[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 χ^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