and 3D coronal fluid attenuated inversion recovery (FLAIR) scans were acquired on a Siemens Magnetom Verio, Numaris/4, Syngo MR B17, 3T MR scanner. TSE and FLAIR scans were used for clinical evaluation and MPRAGE scans were used in the region of interest (ROI) analysis.

**Image Processing:** For image processing we used FreeSurfer Software and it's recommended mainstream pipeline to segment gray matter volumes.

**Statistics:** Sociodemographic and clinical variables were compared by t- or chi-square tests for MDD vs Controls and HRFD vs LRFD separately. Analyses of co-variance (ANCOVA) were used to compare the grey matter volume in each ROI. Total Intracranial Volume (ICV) was accepted nuisance variable for ANCOVA analyses. Due to multiple comparisons, we reported both uncorrected and false discovery rate (FDR) corrected p values adjusted to 0.05. The correlation between grey matter volumes in ROIs with clinical parameters were assessed by Pearson correlation test.

**RESULTS:**

**Sociodemographic and Clinical Variables:** There were no differences in age or education status among the MDD vs controls and HRFD vs LRFD. We observed higher Beck and HAM-D scores not only in MDD but also in the HRFD compared to controls and LRFD.

**Neuroimaging Variables:** We observed greater grey matter volumes in right anterior cingulate and entorhinal cortexes in HRFD compared to LRFD. The difference in the right anterior cingulate cortex was preserved after FDR correction.

We observed smaller ICV in the control group compared to MDD ($t=3.2$ $df=46$ $p<0.01$). ANCOVA relieved that MDD had greater grey matter volume in left inferior frontal cortex. However, this difference was disappeared after FDR correction.

There were no correlation between any of the clinical variables and the GM values obtained from ROIs.

**DISCUSSION:** This study investigated the cortical GMV of a group of young women who were at risk for familial depression and was able to confirm altered GMV in the right anterior cingulate and entorhinal cortex in this population. Our secondary aim of comparing GMV alterations observed in HRFD with their depressed mothers was partially reached because of weak differences between MDD and control groups. Despite our expectations, we found increased GMV in MDD group at left inferior frontal cortex, which was lost with multiple comparisons correction.

The most prominent finding of this study is increased GMV at the right anterior cingulate cortex (ACC) in HRFD while there was no volume alteration in the depressed mothers. ACC has connections with various brain areas including limbic system and dorsolateral prefrontal cortex. These two regions with ACC have significant role in executing working memory, language, attention, and information processing and affect regulation. It is well known that those cognitive functions and affect regulation are impaired in depressive patients. Therefore, it is thought that ACC is one of the major dysfunctional areas in MDD. While the functional neuroimaging studies have consistently supported dysfunctional ACC in MDD patients, such consistency has not emerged from the studies using structural neuroimaging methodology. One study investigated the rostral ACC in healthy children with depressed mood and found significant reduction only in male children[3]. In a three generation study, Peterson et al showed cortical thinning in the lateral surface of right hemisphere while thickening in the subgenual, anterior and posterior cingulate cortex[4]. With the current non-depressed status of HRFD group, our findings of increased GMV in ACC and entorhinal cortex -which were absent in their depressed mothers- might be related to resilience to depression.

We also observed increased GMV in the right entorhinal cortex of HRFD group, which is the main interface between neocortex and hippocampus. It plays an important role in memory formation and consolidation that are impaired in MDD. It has been proposed that volumetric alterations in entorhinal cortex lead to impairment of the cortical-hippocampal circuit and that these structural changes have been implicated in the etiology of depression

We found no major GMV difference between MDD and healthy controls in selected brain regions. In this study, we used ROI based approach that gives the mean values of the whole GMV in the selected regions and smaller local alteration might be missed by this

method. Despite this disadvantage of ROI approach, it has advantages of better registration over voxel-based approach. It should be kept in mind that we investigated certain areas of brain to test our hypothesis. Therefore, it would be premature to conclude that there is no regional GMV differences between MDD and controls.

One strength of this study is to include the mothers and their daughters as couples in both arm of the comparison. On the other hand, the main limitation was small subject number in each group. Obtaining our data from female subjects also limits us to generalize our findings for male high-risk population.

As a conclusion, we provide evidence for GMV alterations in high-risk populations for familial depression. As those regional GMV alterations were not observed in depressed mothers, these regional alterations might help the young women at risk to be depressed free. Longitudinal follow-up studies are needed to interpret the high-risk data and determine the anatomical alterations related to vulnerability and resilience to disease.

**Keywords:** anterior cingulate cortex, familial depression, resilience

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**[Abstract:0822]** ***Addiction***

## Relations between attachment to people, attachment to god, perception of God and addiction severity in an islamic population in Turkey

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**INTRODUCTION:** Alcohol and drug dependency are becoming a serious problem worldwide. While alcohol and drug addiction prevalence varies among countries, addiction prevalence rates have been reported as high as 4-9% in the USA. Lifelong addiction/abuse rates are estimated to be 13.8% for alcohol and 6.2% for drugs.

Addiction increases mortality 4.25-fold in intravenous drug use, and drug users are more prone to contract HIV and genital infections. Recently in our country, mortality events are increasing due to use of "bonsai", which is a local mixture of various addictive drugs. In alcohol/drug abusers, suicidal events are frequent (up to 16-71%), often accompanied by psychiatric disorders such as antisocial personality disorder, schizophrenia, or bipolar mood diseases.

Although Edlund could not find a relationship between drug addiction and religious beliefs, there are many studies reporting an inverse relationship between alcohol / drug addiction and religious faith. Kelly found a higher treatment response among religious cases in their studies, but the mechanism is not clear. Religious people have been found to have a low prevalence of drug and alcohol abuse because almost all religions have a negative attitude towards addiction and abuse.

Studies involving religious living and belief in God in psychiatric diseases are limited in Muslim countries. In our study, we aimed to investigate the influence of religious beliefs on drug/alcohol addiction severity and psychopathologic dynamics among patients.

**METHODS:** We studied 139 patients who had been admitted consecutively to the outpatient clinic for Alcohol and Drug Research, Treatment and Training Center (AMATEM) at Ankara Numune Hospital in Turkey between May and July 2013 with a diagnosis of drug and alcohol dependency. We performed a cross-sectional study. Instruments we used for the study were Addiction Profile Index (API), God Perception Scale (GPS), Attachment to God Scale (AGS), and Adult Attachment Scale (AAS).

**Addiction Profile Index:** API is a self-report questionnaire consisting of sociodemographic data containing 37 items. API involves the following 5 subscales: characteristics of substance use; diagnosis of dependency; effects of substance use on the user; craving; motivation to quit using substances. Development, validity and reliability assessments of the scale were made by Ogel et al.

**God Perception Scale:** GPS is for measuring an individual's perception of God. There are 22 self-report items. High scores show positive (loving/love based) perception, low scores show negative (punitive/fear-based) perception. Validity and reliability studies of the scale were made by Guler.

**Attachment to God Scale:** It contains 24 self-report items and evaluates the attachment to God as secure or anxious. Validity and reliability studies of the scale were made by Korkmaz.

**Adult Attachment Scale:** There are 18 items in a yes-no response form for the evaluation of three types of attachment, namely, secure, avoidant, and anxious/ambivalent. Validity and reliability of the scale were established by Kesebir.

Statistical analyses were conducted using SPSS Statistics 20.0 program. For comparison of means, student t-test and one-way ANOVA test were used for parametric data, Mann-Whitney U and Kruskal Wallis tests for nonparametric data. Descriptive information is presented as N (%). Categorical group was compared by the Chi-Square test. Correlation analyses were performed by Pearson and Spearman Correlations. P-level was set to 0.05.

**RESULTS:** There were 133 males and 6 females, ages 18-65 years. Mean age was 27.84±8.99 (min 18-max 65). 51.1 percent of patients were between 18 and 25 years. 56 patients (40.3%) had been educated for 13 or more years. 133 patients (95.7%) were men, only 6 patients (4.3%) were women. 103 patients (74.1%) were single and 36 patients (25.9%) were married. 44 patients (31.7%) had children.

19 patients (13.7%) were using alcohol, 68 patients (48.9%) were using heroin and 52 patients (37.4%) were using alcohol and heroin/other substances together. The scores of GPS, AGS and AAS did not differ by type of addictive substance. According to cut-off score of 10.7 at API, 93 (66.9%) of the patients were highly dependent and 46 (33.1%) of the patients were slightly dependent. AGS scores and anxious/ambivalent attachment scores of AAS were significantly higher in the highly dependent group. Conversely PGS scores were high in the slightly dependent patients.

AGS-2 was correlated with Total API scores and subscales exact API-1. Anxious/ambivalent attachment scores of AAS were correlated with Total API and API-4 (craving). API-4 (craving) was correlated with AGS-2 scores (p=0.001, r=0.282), anxious/ambivalent attachment scores of AAS (p=0.010, r=0.218) and PGS scores (p=0.014, r=-0.209). API-5 (treatment motivation) was correlated with AGS-1 and 2.

Anxious/ambivalent attachment of AAS was correlated with AGS-1 (r=-0.190, p=0.026), AGS-2 (r=0.184, p=0.031), PGS (r=-0.516, p=0.000).

**DISCUSSION:** In our study of 139 addicts, 133 were male and 6 were female. Rates of alcohol addiction was 13.7%, heroin addiction 37.4% and mixed addiction was 48.9% among the cases. We found that 66.9% of the patients had high addiction profiles and 33.1% low addiction profiles. Cases with anxious/ambivalent adult attachment had high addiction profiles. Patients with secure and avoidant adult attachments did not exhibit such a relation. A review reported a study with 71 German opiate using, drug dependent adolescents (DDAs) and 39 non-clinical controls. Fearful attachment was predominant in DDAs, while controls were predominantly secure. Severity of drug use was positively correlated with fearful attachment. Our results were in accordance with this study.

The addicts with anxious/ambivalent God attachments showed high addiction profiles, which is not encountered in cases with secure God attachment in this study. Similarly, Horton examined 328 college students and showed that secure attachment to God was not inversely associated with recent alcohol or marijuana use or any other substance use. Avoidant and anxious attachment to God are associated with higher levels of addiction.

The Attachment Theory was first suggested by Bowlby, who is a pediatric psychoanalyst. This theory says that the attachment fashion, which is formed early in the infancy period between mother and baby, does extend into adult life and influences cognitive and emotional development. The attachment pattern between mother and baby determines the person's future self-confidence, social attitudes, self-respect, occupation selection, and marital status. This theory may be applied to religious beliefs and may be used as a tool for explaining of psychologic disorders. Kirkpatrick and Shave tried to bring together attachment theory and spirituality in their study. The correspondence hypothesis of Kirkpatrick makes direct relation between religious attachment and childhood mother attachment.

When we evaluate our results, cases with punitive/fear based God perception showed high addiction profiles, in contrast to low addiction profiles of cases with loving/love based perceptions, as we expected. Almost all schools like the school of subject associations, the transpersonal school, and the phenomenological school in psychotherapy tried to explain the relationship between God perception and the perception of self and the world according to their point of view. As a result, perception of God and its positive or negative fashion is a result of a person's environment, information, and religious background.

In our study, we found a relationship between anxious adult attachments and negative god attachment patterns. However, we could not find this for persons having secure attachments. Such a result suggests a role of negative adult attachment patterns in the formation of negative God attachment patterns. Hence the influence of God attachment may exhibit a positive impact on dealing with psychiatric disorders, especially in addiction. It is believed that persons who are attached to God in a secure pattern live a more positive social and emotional life. They have stronger social relations and more optimistic approaches. According to the Attachment Theory, persons with a lovely/merciful attachment to God have higher self-confidence and self-respect. Persons with anxious attachment to God seek and expect stronger and more emotional religious feelings, while persons with an avoidant attachment pattern frequently avoid having close relations with God and beliefs. In particular, we can think that a punitive God perception may have a stronger impact on a person's adult attachment in an Islamic population.

We found higher craving rates among cases with negative adult attachment pattern, negative God attachments, and negative God

perception in both alcohol and drug users. Thorberg et al. found that anxious attachment partially mediated the relationship with craving in a heavily drinking population. Thus, abusers which attach anxiously probably require a secure field or need unconsciousness to divert in their lives.

While attachment theory may be applied to many other psychologic conditions, our study showed, similar to many previous studies, a probable link between attachment theory and religious perceptions. Negative religious attachments were more linked to severity of alcohol/drug addictions than positive attachments. The attachment starts with the mother-baby relation and probably influences the relation with God and determines our beliefs. According to our study, the addiction pathology was related to religious perceptions, and the type of addictive drug was found related with addiction severity. We also suggest a complete approach in addiction treatment consisting of family life, religious perceptions, and general psychopathology. Such an approach may also be applied to government policies and future studies.

**Keywords:** addiction, attachment, religion

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**[Abstract:0827]** ***Mental health, economics and services research***

## Relationships between psychiatric symptoms and levels of serum serotonin and salivary cortisol in healthy subjects

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**OBJECTIVES:** Healthy individuals may experience Psychiatric symptoms (PS) due to the effect of various stressors. Particularly, fluctuation of serotonin (5-HT) and cortisol levels contribute to psychiatric disorders and their etiologies ad hoc. 5- HT and cortisol levels both influence the etiology and also affect the emergence of psychiatric disorders. In some studies, 5-HT and 5-HT agonists caused to secrete corticotropin-releasing hormone by stimulating the hypothalamo-pituitary-adrenergic axis from the hypothalamus, and interactions with the levels and number of 5-HT receptors have been shown. PSs which do not affect functionality and are encountered in healthy subjects usually have been classified in symptoms checklists. The purpose of this study is to investigate the relationship between PSs and levels of serum serotonin and salivary cortisol in healthy individuals.

**METHODS:** For this study, 320 subjects, including 156 males and 164 females, who do not have a history of psychiatric illness or psychiatric treatment and follow-up were enrolled. The subjects were between 20 and 45 years of age. Participants were informed that the investigation aimed to establish the relationship between PSs and levels of serum serotonin and salivary cortisol. They were interviewed face to face by a psychiatrist. Subsequently, the participants were given the sociodemographic form and the SCL- 90-R. In order to collect salivary samples, we asked them to brush their teeth, not to smoke and not to take any drinks other than water for 8 hours before sampling. On the sampling day, we collected blood and saliva samples from the participants. For the measurements of 5-HT and cortisol, the ELISA method was used. Global symptom index (GSI) was used to assess the cases. If GSI is under or equal to one, psychiatric symptom scores are not assumed psychopathologic. But if it is above 1, they are admitted as psychopathologic. Participants were divided into two groups according to GSI ≤1 and GSI >1 and were compared with sociodemographic subgroups. Data were assessed with SPSS 15.0 version.

**RESULTS:** Baseline characteristics are: 51.2% (n=164) were women, 54.4% (n=174) were single, 55.0% (n=175) had been enrolled in school

for 13-16 years, 52.8% (n=169) were clerks. The mean age of the cases was 29.19±8.41. When we analyzed PSs of the 320 participants in our study, the highest PS scores were in the obsessive-compulsive-symptoms subgroup (0.92±0.80), interpersonal-sensitivity subgroup (0.75±0.55) and depressive-symptoms subgroup (0.72±0.53), respectively. We found a negatively significant correlation between PS scores and levels of 5-HT and cortisol, respectively (somatization; r=-0.209 p<0.001, r=-0.156, p=0.005; anxiety, r=-0.184, p=0.001, r=-0.177, p=0.001; depression, r=-0.209, p<0.001, r=-0.194, p<0.001; obsessive-compulsive, r=-0.136, p=0.015, r=-0.133, p=0.017; psychoticism, r=-0.168, p=0.003, r=-0.147, p=0.008). There was a negatively significant relation between the ages of participants and levels of 5-HT (r=-0.156, p<0.005). In contrast, there was a positively significant correlation between levels of 5-HT and cortisol (r=0.489, p<0.05). In our samples, who had GSI≤1, PS scores were lower and levels of 5-HT and cortisol were higher than in those with GSI>1. We found a significant difference in PS scores according to sex and years of education (groups other than obsessives and additional symptoms). Women's PS scores were higher than men's, but the levels of 5-HT and cortisol were lower. We also found a significant difference in PS scores and levels of 5-HT and cortisol between women and men. There was a negatively significant correlation between somatization and psychoticism scale and levels of 5-HT and between phobic scales and cortisol in men. In contrast, there was a negative correlation between somatization and hostility scales and levels of 5-HT in women. Divorced individuals' PS scores were the highest, levels of 5-HT and cortisol were lower than others'. Single people's PS scores were the lowest, levels of 5-HT and cortisol were higher than others. There was a significant difference between PS scores and levels of 5-HT between the groups. We also found a negatively significant correlation between PS scores and levels of 5-HT and cortisol between the groups. 5-HT and cortisol levels were lowest in 5-8-years educated group. It was the highest in the group who were 9-12 years educated. PS scores of the 17-years-and-more educated were the lowest in this study. PS scores were the highest in cases who went to school between 5 and 8 years. There was a significant difference between PS scores and 5-HT levels among the groups. We found a negatively significant correlation between PS scores and 5-HT levels in the 13-16-years educated and 17-years-and-more educated groups (p<0.05) and also a negatively significant correlation between PS and cortisol levels in the 19-12-years educated. PS scores and 5-HT and cortisol were the highest in self-employed workers, but lowest in employees. There was a significant difference in 5-HT levels among the two groups (p<0.05). We found a negatively significant correlation between PS scores and 5-HT levels in unemployed, but also a negatively significant correlation between PS scores and 5-HT and cortisol levels in clerks. There was no correlation to professional status in the other groups.

**CONCLUSIONS:** Healthy subjects have psychiatric symptoms as well. There was a correlation between PS and 5-HT and cortisol levels. This correlation has arisen from socio-cultural structure and characteristics. Capabilities and defense mechanisms, which they have been used to, allow individuals to overcome these stress factors. Mental symptoms vary from person to person, place of living, socio-cultural characteristics and according to work and stress event. Not only serotonin and cortisol but also the impact of various life events, personal characteristics, and the response to these events are supposed to be effective in determining the onset of these symptoms. There is need for a study of these determinants how they affect the serotonin and cortisol levels.

**Keywords:** cortisol, healthy subject, psychiatric symptom, SCL-90-R, serotonin

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