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HIGHLIGHTS FROM A RECENT ADHD PRESENTATION BY DR. VLADIMIR MALETIC

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The current understanding of ADHD suggests an interesting interaction between genetic, anatomic, and functional differences in the brain of those affected.

Genetics of ADHD

Insight into the genetic underpinnings of ADHD comes from a recent, large-scale genome-wide association study that compared the genetic makeup of ~20,000 individuals with ADHD with that of 35,000 healthy individuals. Interestingly, the genetic makeup associated with ADHD was also associated with increased risk for specific emotional behaviors and several comorbidities (eg, irritability, mood swings, depression and substance use).

Neural network affected by ADHD

- The cognitive-executive network comprises interconnected cortical areas that have a role in executive function, working memory, and selective and sustained attention. Prefrontal cortical areas that connect to premotor cortices participate in the planning of motor activity; whereas dorsal prefrontal cortical areas participate in attention, working memory, executive function and "top–down" regulation of emotion.
- The cortico-striatal-thalamic network is comprised of parallel loops that connect the prefrontal cortex with the basal ganglia and thalamus. This network regulates ascending sensory information that reaches the prefrontal cortex, and inhibition of inappropriate actions and motivations.
- The corticolimbic network originates in the ventral prefrontal cortex and connects with areas in the limbic system (such as the amygdala insular, reward related ventral striatum and hypothalamus) and the brainstem norepinephrine center, which regulates arousal. Dysfunction of these connections may result in emotional lability and deficits in impulsivity and motivation.

Anatomic differences in ADHD

ADHD is associated with structural changes in the dorsolateral prefrontal cortex, and the anterior cingulate cortex. These are some of the most replicated findings in ADHD; both areas are involved with top–down regulation emotions and are hubs for the cognitive-executive network. Additional differences include smaller ventral striatum in the basal ganglia and smaller globus pallidus, thalamus, and putamen in ADHD.

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Hot Topics in ADHD

This issue's Hot Topics were provided by Rakesh Jain, MD, MPH, clinical professor, Department of Psychiatry Texas Tech University School of Medicine—Permian Basin, Odessa, Texas

KEY FINDINGS

- **This study offers more support for the concept of underlying neurobiological perturbations in individuals with ADHD. This study will help explain to parents that the seemingly "bad" behaviors of their children with ADHD have a neurobiological basis in various brain regions that control impulsivity, hyperactivity, inattention, emotional regulation, etc.**
- **Neuroplasticity in individuals with ADHD is positively affected by treatment with methylphenidate**
- **This medication-related improved neuropathology has clinical consequences and transmitting this information to parents in a positive manner may improve long-term adherence with ADHD medications**

Neurobiology of ADHD From Childhood to Adulthood: Findings of Imaging Methods

Kasparek T et al.

OBJECTIVE To review the pattern of morphologic and functional brain changes in both children and adults with ADHD that emerges from the recent literature. Additionally, the task of the present review is to explore how to understand the nature of the brain changes.

METHODS Literature review.

RESULTS Neuroimaging studies provide a multitude of information that currently allows us to expand the notions of ADHD neurobiology beyond its traditional understanding as a manifestation of frontostriatal dysfunction. These studies point to disorders of several other areas of the brain, particularly the anterior cingulum, the dorsolateral and ventrolateral prefrontal cortex, the orbitofrontal cortex, the superior parietal regions, the caudate nucleus, the thalamus, the amygdala, and the cerebellum. Imaging studies point to the persistence of changes in both brain structure and function into adulthood, although there might be a tendency for improvement of caudate nucleus pathology. Changes in neuronal (dendritic) plasticity, which are under the modulatory influence of the dopaminergic system, may be in the background of disorders of brain morphology and anatomical connectivity with subsequent brain dysfunction. Growing evidence suggests that treatment with methylphenidate can lead to improvement of brain changes seen in neuroimaging by its positive effect on neuroplasticity.

CONCLUSION Changes in neuronal plasticity may be behind persistent brain changes in ADHD. Current treatment approaches seem to improve these neuroplastic processes, and, therefore, may have a positive effect on the neuropathology of ADHD.

KEY FINDINGS:

- **"Connectome" is a new buzz word in psychiatry. It is a promising new neurobiological tool to aid in the understanding of how different parts of the brain are connected in health and illness. This study examines the brain anatomy and its connectivity in individuals with ADHD compared with controls**
- **This study found both micro- and macrostructural abnormalities in those with childhood onset of ADHD symptoms; these abnormalities were found in both white matter bundles and in gray matter density**
- **The accuracy of these morphometric abnormalities in diagnosing ADHD accurately was an astonishing 83%, thereby raising the possibility that in the future clinicians might be able to use brain morphometric examination to accurately diagnose ADHD**

Hot Topics in ADHD

The Brain Anatomy of Attention-Deficit/Hyperactivity Disorder in Young Adults–A Magnetic Resonance Imaging Study

Gehricke JG et al.

BACKGROUND This is one of the first studies to examine the structural brain anatomy and connectivity associated with an ADHD diagnosis and child as well as adult ADHD symptoms in young adults. It was hypothesized that an adult ADHD diagnosis and in particular childhood symptoms, are associated with widespread changes in the brain macro- and microstructure, which can be used to develop a morphometric biomarker for ADHD.

METHODS Voxel-wise linear regression models were used to examine structural and diffusion-weighted MRI data in 72 participants (31 young adults with ADHD and 41 controls without ADHD) in relation to diagnosis and the number of self-reported child and adult symptoms.

RESULTS Findings revealed significant associations between ADHD diagnosis and widespread changes to the maturation of white matter fiber bundles and gray matter density in the brain, such as structural shape changes (incomplete maturation) of the middle and superior temporal gyrus and fronto-basal portions of both frontal lobes. ADHD symptoms in childhood showed the strongest association with brain macro- and microstructural abnormalities. At the brain circuitry level, the superior longitudinal fasciculus (SLF) and corticolimbic areas are dysfunctional in individuals with ADHD. The morphometric findings predicted an ADHD diagnosis correctly up to 83% of all cases.

CONCLUSION An adult ADHD diagnosis, and in particular childhood symptoms, are associated with widespread micro- and macrostructural changes. The SLF and corticolimbic findings suggest complex audio visual, motivational, and emotional dysfunctions associated with ADHD in young adults. The sensitivity of the morphometric findings in predicting an ADHD diagnosis was sufficient, which indicates that MRI-based assessments are a promising strategy for the development of a biomarker.

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HIGHLIGHTS FROM A RECENT ADHD PRESENTATION BY DR. VLADIMIR MALETIC

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Functional imaging studies have shown interesting differences in individuals with and without ADHD. In one study, viewing photographs with strong emotional expressions (such as fear) have different limbic system responses. Individuals with ADHD who are not taking medication have a more intense response in the amygdala than individuals without ADHD. The difference is normalized when those with ADHD are treated with medication.

ADHD and neurotransmitters

In addition to genetic and anatomic correlates to ADHD, there are abnormalities in neurotransmission and the neurotransmitter pathways that innervate these cortical and limbic regions. In particular,

- When there is too little norepinephrine and dopamine flowing into the prefrontal cortex, individuals are likely to be distracted or disorganized
- When there is excess norepinephrine and dopamine, these neurotransmitters start to bind to low- affinity receptors or receptors located outside of the synapse, associated with distraction, irritability, anxiety, and difficulty falling asleep

ADHD Patient Resource Corner

To download this resource or provide support for your patients interested in learning more about ADHD, go to: MoreToADHD.com

MORE TO ADHD™

Supernus® Pharmaceuticals

INATTENTIVE ADHD IS MUCH HARDER TO DIAGNOSE

Actor portrayal.

You've asked your child 7 times to brush her teeth, but she's still building with her block set.
The homework in her backpack never makes it to the teacher's desk.
The dishwasher is only half emptied, because something else drew her attention away.

Sound familiar?

Inattentive attention-deficit/hyperactivity disorder (ADHD) is sometimes referred to as an "invisible" disorder because it is often misdiagnosed, or even missed entirely.

Without a proper diagnosis or treatment, your child's inattention can cause poor school performance or conflict at home. Although inattentive ADHD can remain undiagnosed for years, it's never too late to see the benefits from treatment.

Recognizing the 9 Symptoms of Inattentive ADHD

The American Psychiatric Association's diagnostic manual lists the following 9 symptoms of inattentive ADHD. For a diagnosis, a persistent pattern of 6 or more symptoms must be present in children up to age 17. For older teens and adults, at least 5 symptoms are required.

Careless Mistakes: Your child doesn't pay close attention to details.	**Short Attention Spans:** Your child has difficulty paying attention, resulting in incomplete classwork and unfinished tasks at home.	**Poor Listening Skills:** Your child doesn't seem to listen when spoken to—and may seem "elsewhere" in a conversation.
No Follow-Through: Your child has difficulty following instructions and seeing projects through to completion.	**Disorganized:** Your child has difficulty organizing activities, managing time, and keeping things tidy.	**Inability to Focus:** Your child avoids things that require sustained focus (reading assignments or lengthy papers).
Loses Things: Your child may misplace classwork or (if older) keys or cell phone.	**Distracted:** Your child likes to daydream, is easily sidetracked, and often can't stay on task.	**Forgetful:** Your child is forgetful in daily activities (eg, handing in assignments).

Inattentive ADHD is Much Harder to Diagnose

Download this resource to help recognize the 9 symptoms of Inattentive ADHD.

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