Neuropsychological correlates of ADRA2A(rs1800544) and COMT(rs4680) polymorphisms in Turkish ADHD patients

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Introduction
The complex etiology of ADHD has a strong genetic component. ADRA2A (rs1800544) and COMT (rs4680) polymorphisms are two of the most studied gene polymorphisms in ADHD etiology. However, there is still debate about their indication of creating different neuropsychological phenotypes in ADHD. In this study, we aimed to investigate the effects of these polymorphisms on neuropsychological traits among Turkish ADHD patients. Also, the relationship between ADHD symptoms, subtypes and neuropsychological test variables were studied.

Methods
To examine the phenotypic discrepancies of these genotypes, Continuous Performance Test (CPT) and Trail Making Tests (TMTA-TMTB) were conducted for 121 genotyped ADHD patients between 6-18 years old. Omission- commission errors and mean response time were used as CPT variables. Besides this, completing times, errors and corrections were the variables recorded for TMTA and TMTB. Mental retardation was excluded with Wechsler Intelligence Scale for Children-4 (WISC4)/Wechsler Intelligence Scale for Children –Revised (WISC-R) in the study. Diagnosis and subtype discrimination were confirmed and comorbidities except learning and disruptive behaviour disorders were excluded by using the Kiddie Schedule for Affective Disorders and Schizophrenia (K-SADS). Clinical Global Impression –Severity Scale (CGI-S) documented clinical severity, whereas Global Assessment of Functioning Scale (GAS) stated clinical functionality. Conners’ Parent (CPRS) and Teacher Rating Scales (CTRS) were used for determining ADHD symptoms and severity. The statistical analyses were conducted with SPSS 21.0. Mann-Whitney U, Kruskal-Wallis, Spearman correlation tests were used and p<0.05 was accepted as statistically significant for the results.

Results
No relationship was detected between ADRA2A, COMT polymorphisms and CPT, TMT variables. CPT commission errors were found more frequent in the combined subtype, while TMTA corrections were more seen in the inattentive subtype. The learning problem subscale of CPRS and hyperactivity, behaviour problem subscales of CTRS were found associated with CPT commission errors. The hyperactivity, oppositional behaviour subscales of CPRS were related to TMTA errors and corrections whereas behaviour problem subscale of CPRS was only associated with TMTA corrections. The hyperactivity and behaviour problem subscales of CTRS were found correlated with TMTA completing time, errors and corrections. Only attention deficiency subscale of CTRS was found associated both with TMTA corrections and TMTB completing time and errors. CPT parameters were found associated with neither clinical severity nor functioning. However, low clinical functionality (<50% GAS score) was associated with longer TMTA-B completing time and more corrections.

Conclusions
ADRA2A and COMT polymorphisms were not found to be associated with a specific neuropsychological phenotype. While CPT did not predict clinical severity or functioning, longer TMT completing time and more TMT corrections were found associated with lower functionality. Although the results of neuropsychological tests were in accordance with ADHD subtypes, neuropsychological traits did not differ in a homogeneous manner in ADHD patients. Consequently, instead of using the neuropsychological traits in distinguishing groups, they may be helpfully used for supporting clinical evaluation in ADHD. In addition, further studies with whole genome sequencing technics are warranted to better understand the role of polymorphisms in ADHD etiology.