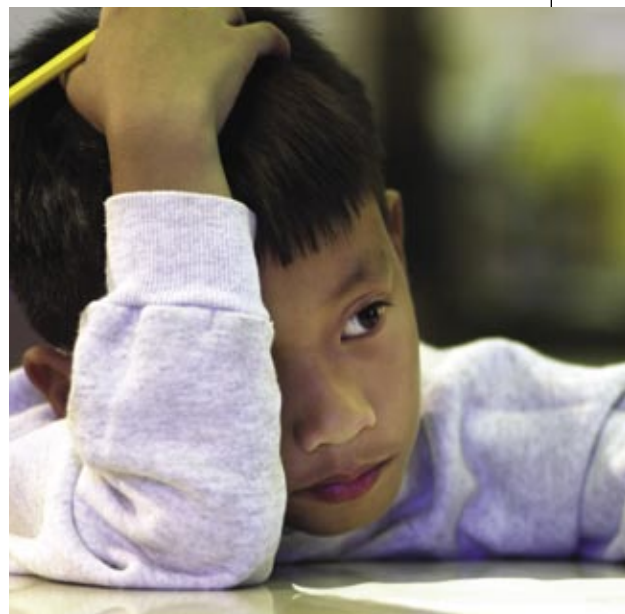


Informing the ADHD Debate

The latest neurological research has injected much needed objectivity into the disagreement over how best to treat children with attention-deficit disorders

By Aribert Rothenberger and Tobias Banaschewski



From the moment Julia entered first grade, she appeared to spend most of her time daydreaming. She needed more time to complete assignments than the other children did. As she moved through elementary school, her test scores deteriorated. She felt increasingly unable to do her homework or follow the teacher's instructions in class. She made few real friends and said her teachers got on her nerves. She complained that her parents pressured her all day long and that nothing she did was right.

Julia was actually very friendly and talkative,

but a lack of self-control made others feel uneasy around her. By age 14, she found that concentrating on assignments seemed impossible. She constantly lost her belongings. Neuropsychological exams showed Julia was of average intelligence but repeatedly interrupted the tests. She was easily distracted and seemed to expect failure in everything she did. So she just gave up. Ultimately Julia was diagnosed with attention-deficit hyperactivity disorder (ADHD) and was treated with methylphenidate, one of the standard drugs for her condition. The medication helped Julia organize her life and tackle her schoolwork more

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readily. She says she now feels better and is much more self-confident.

Julia's symptoms constitute just one profile of a child with ADHD. Other girls and boys exhibit similar yet varied traits, and whereas medication has helped in many cases, for just as many it provides no relief. With the number of cases increasing every year, debate over basic questions has heightened: Is ADHD overdiagnosed? Do drugs offer better treatment than behavior modification? Recent progress in understanding how brain activity differs in ADHD children is suggesting answers.

What Causes ADHD?

ADHD is diagnosed in 2 to 5 percent of children between the ages of six and 16; approximately 80 percent are boys. The typical symptoms of distractibility, hyperactivity and agitation occur at all ages, even in adults who have the condition, but with considerable disparity. Children often

tive diagnosis can be made in those first three years. Physical restlessness often diminishes in teenagers, but attention failure continues and can often become associated with aggressive or anti-social behavior and emotional problems, as well as a tendency toward drug abuse. Symptoms persist into adulthood in 30 to 50 percent of cases.

Longitudinal epidemiological studies demonstrate that ADHD is no more common today than in the past. The apparent statistical rise in the number of cases may be explained by increased public awareness and improved diagnosis. The condition can now be reliably identified according to a set of characteristics that differentiate it from age-appropriate behavior. Nevertheless, debates about overdiagnosis, as well as preferred treatments, are sharper than ever.

Neurologists are making headway in informing these debates. For starters, researchers using state-of-the-art imaging techniques have found differences in several brain regions of ADHD and non-ADHD children of similar ages. On average, both the frontal lobe and the cerebellum are smaller in ADHD brains, as are the parietal and temporal lobes. ADHD seems to be the result of abnormal information processing in these brain regions, which are responsible for emotions and control over impulses and movements.

Yet these variations do not indicate any basic mental deficiency. Currently physicians see the disorder as an extreme within the natural variability of human behavior. On neuropsychological tests such as letter-sequence recognition on a computer, ADHD children have varied but frequently slower reaction times. The reason, experts now believe, is that neural information processing—the foundation of experience and behavior—may break down, especially when many competing demands

suddenly flood the brain. In this circumstance or when faced with tasks requiring speed, thoroughness or endurance, the performance of ADHD brains decreases dramatically compared with the brains of other children. A lack of stimulation, on the other hand, quickly leads to boredom.

The attention deficit is particularly evident whenever children are asked to control their behavior—stopping an impulsive action or maintaining a high level of performance in a given task. The problem is not so much a lack of attention per se but a rapid drop in the ability to continually pay attention.

seem forgetful or impatient, tend to disturb others and have a hard time observing limits. Poor impulse control manifests itself in rash decision making, silly antics and rapid mood swings. The child acts before thinking. And yet ADHD children often behave perfectly normally in new situations, particularly those of short duration that involve direct contact with individuals or are pleasurable or exciting, like watching TV or playing games.

Precursor behaviors such as a difficult temperament or sleep and appetite disorders have often been found in children younger than three who were later diagnosed with ADHD, but no defini-



GETTY IMAGES

A different phenomenon, however, gives hyperactive children the uncontrollable urge to move. Together with the cerebellum, which coordinates movement, various control systems within and underneath the cerebral cortex are responsible for motor functions. This region is where the neurons of the motor cortex, the basal ganglia and the thalamus come together. The motor cortex represents the final stage of neural pro-

tions that lead to a desired behavior when a reward stimulus is presented. But when dopamine is absent, rewards that are minor or presented at the wrong time have no effect.

Genes or Environment

One question that arises from all these findings is why specific brain regions are smaller than others and why certain brain functions are weak

Studies indicate that approximately 80 percent of ADHD cases can be traced to genetic factors.

cessing, after which motor impulses are sent to muscles. When activity in these regions is not balanced, children have difficulty preparing for, selecting and executing movements because they cannot adequately control or inhibit their motor system. Complex movements that require precise sequencing are initiated too early and then overshoot their target. Hyperactivity also often goes hand in hand with deficits in fine-motor coordination and an inability of children to stop speech from bursting forth uncontrollably.

In general, the underlying trait of impulsivity is linked to the development of the brain's so-called executive function: the ability to plan and to monitor working memory. Executive function develops over time as the brain matures. In children with ADHD, however, it tends to remain rudimentary. Anatomically, the executive function stems from neural networks in the prefrontal cortex—the so-called anterior attentional system. Together with the posterior attentional system, located largely in the parietal lobes, it tracks and regulates behavior.

While trying to navigate life without a strong ability to monitor and plan, ADHD children are often in constant battle with their emotions. They are barely able to control their feelings, and they do not endure frustration well. They easily become excited and impatient and tend toward hostility. They also find it hard to motivate themselves for certain tasks. And they are apt to grasp at the first reward that comes their way, no matter how small, rather than wait for a larger, more attractive payoff.

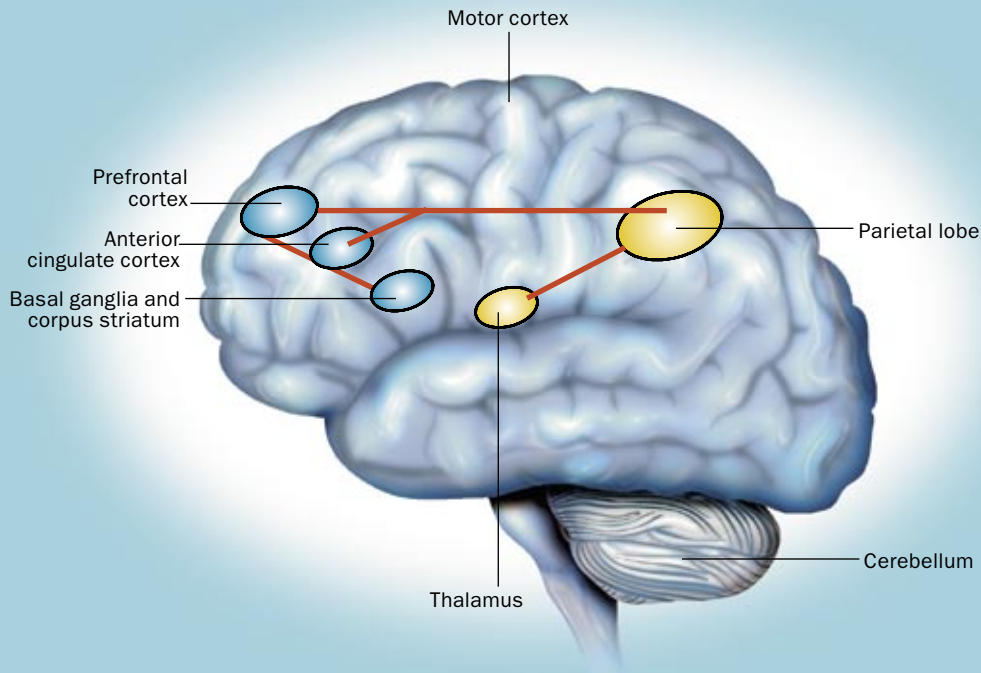
Dopamine plays an important role in the limbic system, which addresses emotional challenges, and ADHD children typically have low levels of this neurotransmitter. Normally, for example, dopamine release strengthens the neural connec-

or unbalanced. Genes may play a considerable role. Comprehensive metastudies of parents and children and identical and fraternal twins, such as those conducted by Anita Thapar, then at the University of Manchester in England, in 1999, Philip Asherson of King's College in London in 2001, and Susan Sprich of Massachusetts General Hospital in 2001, show that heredity greatly influences the occurrence of ADHD. For example, children of parents who have had ADHD are far more likely to suffer similar symptoms. The studies indicate that approximately 80 percent of ADHD cases can be traced to genetic factors.

As a result, researchers have been busily trying to identify which genes might be different in ADHD children. High on the suspect list are genes involved in transferring information between neurons. This group includes genes for proteins that influence the circulation of dopamine at the synapses between neurons—for example, proteins that clear away old messenger molecules so new ones can come through. So far researchers have found that receptor mediation of the dopamine signal is too weak in some patients, and dopamine reuptake is too rapid in others.

The genetics work seems to indicate that behavior problems are associated with insufficient regulation of dopamine metabolism, which derails neural information processing. The neurotransmitter norepinephrine may play a role, too. Although the genetic links between norepinephrine and its receptors and transporters are not as clearly understood as those for dopamine, medications such as atomoxetine that inhibit norepinephrine reuptake by neurons do improve symptoms.

When coupled, the neurotransmitter and brain-imaging evidence imply that the brains of ADHD children may be organized and function differently from an early age. These organic dis-



Uncommon activity in various brain regions is associated with hyperactive behavior in ADHD children. Regions are typically part of the anterior

attentional system (*blue*), which depends on the neurotransmitter dopamine, or the posterior attentional system and norepinephrine (*yellow*).

parities may actually be the cause of behavioral changes and not a consequence of them, as has sometimes been suggested. Another piece of evidence is that in some cases, as children mature, certain physiological peculiarities—such as the size of the corpus striatum—become normal, and ADHD fades.

Still, ADHD cannot yet be tied neatly to known physical, genetic factors. Experts believe that the gene loci discovered to date explain at most 5 percent of problematic behaviors. If more fundamental gene variations are at fault, they have not yet been found. The probability of developing a hyperactivity disorder depends on a combination of many different genes.

Furthermore, there is wide variability in the degree to which these genetic factors are expressed. That means environmental influences must certainly play a role. For example, alcohol and nicotine consumption by a mother during pregnancy tend to increase the risk of ADHD in offspring, much the same way they contribute to extreme prematurity, low birth weight and food allergies.

On the other hand, it is also true that mothers with a genetic predisposition to ADHD have a propensity to smoke and drink during pregnancy. They tend to make basic child-rearing errors, too, such as failing to establish clear rules and effective limits. A chaotic household can strengthen biological ADHD tendencies, leading to a vicious cycle.

Other psychosocial factors, including a non-supportive school environment, marital crises or psychological problems arising between parents, and poor parent-child attachment can also transform a latent tendency into a full-blown disorder.

Medication Dispute

Recent findings about deficits in brain function and neurotransmitters make it clear why certain drugs are likely treatments. And yet the role of environment suggests that behavioral therapy can also be effective. Today uncertainty surrounds both options, and the increasing use of medication has proved divisive. Opinion runs from euphoric endorsement to outright rejection.

The body of evidence suggests that neurotransmitter systems need to be targeted. Psychostimulants such as amphetamine sulfates and methylphenidate, marketed under such names as Ritalin, have had widespread success. Numerous clinical studies show that these medications can decrease or eliminate behavioral disorders in 70 to 90 percent of patients.

(The Authors)

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Latest Leap

Neurofeedback is the newest treatment alternative that therapists are exploring to combat ADHD. It is based on the finding that the electrical brain activity of ADHD children often differs from that of their peers. In this scheme, children play special computer games to learn how to consciously influence their brain waves—and therefore their behavior. For example, they can make themselves calmer and more attentive by strengthening certain electrical activity and decreasing other activity. Sounds, music or movie clips reward them when they can elicit a desired change.

In one game (*photograph*), a child wearing electrodes watches a cartoon of a pole-vaulting mouse. The mouse can only clear the bar when the pole turns red. This feat occurs when the child concentrates, but the pole turns blue when the child does not.

Children in neurofeedback therapy usually undergo three or four 30- to 40-minute sessions a week for six to 10 weeks. Attention, concentration, impulsivity and mild forms of hyperactivity frequently improve. A child's feel-



ings of self-esteem also improve because he sees that he can control his own behavior. Many succeed in transferring the concentration skills they develop to their schoolwork.
—A.R. and T.B.

Administering stimulants to hyperactive children might seem counterintuitive. Yet these substances fix the genetically based dopamine imbalance in the parts of the brain responsible for self-regulation, impulse control and perception. In effect, they prevent the overly rapid reuptake of dopamine at synapses. Other substances with similar modes of action, such as the norepinephrine reuptake inhibitor atomoxetine, work equally well.

Many parents are understandably nervous about subjecting their children to a long-term regimen of medication. News that Ritalin use may be implicated in Parkinson's disease, a dopamine deficiency illness, has added to the worry. Such a connection was suspected because rats that received methylphenidate before sexual maturity exhibited fewer than normal dopamine transporters in their striatum. But to date, not a single case of Parkinson's has been attributed to the use of Ritalin during childhood, and on average Parkinson's patients do not have a history of taking psychostimulants more frequently than other people. Nevertheless, many parents may fear that long-term treatment with psychoactive drugs could leave their child vulnerable to drug or medication abuse in the future.

In 2003, however, Timothy E. Wilens and his colleagues at Harvard Medical School laid these

concerns to rest with a large-scale metastudy. It turns out that the use of psychostimulants significantly *reduces* the risk of future abuse. In comparing ADHD adults with comparable symptoms, those who had not received ADHD medications as children were three times more likely to succumb to drug addiction later in life than those who had received medication.

Drugs Plus Behavior

This does not mean that physicians should prescribe drugs lightly. And under no circumstances should doctors, parents or patients rely exclusively on medication. Studies show that adding behavioral therapy greatly enhances improvements. It also can teach children how to overcome any kind of problematic behavior that might arise in their lifetime. Children learn how to observe and control themselves. Unless ADHD erupts in its most extreme form, behavioral therapy should be the initial treatment of choice. If a child shows no significant signs of improvement after several months, a drug regimen can then be considered.

For the youngest children—those of preschool age—psychostimulants should generally be avoided. Parents should instead try to work daily with their children on their behavior. They would also do well to draw on the expertise of preschool

teachers, who see many different children with a wide range of challenges.

A comprehensive examination conducted in 2000 by the National Institute of Mental Health rated the effectiveness of medical and behavioral treatments of ADHD. Conducted over two years, the Multimodal Treatment Study of Children with ADHD included 579 ADHD children at six different university medical centers. The principal investigators divided the test subjects, all of

family. One common recommendation is to set up written schedules with children so that getting ready for school, for example, does not turn into a contest every morning. Clear rules, specific expectations and known consequences as well as reward points for desired behaviors can all be effective. Particularly with teenagers, parents and even siblings should be included in family therapy.

As neuroscience progresses, therapists continue to try to refine which mixes of drugs and

Studies strongly suggest that a combination of drug and behavioral therapies leads to the highest success.

whom were between the ages of seven and nine, into four groups that had different treatment plans. The results strongly suggest that a combination of drug and behavioral therapies leads to the highest success:

- Routine daily treatment with prescribed medication normalized behavior in 25 percent of children treated.
- Intensive behavioral therapy without medication ended with 34 percent of patients exhibiting no further remarkable symptoms.
- Carefully tailored medical treatment with accompanying counseling for the child and parents helped 56 percent of the children.
- A combination of medication and behavioral therapy resulted in a success rate of 68 percent.

Always Count to 10

These findings allow us to draw concrete conclusions about how parents and educators might best help ADHD children. With or without drugs, it is imperative that children be taught how to handle tasks with more organization and less impulsivity. One common tool, for example, is teaching them to count to 10 before carrying out an impulse, such as jumping up from a table at school. Wall posters or cards shaped like stop signs can remind children to use the various devices they have learned in the heat of a moment. Older children and teenagers can learn how to make detailed plans and how to follow through when complicated tasks threaten to shut them down—for example, when they must straighten a messy bedroom.

Parents also need aids for dealing with trying situations. They can receive guidance in parent training programs that focus on their child-rearing skills as well as their child's interactions within the

behavioral therapy are best for which types of ADHD. More work is needed. Little is known, for example, about what occurs in the brains of ADHD children between birth and the time they enter school. One conclusion has become increasingly clear, however: the varying combinations of behaviors cannot be grouped into a picture of a single disorder. Researchers are now trying to define subgroups that are more coherent in terms of symptoms and neurological causes. To this end, they are looking at other disturbances that are often associated with attention deficit or hyperactivity; approximately 80 percent of ADHD children suffer from at least one other challenge, such as nervous tics, antisocial behavior, anxiety, or reading and spelling problems.

In the meantime, as parents and teachers do the best they can, they must remember that ADHD children possess many positive traits. They tend to be free-spirited, inquisitive, energetic and funny, as well as intelligent and creative. Their behavior is often spontaneous, helpful and sensitive. Many ADHD children are talented multitaskers, last-minute specialists and improvisationalists. Parents and educators should encourage these strengths and let their children know whenever possible that these qualities are highly valued. That will help them feel less under attack, a relief that all by itself can help them begin to turn the corner. **M**

(Further Reading)

- ◆ **Driven to Distraction: Recognizing and Coping with Attention Deficit Disorder from Childhood through Adulthood.** Reprint edition. Edward M. Hallowell and John J. Ratey. Touchstone, 1995.
- ◆ **Does Stimulant Therapy of Attention-Deficit/Hyperactivity Disorder Beget Later Substance Abuse? A Meta-Analytic Review of the Literature.** T. E. Wilens, S. V. Faraone, J. Biederman and S. Gunawardene in *Pediatrics*, Vol. 111, pages 179–185; January 2003.

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