Attention-Deficit Hyperactivity Disorder

A new theory suggests the disorder results from a failure in self-control. ADHD may arise when key brain circuits do not develop properly, perhaps because of an altered gene or genes

by Russell A. Barkley

YAN NASCIMBENE

As I watched five-year-old Keith in the waiting room of my office, I could see why his parents said he was having such a tough time in kindergarten. He hopped from chair to chair, swinging his arms and legs restlessly, and then began to fiddle with the light switches, turning the lights on and off again to everyone's annoyance—all the while talking nonstop. When his mother encouraged him to join a group of other children busy in the playroom, Keith butted into a game that was already in progress and took over, causing the other children to complain of his bossiness and drift away to other activities. Even when Keith had the toys to himself, he fidgeted aimlessly with them and seemed unable to entertain himself quietly. Once I examined him more fully, my initial suspicions were confirmed: Keith had attention-deficit hyperactivity disorder (ADHD).

Since the 1940s, psychiatrists have applied various labels to children who are hyperactive and inordinately inattentive and impulsive. Such youngsters have been considered to have "minimal brain dysfunction," "brain-injured child syndrome," "hyperkinetic reaction of childhood," "hyperactive child syndrome" and, most recently, "attention-deficit disorder." The frequent name changes reflect how uncertain researchers have been about the underlying causes of, and even the precise diagnostic criteria for, the disorder.

Within the past several years, however, those of us who study ADHD have begun to clarify its symptoms and causes and have found that it may have a genetic underpinning. Today's view of the basis of the condition is strikingly different from that of just a few years ago. We are finding that ADHD is not a disorder of attention per se, as had long been assumed. Rather it arises as a developmental failure in the brain circuitry that underlies inhibition and self-control. This loss of self-control in turn impairs other important brain functions crucial for maintaining attention, including the ability to defer immediate rewards for later, greater gain.

ADHD involves two sets of symptoms: inattention and a combination of hyperactive and impulsive behaviors [*see table on next page*]. Most children are more active, distractible and impulsive than adults. And they are more inconsistent, affected by momentary events and dominated by objects in their immediate environment. The younger the children, the less able they are to be aware of time or to give priority to future events over more immediate wants. Such behaviors are signs of a problem, however, when children display them significantly more than their peers do.

CHILDREN WITH ADHD cannot control their responses to their environment. This lack of control makes them hyperactive, inattentive and impulsive.

Boys are at least three times as likely as girls to develop the disorder; indeed, some studies have found that boys with ADHD outnumber girls with the condition by nine to one, possibly because boys are genetically more prone to disorders of the nervous system. The behavior patterns that typify ADHD usually arise between the ages of three and five. Even so, the age of onset can vary widely: some children do not develop symptoms until late childhood or even early adolescence. Why their symptoms are delayed remains unclear.

Huge numbers of people are affected. Many studies estimate that between 2 and 9.5 percent of all school-age children worldwide have ADHD; researchers have identified it in every nation and culture they have studied. What is more, the condition, which was once thought to ease with age, can persist into adulthood. For example, roughly two thirds of 158 children with ADHD my colleagues and I evaluated in the 1970s still had the disorder in their twenties. And many of those who no longer fit the clinical description of ADHD were still having significant adjustment problems at work, in school or in other social settings.

To help children (and adults) with ADHD, psychiatrists and psychologists must better understand the causes of the disorder. Because researchers have traditionally viewed ADHD as a problem in the realm of attention, some have suggested that it stems from an inability of the brain to filter competing sensory inputs, such as sights and sounds. But recently scientists led by Joseph A. Sergeant of the University of Amsterdam have shown that children with ADHD do not have difficulty in that area; instead they cannot inhibit their impulsive motor responses to such input. Other researchers have found that children with ADHD are less capable of preparing motor responses in anticipation of events and are insensitive to feedback about errors made in those responses. For example, in a commonly used test of reaction time, children with ADHD are less able than other children to ready themselves to press one of several keys when they see a warning light. They also do not slow down after making mistakes in such tests in order to improve their accuracy.

The Search for a Cause

No one knows the direct and immediate causes of the difficulties experienced by children with ADHD, although advances in neurological imaging techniques and genetics promise to clarify this issue over the next five years. Already they have yielded clues, albeit ones that do not yet fit together into a coherent picture.

Imaging studies over the past decade have indicated which brain regions might malfunction in patients with ADHD and thus account for the symptoms of the condition. That work suggests the involvement of the prefrontal cortex, part of the cerebellum, and at least two of the clusters of nerve cells deep in the brain that are collectively known as the basal ganglia [*see illustration on page 69*]. In a 1996 study F. Xavier Castellanos, Judith L. Rapoport and their colleagues at the National Institute of Mental Health found that the right prefrontal cortex and two basal ganglia called the caudate nucleus and the globus pallidus are significantly smaller than normal in children with ADHD. Earlier this year Castellanos's group found that the vermis region of the cerebellum is also smaller in ADHD children.

The imaging findings make sense because the brain areas that are reduced in size in children with ADHD are the very ones that regulate attention. The right prefrontal cortex, for example, is involved in "editing" one's behavior, resisting distractions and developing an awareness of self and time. The caudate nucleus and the globus pallidus help to switch off automatic responses to allow more careful deliberation by the cortex and to coordinate neurological input among various regions of the cortex. The exact role of the cerebellar vermis is unclear, but early studies suggest it may play a role in regulating motivation.

What causes these structures to shrink in the brains of those with ADHD? No one knows, but many studies have sug-

Diagnosing ADHD

Psychiatrists diagnose attention-deficit hyperactivity disorder (ADHD) if the individual displays six or more of the following symptoms of inattention or six or more symptoms of hyperactivity and impulsivity. The signs must occur often and be present for at least six months to a degree that is maladaptive and inconsistent with the person's developmental level. In addition, some of the symptoms must have caused impairment before the age of seven and must now be causing impairment in two or more settings. Some must also be leading to significant impairment in social, academic or occupational functioning; none should occur exclusively as part of another disorder. (Adapted with permission from the fourth edition of the *Diagnostic and Statistical Manual of Mental Disorders.* ©1994 American Psychiatric Association.)

INATTENTION

- Fails to give close attention to details or makes careless mistakes in schoolwork, work or other activities
- Has difficulty sustaining attention in tasks or play activities
- Does not seem to listen when spoken to directly
- Does not follow through on instructions and fails to finish schoolwork, chores or duties in the workplace
- Has difficulty organizing tasks and activities
- Avoids, dislikes or is reluctant to engage in tasks that require sustained mental effort (such as schoolwork)
- Loses things necessary for tasks or activities (such as toys, school assignments, pencils, books or tools)
- Is easily distracted by extraneous stimuli
- Is forgetful in daily activities

HYPERACTIVITY AND IMPULSIVITY

- Fidgets with hands or feet or squirms in seat
- Leaves seat in classroom or in other situations in which remaining seated is expected
- Runs about or climbs excessively in situations in which it is inappropriate (in adolescents or adults, subjective feelings of restlessness)
- Has difficulty playing or engaging in leisure activities quietly
- Is "on the go" or acts as if "driven by a motor"
- Talks excessively
- Blurts out answers before questions have been completed
- Has difficulty awaiting turns
- Interrupts or intrudes on others

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gested that mutations in several genes that are normally very active in the prefrontal cortex and basal ganglia might play a role. Most researchers now believe that ADHD is a polygenic disorder—that is, that more than one gene contributes to it.

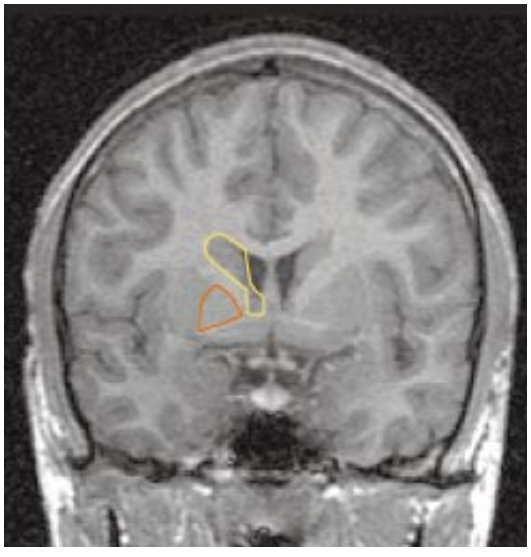
Early tips that faulty genetics underlie ADHD came from studies of the relatives of children with the disorder. For instance, the siblings of children with ADHD are between five and seven times more likely to develop the syndrome than children from unaffected families. And the children of a parent who has ADHD have up to a 50 percent chance of experiencing the same difficulties.

The most conclusive evidence that genetics can contribute to ADHD, however, comes from studies of twins. Jacquelyn J. Gillis, then at the University of Colorado, and her colleagues reported in 1992 that the ADHD risk of a child whose identical twin has the disorder is between 11 and 18 times greater than that of a nontwin sibling of a child with ADHD; between 55 and 92 percent of the identical twins of children with ADHD eventually develop the condition.

One of the largest twin studies of ADHD was conducted by Helene Gjone and Jon M. Sundet of the University of Oslo with Jim Stevenson of the University of Southampton in England. It involved 526 identical twins, who inherit exactly the same genes, and 389 fraternal twins, who are no more alike genetically than siblings born years apart. The team found that ADHD has a heritability approaching 80 percent, meaning that up to 80 percent of the differences in attention, hyperactivity and impulsivity between people with ADHD and those without the disorder can be explained by genetic factors.

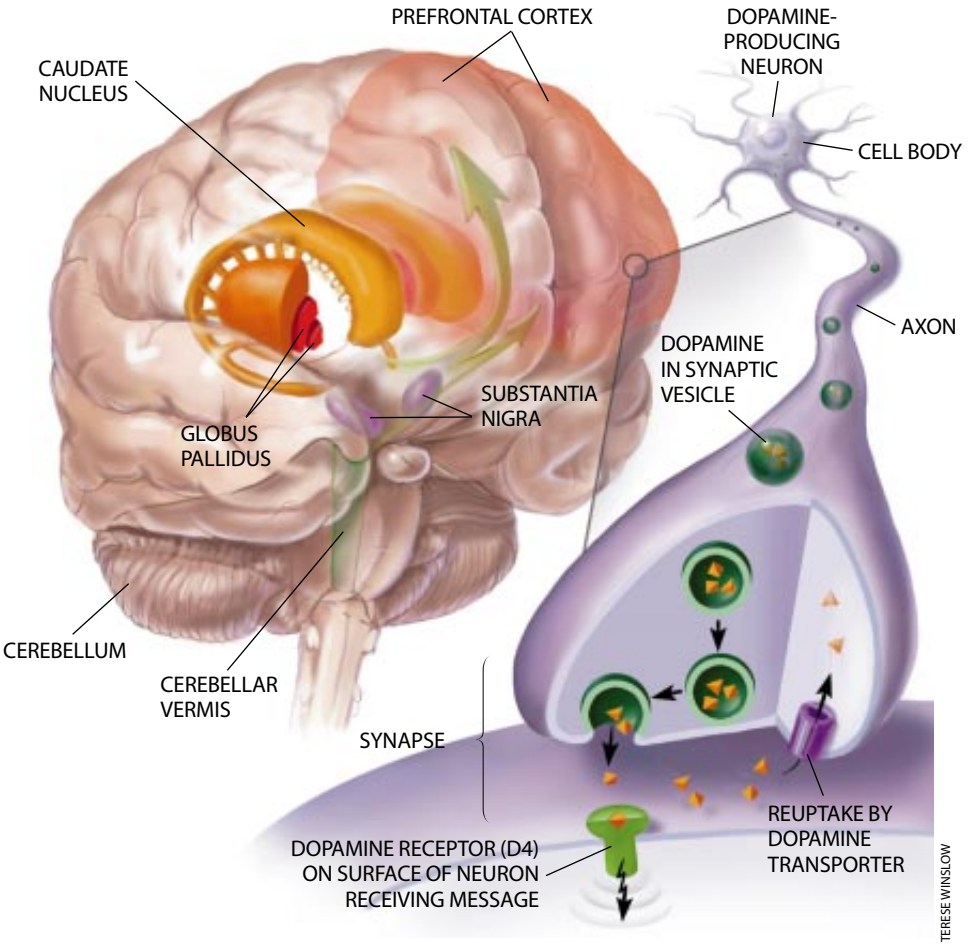
Nongenetic factors that have been linked to ADHD include premature birth, maternal alcohol and tobacco use, exposure to high levels of lead in early childhood and brain injuries—especially those that involve the prefrontal cortex. But even together, these factors can account for only between 20 and 30 percent of ADHD cases among boys; among girls, they account for an even smaller percentage. (Contrary to popular belief, neither dietary factors, such as the amount of sugar a child consumes, nor poor child-rearing methods have been consistently shown to contribute to ADHD.)

Which genes are defective? Perhaps those that dictate the way in which the brain uses dopamine, one of the chemicals known as neurotransmitters that convey messages from one nerve cell, or neuron, to another. Dopamine is secreted by neurons in specific parts of the brain to inhibit or modulate the activity of other neurons, particularly those involved in emotion and movement. The movement disorders of Parkinson's disease, for example, are caused by the death of dopamine-secreting neurons in



NORMAL BRAIN image outlines the right caudate nucleus (*yellow*) and the globus pallidus (*red*), brain structures that regulate attention and that are reduced in size in children with ADHD.

F. XAVIER CASTELLANOS AND JAY N. GIEDD *National Institute of Mental Health*



BRAIN STRUCTURES affected in ADHD use dopamine to communicate with one another (*green arrows*). Genetic studies suggest that people with ADHD might have alterations in genes encoding either the D4 dopamine receptor, which receives incoming signals, or the dopamine transporter, which scavenges released dopamine for reuse. The substantia nigra, where the death of dopamine-producing neurons causes Parkinson's disease, is not affected in ADHD.

a region of the brain underneath the basal ganglia called the substantia nigra.

Some impressive studies specifically implicate genes that encode, or serve as the blueprint for, dopamine receptors and transporters; these genes are very active in the prefrontal cortex and basal ganglia. Dopamine receptors sit on the surface of certain neurons. Dopamine delivers its message to those neurons by binding to the receptors. Dopamine transporters protrude from neurons that secrete the neurotransmitter; they take up unused dopamine so that it can be used again. Mutations in the dopamine receptor gene can render receptors less sensitive to dopamine. Conversely, mutations in the dopamine transporter gene can yield overly effective transporters that scavenge secreted dopamine before it has a chance to bind to dopamine receptors on a neighboring neuron.

In 1995 Edwin H. Cook and his colleagues at the University of Chicago reported that children with ADHD were more likely than others to have a particular variation in the dopamine transporter gene *DAT1*. Similarly, in 1996 Gerald J. LaHoste of the University of California at Irvine and his co-workers found that a variant of the dopamine receptor gene *D4* is more common among children with ADHD. But each of these studies involved 40 or 50 children—a relatively small number—so their findings are now being confirmed in larger studies.

From Genes to Behavior

How do the brain-structure and genetic defects observed in children with ADHD lead to the characteristic behaviors of the disorder? Ultimately, they might be found to underlie impaired behavioral inhibition and self-control, which I have concluded are the central deficits in ADHD.

Self-control—or the capacity to inhibit or delay one's initial motor (and perhaps emotional) responses to an event—is a critical foundation for the performance of any task. As most children grow up, they gain the ability to engage in mental activities, known as executive functions, that help them deflect distractions, recall goals and take the steps needed to reach them. To achieve a goal in work or play, for instance, people need to be able to remember their aim (use hindsight), prompt themselves about what they need to do to reach that goal (use forethought), keep their emotions reined in and motivate themselves. Unless a person can inhibit interfering thoughts and impulses, none of these functions can be carried out successfully.

In the early years, the executive functions are performed externally: children might talk out loud to themselves while remembering a task or puzzling out a problem. As children mature, they internalize, or make private, such executive functions, which prevents others from knowing their thoughts. Children with ADHD, in contrast, seem to lack the restraint needed to inhibit the public performance of these executive functions.

The executive functions can be grouped into four mental activities. One is the operation of working memory—holding information in the mind while working on a task, even if the original stimulus that provided the information is gone. Such remembering is crucial to timeliness and goal-directed behavior: it provides the means for hindsight, forethought, preparation and the ability to imitate the complex, novel behavior of others—all of which are impaired in people with ADHD.

The internalization of self-directed speech is another executive function. Before the age of six, most children speak out loud to themselves frequently, reminding themselves how to perform a particular task or trying to cope with a problem, for example. ("Where did I put that book? Oh, I left it under the desk.") In elementary school, such private speech evolves into inaudible muttering; it usually disappears by age 10 [see "Why Children Talk to Themselves," by Laura E. Berk; Scientific American, November 1994]. Internalized, self-directed speech allows one to

A Psychological Model of ADHD

A loss of behavioral inhibition and self-control leads to the following disruptions in brain functioning:

IMPAIRED FUNCTION	CONSEQUENCE	EXAMPLE
Nonverbal working memory	Diminished sense of time Inability to hold events in mind Defective hindsight Defective forethought	Nine-year-old Jeff routinely forgets important responsibilities, such as deadlines for book reports or an after-school appointment with the principal
Internalization of self-directed speech	Deficient rule-governed behavior Poor self-guidance and self-questioning	Five-year-old Audrey talks too much and cannot give herself useful directions silently on how to perform a task
Self-regulation of mood, motivation and level of arousal	Displays all emotions publicly; cannot censor them Diminished self-regulation of drive and motivation	Eight-year-old Adam cannot maintain the persistent effort required to read a story appropriate for his age level and is quick to display his anger when frustrated by assigned schoolwork
Reconstitution (ability to break down observed behaviors into component parts that can be recombined into new behaviors in pursuit of a goal)	Limited ability to analyze behaviors and synthesize new behaviors Inability to solve problems	Fourteen-year-old Ben stops doing a homework assignment when he realizes that he has only two of the five assigned questions; he does not think of a way to solve the problem, such as calling a friend to get the other three questions

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reflect to oneself, to follow rules and instructions, to use self-questioning as a form of problem solving and to construct "meta-rules," the basis for understanding the rules for using rules—all quickly and without tipping one's hand to others. Laura E. Berk and her colleagues at Illinois State University reported in 1991 that the internalization of self-directed speech is delayed in boys with ADHD.

A third executive mental function consists of controlling emotions, motivation and state of arousal. Such control helps individuals achieve goals by enabling them to delay or alter potentially distracting emotional reactions to a particular event and to generate private emotions and motivation. Those who rein in their immediate passions can also behave in more socially acceptable ways.

The final executive function, reconstitution, actually encompasses two separate processes: breaking down observed behaviors and combining the parts into new actions not previously learned from experience. The capacity for reconstitution gives humans a great degree of fluency, flexibility and creativity; it allows individuals to propel themselves toward a goal without having to learn all the needed steps by rote. It permits children as they mature to direct their behavior across increasingly longer intervals by combining behaviors into ever longer chains to attain a goal. Initial studies imply that children with ADHD are less capable of reconstitution than are other children.

I suggest that like self-directed speech, the other three executive functions become internalized during typical neural development in early childhood. Such privatization is essential for creating visual imagery and verbal thought. As children grow up, they develop the capacity to behave covertly, to mask some of their behaviors or feelings from others. Perhaps because of faulty genetics or embryonic development, children with ADHD have not attained this ability and therefore display too much public behavior and speech. It is my assertion that the inattention, hyperactivity and impulsivity of children with ADHD are caused by their failure to be guided by internal instructions and by their inability to curb their own inappropriate behaviors.

Prescribing Self-Control

If, as I have outlined, ADHD is a failure of behavioral inhibition that delays the ability to privatize and execute the four executive mental functions I have described, the finding supports the theory that children with ADHD might be helped by a more structured environment. Greater structure can be an important complement to any drug therapy the children might receive. Currently children (and adults) with ADHD often receive drugs such as Ritalin that boost their capacity to inhibit and regulate impulsive behaviors. These drugs act by inhibiting the dopamine transporter, increasing the time that dopamine has to bind to its receptors on other neurons.

Such compounds (which, despite their inhibitory effects, are known as psychostimulants) have been found to improve the behavior of between 70 and 90 percent of children with ADHD older than five years. Children with ADHD who take such medication not only are less impulsive, restless and distractible but are also better able to hold important information in mind, to be more productive academically, and to have more internalized speech and better self-control. As a result, they tend to be liked better by other children and to experience less punishment for their actions, which improves their self-image.

My model suggests that in addition to psychostimulants—and perhaps antidepressants, for some children—treat-

PSYCHOLOGICAL TESTS used in ADHD research include the four depicted here. The tower-building test (*upper left*), in which the subject is asked to assemble balls into a tower to mimic an illustration, measures forethought, planning and persistence. The math test (*upper right*) assesses working memory and problem-solving ability. In the auditory attention test (*below*), the subject must select the appropriate colored tile according to taped instructions, despite distracting words. The time estimation test (*lower right*) measures visual attention and subjective sense of time intervals. The subject is asked to hold down a key to illuminate a lightbulb on a computer screen for the same length of time that another bulb was illuminated previously.

PHOTOGRAPHS BY STEPHEN ROSE *Gamma Liaison*

ment for ADHD should include training parents and teachers in specific and more effective methods for managing the behavioral problems of children with the disorder. Such methods involve making the consequences of a child's actions more frequent and immediate and increasing the external use of prompts and cues about rules and time intervals. Parents and teachers must aid children with ADHD by anticipating events for them, breaking future tasks down into smaller and more immediate steps, and using artificial immediate rewards. All these steps serve to externalize time, rules and consequences as a replacement for the weak internal forms of information, rules and motivation of children with ADHD.

In some instances, the problems of ADHD children may be severe enough to warrant their placement in special education programs. Although such programs are not intended as a cure for the child's difficulties, they typically do provide a smaller, less competitive and more supportive environment in which the child can receive individual instruction. The hope is that once children learn techniques to overcome their deficits in self-control, they will be able to function outside such programs.

There is no cure for ADHD, but much more is now known about effectively coping with and managing this persistent and troubling developmental disorder. The day is not far off when genetic testing for ADHD may become available and more specialized medications may be designed to counter the specific genetic deficits of the children who suffer from it. SA

The Author

RUSSELL A. BARKLEY is director of psychology and professor of psychiatry and neurology at the University of Massachusetts Medical Center in Worcester. He received his B.A. from the University of North Carolina at Chapel Hill and his M.A. and Ph.D. from Bowling Green State University. He has studied ADHD for nearly 25 years and has written many scientific papers, book chapters and books on the subject, including *ADHD and the Nature of Self-Control* (Guilford Press, 1997) and *Attention-Deficit Hyperactivity Disorder: A Handbook for Diagnosis and Treatment* (Guilford Press, 1998).

Further Reading

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