

# The Good, Bad, & Ugly of Attention Deficit Hyperactivity Disorder Medications

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## ABSTRACT

The medications often used to treat attention deficit hyperactivity disorder (ADHD) include stimulants like methylphenidate and other amphetamines. Some evidence is beginning to show that these pharmaceuticals may help mitigate functional, and possibly structural brain alterations as well as behavioral symptoms associated with ADHD diagnoses. These medications are thought to facilitate concentration, focus, and regulate altered brain function by increasing dopamine. However, additional research portrays an alternate perspective on the drugs. In some cases, the use of these medications has been associated with serious side effects including risks of psychosis, risk for problematic substance use, and other externalizing behaviors. Evidence is still lacking as to whether long-term treatment with these medications is leading to a risk for psychosis, substance use, and externalizing behaviors. Magnetic resonance imaging (MRI) scans of the brain contribute more knowledge but also motivate additional questions that remain to be answered. In this review, we specifically focus on the benefits and potential dangers of these medications for the developing brain. Further, we will discuss evidence of altered functioning among individuals living with ADHD in various large-scale brain networks and the consequences of attention and behavior. Additionally, we will summarize evidence of the various short-term and long-term impacts of a variety of different ADHD medications prescribed at different doses. Overall, more studies are needed to enhance understanding of these medications, their benefits, and potential risks.

## **The Effects of Stimulant ADHD Medications On Brain Function**

ADHD is a neurodevelopmental disorder that affects a person's ability to focus, control impulses, and regulate behavior. Stimulants are a commonly prescribed medication for people with ADHD. Stimulants work by increasing the levels of dopamine in the brain, which can help improve attention and decrease impulsivity. One of the most significant effects of stimulants on someone with ADHD is an increase in focus [JF1]. People with ADHD often struggle with maintaining attention on tasks for extended periods. Stimulants can help improve focus by increasing the levels of certain neurotransmitters in the brain that, when dysregulated in ADHD, are thought to contribute to attentional deficits. In a lot of cases, stimulants such as methylphenidate block 60 to 70% of dopamine transporters (DAT) and 70 to 80% of norepinephrine transporters which are involved in the reuptake of these neurotransmitters (1). Thus, at therapeutic doses, methylphenidate increases extracellular levels of both dopamine and norepinephrine (1). This increase in dopamine and norepinephrine is thought to result in an increase in focus and attention as well as a decrease in impulsivity in people with ADHD. (1). Impulsivity is a common symptom of ADHD; it can lead to problems in social, academic, and occupational settings (5). These pharmacological treatments for ADHD have been shown to reduce symptoms in about 70% of patients (1).

## **The Acute Effects Of ADHD Stimulants On Default Mode Network Function**

The default mode network (DMN) is made up of brain regions that are commonly active when a person is at rest and not engaged in a specific task. This network is associated with self-referential thinking, mind wandering, and day-dreaming. The DMN, one of the most consistently observed functional networks of the brain, is known to be involved in focus and attention on internal stimuli vs external (6). Recent research has suggested that the DMN may be involved in ADHD. Studies have shown that compared to individuals without ADHD, individuals with ADHD have increased connectivity within the DMN, which may be associated with the symptoms of the disorder. One theory is that the increased DMN connectivity may underlie excessive mind wandering and distractibility, which are symptoms of ADHD. Connectivity between the DMN and other task-positive networks like the executive control network (ECN) and salience network (SN) is also thought to be involved in the regulation of attention and the ability to switch between different tasks, which are a challenge for individuals with ADHD. Studies have shown that individuals with ADHD have altered DMN connectivity with other brain regions involved in attention and task switching, which may contribute to the symptoms of the disorder. In line with this hypothesis, Quern et al.'s, 2017 article demonstrated that drug-naive adolescents with ADHD showed increased synchronization between the DMN and other task-positive networks involved in regulating task attention when compared to typically developing adolescents. Interestingly, the adolescents with ADHD that were medicated showed anti-correlations between these networks more like the typically developing participants. Importantly, this reduced synchronization between the DMN and task-positive networks was associated with poorer behavioral performance on a response inhibition task (2). In addition to these findings, research has suggested that DMN connectivity may be related to behavioral response to treatment for ADHD. Studies have shown that individuals with ADHD who respond well to medication have different patterns of DMN connectivity and those who do not respond well to medication. This suggests that DMN connectivity may be a useful biomarker for predicting treatment response and tailoring treatment to individual patients. [JF2] Further research is needed to better understand the role of DMN in ADHD and inform targeted treatments based on DMN dysfunction.

## **The Long-Term Effects of ADHD Stimulants On Brain Development**

Approximately 5% of children and 2.5% of adults worldwide have been prescribed stimulant medications, as a treatment for ADHD symptoms (3). However, concerns have been raised about the long-term effects of these medications on brain development. Studies have shown that stimulant medications can alter brain development potentially in a therapeutic way. For example, evidence has shown three areas of the brain that may be smaller in children with ADHD: the prefrontal cortex, frontal-striatal-cerebellar projections, and the caudate nucleus. Not surprisingly, these areas of the brain are critical for a child's ability to plan, focus, learn, and retain information (3). Some evidence suggests that long-term use of stimulants might even be able to reverse these structural changes associated with ADHD, such that adults with ADHD who took medications throughout development do not show reduced volume in these regions (3). However, long-term use of stimulant medications can lead to changes in the structure and function of the prefrontal cortex that may also be detrimental, which is part of the brain responsible for executive functions such as attention, working memory, and decision-making. These changes may persist even after the medication is discontinued. The prefrontal cortex is particularly vulnerable to the effects of stimulant medications because it is still developing during childhood and adolescence. Studies[3] have shown that chronic use of stimulant medications can lead to a decrease in the thickness[4] of the prefrontal cortex, which may be associated with cognitive deficits and an increased risk of developing other psychiatric disorders such as depression and anxiety (7). In addition to the structural changes, studies have shown that chronic use of stimulant medications can lead to changes in the dopamine system, which is involved in reward processing and motivation. These changes may even contribute to the development of addiction and other substance use disorders later in life. While the long-term effects of brain stimulant medications are still not fully understood, these medications can have significant effects on brain development. While stimulant medications are the most commonly prescribed treatment for ADHD, concerns have been raised about the long-term effects of these medications on brain development. Overall, it is important for clinicians to carefully monitor children and adolescents

who are prescribed stimulant medications for ADHD and to consider the potential risks and benefits of long-term use. [JF5]

## **The Impact of ADHD Stimulants On Cognitive Function and Academic Performance**

ADHD can have a significant impact on academic performance, including cognitive function. Another common side effect of ADHD is difficulty with social relationships. People with ADHD may struggle with social cues and may have difficulty with interpersonal relationships. They may also struggle with impulse control, which can lead to social problems such as interrupting others or speaking out of turn. ADHD is also associated with difficulties in organization and time management such that people with ADHD may struggle with keeping track of appointments, deadlines, and other important tasks. They may also have difficulty with planning and prioritizing tasks, which can lead to procrastination and missed deadlines. These symptoms, if untreated can then lead to poor academic performance and lower grades. As previously mentioned, medications can work by increasing levels of dopamine which can improve these attentional symptoms and cognitive function. Supporting this notion, studies have shown that stimulant medications can improve academic performance in children with ADHD, including improvements in attention, memory, and executive function. [JF6] It is also important to consider the role of nonpharmacological interventions for improving academic performance in children with ADHD. Behavioral interventions, such as parent training and school-based interventions, are effective in improving academic performance and reducing symptoms of ADHD[7] . These interventions can also be used in combination with stimulant medications to improve outcomes for children with ADHD.

## **The Potential Risks and Side Effects of ADHD Stimulant Use On the Brain and Body**

Though stimulant medications can improve academic performance in the short term, the long-term effects of these medications on brain development are still not fully understood. While ADHD and psychosis are typically thought of as separate conditions, recent research has suggested that there may be an overlap between the two, with some individuals with ADHD experiencing symptoms of psychosis. Among adolescents and young adults with ADHD who were receiving prescription stimulants, new-onset psychosis occurred in approximately 1 in 660 patients (4). The relationship between ADHD and psychosis is complex and not yet fully understood. Psychosis is a condition in which an individual experiences a loss of contact with reality, including delusions and hallucinations. Individuals with ADHD who experience symptoms of psychosis may have difficulty distinguishing between reality and fantasy, which can lead to confusion and distress. They may also experience delusions or hallucinations that can be frightening or disturbing. These symptoms can interfere with daily functioning, including academic and occupational performance, and can lead to social isolation and other negative outcomes. A study published in the Journal of child psychology and Psychiatry found that individuals with ADHD are more likely to experience symptoms than individuals without ADHD. The exact mechanisms underlying the relationship between ADHD and psychosis are not yet clear. However, it is thought that both conditions may be related to abnormalities in dopamine signaling in the brain. Dopamine is a neurotransmitter that plays a role in regulating attention, motivation, and reward processing. Abnormalities in dopamine signaling have been implicated in both ADHD and psychosis. Treatment for individuals with ADHD and psychosis typically involves a combination of pharmacological and normal behavioral interventions. Non-pharmacological interventions, such as cognitive behavioral therapy, may also be used to help individuals with ADHD and psychosis learn coping strategies and improve their overall functioning. While the relationship between ADHD and psychosis is not yet fully understood, there is evidence to suggest that individuals with ADHD may be at increased risk for experiencing symptoms of psychosis. The effects of psychosis associated with ADHD can be significant, interfering with daily functioning and leading to social isolation and other negative outcomes. Further research is needed to

better understand the relationship between these two conditions and to develop more effective treatments for individuals who experience symptoms of both ADHD and psychosis.

## Stimulant vs. Non-Stimulant Alternatives

Though stimulant medications are commonly used to treat ADHD, non-stimulant alternatives are also available. Non-stimulant medications work differently than stimulants and may be preferred by some individuals due to their lower risk of side effects or potential for abuse. Nonstimulant medications may take longer to start working than stimulant medications, and their effects may not be as dramatic. They are generally taken once or twice a day, and it may take several weeks for the full effects to be felt. While non-stimulant medications are generally safe and effective, they do come with some side effects, most commonly dizziness, dry mouth, and upset stomach (8). Non-stimulant medications are a viable option for individuals with ADHD who do not respond well to stimulant medications or who have a history of substance abuse or heart problems. They work by increasing the levels of certain chemicals in the brain that are responsible for regulating attention, mood, and behavior. While they do come with some side effects they are generally safe and effective and are used as directed by a healthcare professional.

## Conclusion

In conclusion, ADHD is a complex neurodevelopmental disorder that can be effectively treated with a variety of medications, including stimulant and non-stimulant options. Stimulant medications are often the first line of treatment, but non-stimulant alternatives may be preferred by some individuals due to their lower risk of side effects. ADHD is a complex disorder that can have a significant impact on an individual's life. While there is no cure for ADHD, there are a variety of treatments available that can help manage symptoms and improve quality of life. These treatments range from medication to behavioral therapy and lifestyle modifications. The most effective treatment plan will vary from person to person, and individuals with ADHD need to work closely with their healthcare provider to find the right approach for them. With the right treatment, individuals with ADHD can thrive and reach their full potential. It is also important to continue raising awareness about ADHD and reduce the stigmas about the disorder to ensure that those affected receive the support and resources they need to succeed.

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