Attention-deficit/hyperactivity disorder (ADHD) often persists beyond childhood into adulthood. One of the therapeutic challenges of treating ADHD is identifying comorbidities, including underlying mood and anxiety disorders, and ongoing substance abuse. Effective treatment modalities tend to prioritize management of substance abuse, but the patient’s age may dictate the overall assessment plan.

So-called ‘reward’ center
Treating childhood ADHD with stimulants might reduce the risk for future drug abuse. It is estimated that approximately 10 million people with ADHD are undiagnosed in the United States; characteristic ADHD symptoms—inattention, hyperactivity, impulsivity—can persist in adulthood, and affected persons might not meet societal expectations. Previously unidentified attention difficulties may emerge during early adulthood because of increasingly complex tasks at school and work.

Persons with undiagnosed ADHD might turn to potentially self-destructive means of placating inner tension. Cocaine has pharmacological properties in common with stimulants such as methylphenidate, which often is prescribed for ADHD. Cocaine and methylphenidate both work on altering brain chemistry with a similar mechanism of action, allowing for increased dopamine in the nucleus accumbens, also known as the “reward center” of the brain.

Adults with ADHD have a 300% higher risk of developing a substance use disorder than adults without ADHD. An estimated 15% to 25% of adults with substance abuse have comorbid ADHD. Although these patients abuse a variety of substances including Cannabis and alcohol, cocaine is one of the most commonly abused substances among this population. These observations could point to a self-medication hypothesis.

Why self-medicate?
The self-medication hypothesis, formulated by Khantzian in 1985, was based on several clinical observations. Khantzian stated that an abuser’s drug of choice is not selected at random but, rather, by an inherent desire to suppress the attributes of the condition that seems to otherwise wreak havoc on his (her) life. Almost a century earlier, Freud mentioned that cocaine is an antidepressant. Among persons with ADHD who have not been given that diagnosis, or treated for the disorder, cocaine is a popular drug. Because of the antidepressant features of cocaine and its ability to produce a rapid increase of dopamine levels that exert a pro-euphoric effect, coupled with a seemingly paradoxical calming influence that leads to increased productivity, it is not surprising to find that cocaine is abused. Reportedly, persons who have not been treated because their ADHD is undiagnosed turn to cocaine because it improves attention, raises self-esteem, and allows users to harness a level of focus that they could not otherwise achieve.

Mechanism of action
Methylphenidate reduces ADHD symptoms by increasing extracellular dopamine in the brain, acting by means of a mechanism
that is similar to that of cocaine. By blocking reuptake of dopamine and allowing an extracellular surplus, users continue to experience the pleasurable effect the neurotransmitter produces. Methylphenidate has been shown to be an even more potent inhibitor of the same autoreceptors. Injecting methylphenidate has been shown to produce a rapid release of dopamine similar to that of cocaine.

However, methylphenidate causes a much slower increase in dopamine; its effect on the brain has been shown to be similar to that of cocaine without the increased abuse potential. Cocaine use remodels the brain by reconfiguring connections that are essential for craving and self-control. Therefore, substituting methylphenidate for cocaine could help ADHD patients by:

- improving overall executive functioning
- decreasing feelings of low self-worth
- increasing daily functioning
- minimizing craving and the risk of subsequent cocaine abuse.

**Treatment recommendations**

Carefully consider pharmacodynamics and pharmacokinetics when prescribing ADHD medication. In general, children and adolescents with ADHD respond more favorably to stimulants than adults do. In children, the mainstay of treatment is slow-dose stimulants such as methylphenidate; second-line treatments are immediate-release stimulants and atomoxetine, a selective norepinephrine reuptake inhibitor. Adults with ADHD might benefit from a nonstimulant, in part because of the presence of complex comorbidities. Modafinil often is prescribed for adults with ADHD.

Atomoxetine readily increases norepinephrine and dopamine in the prefrontal cortex as it bypasses the nucleus accumbens. Although atomoxetine is not a stimulant, the efficacy of the drug is based on its ability to increase norepinephrine through selective inhibition of the norepinephrine transporter. Norepinephrine modulates higher cortical functions—attention, executive function, arousal—that lead to a reduction in hyperactivity, inattention, and impulsivity.

Because dopamine is released in the prefrontal cortex—not in the nucleus accumbens—the addiction potential of atomoxetine is low. The drug might be an effective intervention for patients who are using cocaine to self-medicate. Stimulants such as methylphenidate have proven effective in safely mimicking the mechanism of action of cocaine. Nonstimulants, such as atomoxetine and modafinil, lack abuse potential and are excellent options for treating adults with ADHD.

Clinicians generally are advised to treat a patient’s underlying ADHD symptoms before addressing ongoing substance abuse. If a patient abruptly discontinues cocaine use before ADHD symptoms are properly controlled, her (his) condition might deteriorate further and the treatment plan might fail to progress. Some patients have experienced a reduction in craving for cocaine after they began stimulant therapy; these people no longer felt a need to self-medicate because their symptoms were being addressed.

**References**