Is ADHD a Spectrum Disorder?

New research suggests that ADHD comprises several meaningful subgroups — each one tied to a weak connection in the brain's neural networks. Here, Joel Nigg, Ph.D. maps the regions of the brain that control attention, impulsivity, and emotion, and explains why scientists are studying the "white matter" connections between these circuits.

BY JANICE RODDEN, JOEL NIGG, PH.D., ADDITUDE EDITORS

According to the *Diagnostic and Statistical Manual of Mental Disorders (DSM-V)*, ADHD comprises two predominant sub-types: inattentive and hyperactive/impulsive. Joel Nigg, Ph.D., professor of psychiatry at Oregon Health & Science University, and other researchers studying the neuroscience of ADHD believe the condition is far more nuanced.

"Some kids are anxious. Some are angry. Some don't have problems with emotions, but can't pay attention. ADHD is variable," Nigg says. "Children with ADHD appear to exhibit different profiles of emotional regulation and attention problems, perhaps associated with different patterns of maturation of brain networks." The ADHD brain is quite different.

The Biology of the Brain

Brain networks, of course, are numerous and complicated. At a cellular level, neurons transmit messages and make connections between and within different brain regions — the frontal lobe, the temporal lobe, the parietal lobe, and the occipital lobe — as well as subcortical structures. Brain scans show us that ADHD brains are, on average, about 10% smaller than neurotypical brains. Other scans show that connections in the brain networks are underdeveloped, suggesting problems with the quality of the connections between neurons, which are called axons.

"As a child matures, the white matter – or the myelin sheath – around the axons continues to develop and mature until the 20s. For people with ADHD, the brain could continue to mature until the 30s. This growth in myelin is like replacing a dial-up telephone Internet connection with a fiber optic cable. It makes neural transmissions faster and more efficient," Nigg says. "Recent research has shown that there are changes to axon growth in the ADHD brain as well. Recent neuropsychological studies suggest that people with the condition process information more slowly, and there is more 'noise' during their processing. This may be related to immaturity of myelin fibers, which makes the axon's neural transmission between certain brain circuits less efficient."

In his research, Nigg and his collaborators have concentrated specifically on the connections between and within the frontal cortex, the parietal cortex, the basal ganglia, the thalamus, and the nucleus accumbens. Underdeveloped axonal fibers in the connections between these regions may help to explain the inattention, impulsivity, and emotional regulation problems so common in people with ADHD, Nigg says.

"The fronto-cerebellar network links the frontal cortex to the cerebellum. The executive function network links the frontal cortex, the parietal cortex, and the subcortical areas (basal

ganglia). The attentional network links the frontal cortex to the supplementary motor cortex and the parietal cortex. Each network could be a locus of dysfunction for people with ADHD."

Two fundamental kinds of brain signaling must be considered to understand ADHD.

Bottom-Up Signaling: "The signaling from the back of the brain to the front of the brain, and from the interior of the brain to the outer part of the brain is bottom-up signaling. Those signals respond to sensory input — what you see and hear — and immediately trigger attentional capture or emotional reaction."

Top-Down Signaling: "In response to these bottom-up signals, top-down signals come from neurons projecting either from the prefrontal cortex backward towards the back of the cortex or downward into the interior of the brain to modulate the spontaneous bottom-up signals. The top-down modulatory signals are based on your goals, your learning, or what you want to be doing. They respond to internal signals instead of external signals."

In a neurotypical brain, he says, "There is a good balance of bottom-up and top-down signaling. Bottom-up systems appropriately interrupt attention when something important happens (e.g., someone physically draws near, a loud sound, or if you are a child – the teacher frowns). These are occurrences that your brain recognizes as something unexpected, not-supposed-to-happen in the moment, and makes you notice so you can modify your top-down response."

The ADHD Brain

In ADHD brains, however, these top-down signals are relatively weak. One hypothesis is that they are overpowered by the much more powerful bottom-up signals. And that imbalance manifests in several different ways, depending the area of the brain impacted. Nigg and his team have focused on three common manifestations of this imbalance: inattention, impulsivity, and emotional regulation.

Inattention

The problem: A child with ADHD becomes so hyperfocused on a video game that it is not easy for him to stop playing. Or he can't focus on his homework when siblings are watching TV or playing nearby.

The explanation: The "automatic attention capture system" in the brain is activated by the stimulation of the video game or the enticing distractions nearby. It sends a bottom-up signal to the parietal lobe, which should reply with a top-down signal reminding the brain of its long-term goals and obligations. In ADHD brains, the axonal fibers in this top-down reply are underdeveloped, so the message to ignore the environment and refocus on the goals is lost. There is not enough top-down control.

"Studies that observe the brain using an fMRI scanner while children work on an attention task (like a math problem), show the frontal-parietal attention network functions poorly," Nigg says. "Additionally, in research that examines the axon fibers connecting the attention circuits of the brain, it's found that certain fibers are underdeveloped, which could explain the under-

functioning of the front and back areas of the attention network. It's as if they are not well-connected, so they are not talking to each other. Because the front of the brain can't capture attention, the behavior is not suppressed."

Impulsivity

The problem: A child with ADHD blurts out answers in class, says something hurtful to a friend without stopping to consider the consequences, or literally leaps without looking and ends up injured.

The explanation: The thalamus is the interior area of the brain that helps to signal the need for response inhibition; in other words, it helps stop you from performing a behavior that is not in your best interest. It operates like a gate, sending signals to allow and stop behaviors as is appropriate. In ADHD brains, the limbic-hippocampal connections relaying these warning signals from the thalamus to the frontal cortex are impaired. It's as if the gate is broken, and behavior doesn't get suppressed when it should.

"People without ADHD have the ability to stop, mid-stream, if they recognize a person is not smiling or responding well to something they are saying," Nigg says. "The average adult needs only 200 milliseconds of warning to interrupt something they are about to do, even if they started doing it. The average child needs about 280 milliseconds. The child with ADHD needs 20 to 30 milliseconds longer warning, which is an eternity when it comes to behavior control because behavior is so fluid."

Emotional Control

The problem: A child with ADHD responds in overblown, extremely emotional ways to small setbacks or challenges that most children would shrug off. Perhaps she suffers from anxiety or worry due to school frustrations, or she throws temper tantrums that last hours because she can't regulate her anger. Long-term rewards are meaningless; immediate gratification is everything.

The explanation: The amygdala are two internal brain regions that are involved in emotional reactions and decision making. When flooded with anger or worry, these regions deploy bottom-up signals to the cerebral cortex. The insula, a region of the cerebral cortex, should then respond with top-down strategies and goals designed to inhibit an individual's emotional response in line with the goal. This is what helps you take a deep breath and think before acting on a sudden emotion. In ADHD brains, this insula-amygdala connection is weak, which "can lead to a breakdown in regulating negative emotions," Nigg says. "Emotion regulation is a big part of ADHD that has been traditionally ignored."

"At the same time, people with ADHD over-respond to rewards when they are immediate, and don't remember or value future rewards, which indicates a potential breakdown in the regulatory system," Nigg says. "When comparing ADHD brains to people without ADHD, we see that the connection between the prefrontal cortex and the reward system (which is partly in the nucleus accumbens) has reduced activation, especially in the dorsal part of the prefrontal cortex. This

could explain overexcitement, frustration and anger, and inability to respond to delayed rewards."

Not all Kids with ADHD Are the Same

"ADHD is not a breakdown of the brain in one spot. It's a breakdown in the connectivity, the communication networks, and an immaturity in these networks," Nigg says. "These brain networks are interrelated around emotion, attention, behavior, and arousal. People with ADHD have trouble with global self-regulation, not just regulation of attention, which is why there are attentional and emotional issues."

In the future, brain imaging may lead us to classify ADHD according to various valid sub-types like those explained above. Currently, though, "brain types determined by brain scans are just speculation by physicians," Nigg says. Due to variability in brain-imaging equipment and analysis procedures, Nigg says he does not recommend pursuing a brain scan to help diagnose symptoms of ADHD in anyone.

"My own view of this [brain-imaging] data is [that] it's not worth the money that it's going to cost you to have this test," he says. "It may give the clinician a little more confidence in their ADHD diagnosis, but that may not be valid; it's important to note there's an improvement in accuracy from simply using a standardized rating scale too, and that's a lot less expensive."

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