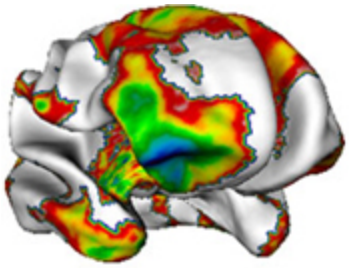
A Neurological Basis for ADHD

Scientists have identified a genetically determined pattern of brain development linked to ADHD.

by Emily Singer, 2007

1 A genetic variation that boosts risk for Attention Deficit Hyperactivity Disorder (ADHD) paradoxically appears to predict who will grow out of the learning disability. Scientists found that brain development in ADHD-afflicted children with this variation was out of whack at age 8 but normalized by 16. ADHD symptoms in this group were also more likely to disappear with age. The study is the first to identify a genetically-determined pattern of brain development linked to ADHD. And it indicates a real neurological basis for the disorder, which has been viewed by some as a scheme of medication promoters or the product of bad parenting.



2 ADHD brains: Scientists found that children with ADHD who had a particular genetic variation started out with an unusually thin cortex in the parts of the brain important for attention. But over time, their brains became similar to those of healthy teens. This time-lapse series of images shows how their brains normalized over time. The brightly colored sections indicate the parts of the brain that were most different in the ADHD group. These sections disappear as the children aged.

3 “This is the first step in individualizing treatment for ADHD based on genetic make-up,” says Philip Shaw, a neuroscientist at the National Institute of Mental Health in Bethesda, MD. Shaw led the study.

4 ADHD is one of the most common childhood disorders in the United States. It affects about three to five percent of school-aged kids. Scientists have already found several genetic variations that raise risk for ADHD, which is likely caused by a complex combination of genetic and other factors. The biggest genetic factor identified so far is a variation in a receptor for dopamine, one of the brain’s molecules that sends signals. This variation increases risk for ADHD by 20 to 30 percent.

5 To try to understand how this variation influences attention, Shaw and colleagues scanned the brains of 105 children with ADHD and 103 healthy controls between 8 and 16 years old. They repeated the scans in a subset of children through their teen years. They also determined how many copies, if any, the children carried of the target variation.

6 Scientists found that ADHD-afflicted children with the high-risk genetic variation seemed to be worse off at younger ages. Parts of the cortex crucial for attention were thinner in this group than in both their normal counterparts and in children with ADHD lacking that variation. However, the high-risk variant group also showed the best chance of recovery. In contrast to other children with ADHD, the cortices of these children naturally became normal by age 16. Like teenagers growing into their too-long limbs, they were also most likely to have grown out of their ADHD symptoms. “People who have the risk gene have a distinctive pattern of brain growth that normalizes with age,” says Shaw. “That might be what’s driving the good clinical outcome they have.” The findings were published this week in the Archives of General Psychiatry.

7 Scientists don’t yet know exactly how this genetic marker contributes to differences in brain size or in behavior. But previous research has shown that receptors with the variation don’t respond to dopamine as much as other forms of the gene. “That biological action of the brain may help to explain why in this study, the cortical thickness was thinner in the people who carried this variant,” says James Kennedy, professor of psychiatry at the University of Toronto. “The reasoning would be that people with that allele would have a bit less nerve-transmission activity in areas of their brain where this is located.” Kennedy compares gray matter in the brain to muscle, which gets bigger with exercise. “The more you use it, the more synapses are formed and the more volume is created.”

8 Shaw and others caution that it's too early to use the findings to diagnose the disorder or to influence treatment. "But with more research, it may be possible to do an MRI study before starting medication, and then predict what type of treatment might be best for that individual based on their brain image and genotype," says Kennedy.

9 The findings may also help put an end to some controversy surrounding the disorder. ADHD is diagnosed mainly by a child's behavior. Some have argued that pushy drug companies, impatient parents and overburdened teachers have led to frequent overdiagnosis and unnecessary medication of children. Identifying a way in which a genetic allele might influence ADHD helps solidify a neurological basis of the disorder.

10 In addition, the study supports the idea that ADHD sometimes disappears in adulthood. While that idea had gone out of favor, recent large-scale follow-up studies suggest that some children do get better and stay better, says James Swanson, professor of psychiatry at University of California, Irvine. The new findings may provide a biological basis for this pattern, he says.

11 He adds that the gene itself is very interesting. The variation linked to ADHD shows signs that it was selected for during evolution. This suggests that it provides some kind of advantage. "[The variation] might be linked to a different way of thinking or acting that is diagnosed as ADHD in childhood but could be beneficial at other times in development," says Swanson.