Methylphenidate 'normalizes' activation in key brain areas in kids with ADHD

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The stimulant drug methylphenidate "normalizes" activation of several brain areas in young patients with attention-deficit/hyperactivity disorder (ADHD), according to a review published in the May *Harvard Review of Psychiatry*.

Studies using functional magnetic resonance imaging (fMRI) show increased activation of key brain areas after a dose of methylphenidate in young patients with ADHD, according to the systematic review by Constance A. Moore, PhD, and colleagues of the University of Massachusetts Medical School. They write, "In most cases, this increase 'normalized' activation of at least some brain areas to levels seen in typically developing children."

How Do ADHD Medications Affect the Brain in ADHD Patients?

In a research review, Dr Moore and colleagues identified nine previous studies using fMRI to study patterns of brain activation in response to a single dose of methylphenidate. Perhaps best known by the brand name Ritalin, methylphenidate is a common and effective treatment for ADHD. "Although methylphenidate has been shown to significantly improve the behavioral symptoms associated with ADHD, both the mechanism behind its therapeutic effect and its direct effects on brain function are unknown," the researchers write.

The studies evaluated methylphenidate-induced fMRI changes in various brain areas, as the participants performed different types of tasks. Most of the studies included adolescent boys with ADHD, along with matched groups of young people without ADHD.

Methylphenidate altered activation patterns in widely distributed areas of the brain in ADHD patients, the results showed. The main brain areas involved were the frontal lobes, the basal ganglia, and cerebellum: "Abnormalities in these regions have all been implicated in patients with ADHD," Dr Moore and coauthors write.

Different areas were activated during different types of fMRI tasks. Several studies assessed performance on "inhibitory control" tasks—the ability to control certain types of accustomed ("prepotent") responses. In three out of five studies, methylphenidate "at least partially normalized" brain activation in ADHD patients, compared to healthy young people.

Different Tasks Affect Different Brain Areas

A few studies showed similar normalization of brain responses with methylphenidate on tasks of selective attention and time perception—although not on tasks evaluating working memory. Methylphenidate mainly affected activation in the frontal lobes during inhibitory control tasks. During selective attention tasks, a wider range of brain areas were affected.

Since none of the studies evaluated ADHD symptoms on and off methylphenidate, there was no way to link the changes in brain activation with clinical improvement. Brain activation patterns with methylphenidate differed for patients who were versus were not previously treated with stimulants for ADHD.

Patients with ADHD have "age-inappropriate frequency or severity of

inattentive or hyperactive-impulsive behaviors," according to the authors. It affects about five percent of children worldwide, and a growing body of evidence suggests that ADHD persists throughout adolescence and into adulthood. Functional fMRI provides a safe, noninvasive way to study how stimulants like methylphenidate may act in the brain of ADHD patients.

The new analysis suggests that methylphenidate partially normalizes activation in key brain areas thought to be involved in ADHD. The studies "may provide evidence that methylphenidate facilitates the return of brain function in ADHD patients to, or close to, a typically functioning state," Dr Moore and colleagues write. They call for further research to confirm that methylphenidate-induced changes in specific brain areas are correlated with improvement in ADHD symptoms.

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