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1400 London Time (BST) / 0900 US Eastern time Wednesday 25 June 2200 Japanese Time / 2300 Australian Eastern time Wednesday 25 June

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## Enzyme variant may contribute to off-task behavior in ADHD

A single genetic change to an enzyme that regulates dopamine in the brain could account for the difficulties some children with attention-deficit hyperactivity disorder (ADHD) have staying on task. If confirmed, this finding could lead to a better understanding of the biological causes of this prevalent childhood disorder.

ADHD affects 8-12% of school-aged children worldwide with symptoms such as chronic problems with attention and hyperactive or impulsive behaviour. Recent research suggests that these children may also exhibit problems with 'executive function' – the higher-level thinking used to complete goals and stay on task.

Online in *Neuropsychopharmacology* this week, Ridha Joober and colleagues find that children with ADHD who have a specific genetic variant of the enzyme known as COMT are more likely to stray off task. Neuroscientists have demonstrated that COMT regulates dopamine levels in the prefrontal cortex, an area of the brain that controls executive function. The researchers

speculate that this particular variant of COMT is more active than the standard form of the enzyme, inducing greater clearance of the brain chemical dopamine, which helps maintain focus.

Despite this role, the COMT variant did not interfere with the efficacy of methylphenidate, a commonly prescribed treatment for ADHD that increases dopamine levels by blocking its transport primarily in the motor portion of the brain, the striatum. These findings suggest the importance of both the prefrontal cortex and the striatum in coordinating task-oriented behavior and how their dysregulation may contribute to the pathology of ADHD.

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