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The association of catechol-O-methyltransferase (*COMT*) gene variants with childhood attention-deficit/hyperactivity disorder (ADHD)

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Background: Attention-deficit/hyperactivity disorder (ADHD) is a multifactorial, highly heritable developmental disorder characterized by behavioral symptoms of impulsivity, hyperactivity and/or inattention. The enzyme catechol-O-methyl transferase (*COMT*), which is responsible for the degradation of catecholamines, could have an important role in genetic susceptibility to ADHD. *COMT* could play a significant role in modulating dopamine levels in the prefrontal cortex which was implicated in ADHD aetiology. We aimed to analyze the association of *COMT* Val108/158Met (rs4680) polymorphism which affects *COMT* activity with ADHD features since genetic studies of the functional Val158Met polymorphism in ADHD have been inconsistent.

Methods: The study included 113 medication free children with ADHD diagnosed according to the DSM-IV criteria and 187 children without psychiatric diagnoses and free of medication that served as control group. Genotyping was done using the TaqMan SNP Genotyping Assay.

Results: We found an association between Val108/158Met polymorphism and the symptoms of ADHD in male, but not in female children. Lack of association in female children is probably due to a small number of female patients with ADHD, which represents the limitation of this study. An association with ADHD features was also found when comparing Val carriers to Met/Met homozygotes in male children. These differences were especially significant when comparing male patients with combined type of ADHD with healthy control subjects.

Conclusions: Our results confirmed the association between *COMT* variants and ADHD in male children, which was due to the higher frequency of Met/Met homozygotes in children with ADHD compared to healthy controls. These results suggest that carriers of the high activity *COMT* variant are less prone to develop ADHD. This study also suggests that *COMT* Val108/158Met polymorphism is associated with the ADHD combined subtype.