

# ADHD appears to be associated with depressed dopamine activity in the brain

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Adults with attention-deficit/hyperactivity disorder (ADHD) show a blunted response to the drug methylphenidate (Ritalin), which increases brain dopamine levels, according to a report in the August issue of *Archives of General Psychiatry*, one of the JAMA/Archives journals. This suggests that dopamine dysfunction may be involved with ADHD symptoms and may contribute to substance abuse that often occurs simultaneously.

ADHD is the most prevalent psychiatric disorder among children, according to background information in the article. "Despite decades of research, the specific neurobiological mechanisms underlying this disorder still remain unclear," the authors write. "Genetic, clinical and imaging studies point to a disruption of the brain dopamine system, which is corroborated by the clinical effectiveness of stimulant drugs (methylphenidate hydrochloride and amphetamine), which increase extracellular dopamine in the brain."

Nora D. Volkow, M.D., of the National Institute on Drug Abuse, Bethesda, Md., and colleagues studied 19 adults with ADHD (average age 32) who had never received medication and 24 healthy controls (average age 30). Brain scans were performed using positron emission tomography (PET) and a drug known as raclopride labeled with carbon 11 ([<sup>11</sup>C]raclopride), which binds with dopamine receptors. Scans were performed twice, after injections of placebo and of methylphenidate; the participants did not know which drug they had received. Participants also were asked to report the severity of their ADHD symptoms, whether they could detect the drug, if they liked or disliked it, and if it made them feel "high," tired, alert, anxious or restless.

In individuals with ADHD, methylphenidate caused less of a decrease in the amount of [<sup>11</sup>C]raclopride that bound to dopamine receptors in areas of the brain associated with attention than it did in those without ADHD. Since levels of methylphenidate in

the blood were the same in both groups, this suggests that those with ADHD released less dopamine in response to the drug than controls. This blunted response was associated with symptoms of inattention. Exploratory analyses also found evidence of reduced [<sup>11</sup>C]raclopride binding in the hippocampus and amygdala in those with ADHD. These areas of the brain are part of the limbic system, involved in emotional responses as well as consolidating and retrieving memories.

"The findings of reduced dopamine release in subjects with ADHD are consistent with the notion that the ability of stimulant medications to enhance extracellular dopamine underlies their therapeutic effects in ADHD," the authors write.

Individuals with ADHD also reported liking methylphenidate more than individuals without ADHD, the authors note. "The reinforcing responses to methylphenidate were negatively correlated with the dopamine increases, suggesting that decreased dopaminergic activity may also be involved in modulating the magnitude of the reinforcing effects of methylphenidate," they continue. "This suggests that dopamine dysfunction is involved with symptoms of inattention but may also contribute to substance abuse comorbidity in ADHD."

Source: JAMA and Archives Journals

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