The divergent impact of COMT Val158Met on executive function in children with and without attention-deficit/hyperactivity disorder.


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Abstract
BACKGROUND:
Children with attention-deficit/hyperactivity disorder (ADHD) usually display deficits in executive function (EF), which are primarily mediated by prefrontal cortex (PFC). The functional polymorphism of COMT, Val158Met (rs4680), leads to observed polymorphic differences in the degradation of dopamine (DA) within PFC. Our present study aimed to explore the effect of rs4680 on EF using case-control design. In addition, considering the dynamic development of EF, we also attempted to investigate whether this genetic influence changes during development or not.

METHODS:
A total of 597 ADHD children and 154 unaffected controls were recruited. EF was evaluated using Rey-Osterrieth Complex Figure Test (RCFT), Trail Making Test (TMT) and Stroop Color-Word Test for working memory, shifting and inhibition. Association between genotype and EF was analyzed using analysis of covariance (ANCOVA).

RESULTS:
The results showed significant interaction effect of genotype and ADHD diagnosis on RCFT performance (P<0.001). However, the associated genotypes between ADHD and controls were divergent. In ADHD, the Met carriers performed better than the Val homozygotes on detail immediate [(10.38 ± 6.90) versus (9.33 ± 6.92), P=0.007] and detail delay [(9.96 ± 6.86) versus (8.86 ± 6.89), P=0.004], while Val/Val homozygotes showed better performance compared with Met carrier controls [for detail immediate (14.55 ± 6.18) versus (11.10 ± 6.45), P<0.001; for detail delay (14.31 ± 5.96) versus (11.31 ± 6.96), P=0.001]. We did not find significant interaction between genetic variant and development.

CONCLUSION:
COMT Val158Met (rs4680) may have divergent effect on working memory in ADHD children compared with healthy controls.