Differences in Brain Function Found for ADD

Source: Stanford University

Stanford neuroscientists have found a clear difference in brain functioning between boys who have attention deficit disorder [ADD] and those who do not, a step that could lead to better diagnosis of the most common developmental disorder of childhood.

Follow-up studies will be required before the results of this study on a small number of boys can lead to brain-based methods of diagnosis, caution the lead researchers, Research Associate Chandan Vaidya and Associate Professor John Gabrieli of Stanford's Department of Psychology.
Theirs is the first study, however, to show that Ritalin, the drug most commonly used to treat ADD, has different effects on the brains of people with and without ADD, and where those differences occur in the brain. The findings are reported in the Nov. 24 issue of the Proceedings of the National Academy of Sciences.

The study is also the first to use functional magnetic resonance imaging [FMRI] in the study of ADD. This imaging method can show brain differences in individual people, instead of in averages of differences of two groups. This is critical for diagnosis, which has to be established on an individual basis.

Unlike methods used in other studies of ADD, FMRI does not require injection or inhalation of radioactive substances. It relies instead on naturally occurring changes in brain function, which makes it appropriate for research and clinical purposes for children.

Co-authors of the study are medical doctors Glenn Austin and Hugh Ridlehuber and school psychologist Gary Kirkorian of the Community/Academia Coalition in Los Altos, Calif. and Gary Glover and John Desmond of the Stanford Medical Center's Radiology Department.

The findings have drawn considerable attention from neuroscientists because "ADD is so widespread, so controversial and confusing, and these are among the few clear findings in that field," said Gabrieli, who heads the brain imaging laboratory where the research was done.

Attention deficit disorder, which often includes hyperactivity, is currently diagnosed on the basis of subjective observations of youngsters' behavior. If the new findings can be replicated, he said, it might be possible to make a biological diagnosis of the disorder by using FMRI.

Since the common treatment for ADD is a prescription drug whose long-term effects on brain function are not known, parents and pediatricians most likely would welcome a more definitive way to diagnose the disorder.

In the study, 16 boys between the ages of 8 and 13 were asked individually to play a mental game while lying in a magnetic resonance imaging device, which was set to image front portions of the brain, including the frontal-lobe cortex and the striatal structures below it.

The boys, 10 of whom had been diagnosed with ADD and 6 of whom had not, were instructed to press a button when they saw any letter of the alphabet except the letter X on a display screen. Because most of the letters were not X, each child built up a predisposition to press the button and needed to control his impulse to press the button when he saw an X. The task was expected to be, and in fact proved to be, more difficult for the boys with ADD, because poor impulse control is one of the disorder's symptoms.

Comparing the brain images later, researchers found a clear difference in the activation of neuronal tissue in two structures in the striatal region, which is known to be involved in motor control. The brain activation differences between the boys with ADD and those without were even more dramatic when the subjects were asked to perform the same task after taking the drug Ritalin. Ritalin is a stimulant medication used to temporarily relieve symptoms of ADD, such as inattention, impulsivity and hyperactivity.

"Both the normal kids and the ADD kids got better in their impulse control when they had taken the drug," Vaidya said. "Ritalin improved everyone's performance, but how it actually did it differed in the brains."

The boys with ADD showed more activity in the affected striatal structures (specifically known as the caudate and putamen) when taking the drug than when not. The healthy boys, in contrast, showed the reverse - less activity in those areas when taking the drug than when not.

"From past work with adults and children, some of which required injecting radioactive material, a consensus developed that it is the frontal striatal circuitry of the brain that is what's not right with this disorder," Vaidya said. "That is why we imaged this part of the brain, and our study confirmed that these structures are, indeed, important for ADD."

Ritalin primarily, but not exclusively, influences dopamine neurotransmission. The opposite effects of Ritalin on boys with ADD and boys without the disorder suggest that ADD involves atypical dopamine modulation in the striatum, she said.

The researchers caution that the study was conducted with a small group and needs to be replicated with girls as well as with more boys before they can be certain they have found a universal neurobiological marker for the disorder. They also reported that they tried the experiment on three other boys who had not been diagnosed with ADD but who had siblings with the diagnosis. Two of the three siblings of ADD boys showed some Ritalin enhancement of the striatum, as did their affected brothers.

"This would lend some support to the idea that ADD may involve atypical genetic influences on dopamine modulation," Vaidya said, but more studies would be necessary to establish a genetic influence.

Because of the widespread interest in ADD, the researchers also were careful to point out other limitations of their study. A fraction of people diagnosed with ADD have not responded to Ritalin treatment, and this study did not include such children, they said. It also did not attempt to investigate possible changes in brain activation that might occur with the drug over time. The ADD boys did show a different brain activation level when not on the drug, but all of them had been taking Ritalin previously as part of their ongoing treatment.

Despite these limitations, the study points to new directions for research into brain function that could improve individuals' performance.

"This is one of the few studies to examine brain function in children, and to further our knowledge about normal and abnormal brain development," Gabrieli said. "It suggests that FMRI is a powerful tool to examine brain and behavior in the context of both normal and abnormal development."

Currently, ADD impairs the function of an estimated 3 to 7 percent of youngsters in home and school, and the long-term consequences include lower educational and vocational accomplishments for them as adults as well as an increased risk for drug abuse and other risky behaviors.

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