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DR. COOPER-KAHN: Research shows that there is a higher rate of cannabis use disorder among those with ADHD than in the general population. Can you break that down? Is there a higher rate in both males and females? At all ages?

DR. GRAY: A recent publication highlights the genetic overlap and causal relationship between ADHD and cannabis use:

 Soler Artigas M, Sánchez-Mora C, Rovirar P, et al. Attentiondeficit/hyperactivity disorder and lifetime cannabis use: genetic overlap and causality. *Molecular Psychiatry*. 2019. [doi:10.1038/ s41380-018-0339-3]

This group's research, drawn from the largest available metaanalyses of genome-wide association studies, indicates that having "ADHD is causal for lifetime cannabis use, with an odds ratio of 7.9 for cannabis use in individuals with ADHD in comparison to individuals without ADHD."

Generally speaking, the increased risk for cannabis use, and progression to cannabis use disorders, cuts across demographics among those with ADHD. The age of use tends to parallel general rates of use in the general population, with peak onset during adolescence and peak use (and peak rates of cannabis use disorder) during young adulthood.

COOPER-KAHN: How do you explain the over-representation of cannabis use disorder in the ADHD population?

GRAY: The abovementioned article suggests shared genetic risk, which is likely an important factor. Beyond that, it is well established that rates of substance use and substance use disorders, in general, are higher among those with ADHD than those without ADHD. A number of clinical observations help place this in context. Impulsivity, a core symptom of ADHD, reliably predicts substance use.Interestingly, another recent article suggested sex differences in ADHD symptom profiles that predict problematic cannabis use:

Kolla NJ, van der Maas M, Toplak ME, et al. Adult attention deficit hyperactivity disorder symptom profiles and concurrent problems with alcohol and cannabis: sex differences in a representative, population survey. BMC Psychiatry. 2016; 16:50.

While hyperactive symptoms predicted problems with cannabis use in men, inattentive symptoms predicted problems with cannabis use in women. In contrast, an earlier adolescent-focused study indicated that hyperactivity/impulsivity predicted later substance problems in both males and females, with inattention posing less risk:

Elkins IJ, McGue M, Iacono WG. Prospective effects of attention-deficit/hyperactivity disorder, conduct disorder, and sex on adolescent substance use and abuse. *Archives of General Psychiatry*. 2007; 64(10): 1145-1152.

Cannabis can appear to be desirable for individuals with ADHD, given a general "calming" effect. However, while this may reduce the appearance of hyperactivity/impulsivity, cannabis impairs cognition and may compound issues with inattention. The only randomized controlled trial of cannabinoids for ADHD investigated nabiximols (an orally administered combination of tetrahydrocannabinol and cannabidiol) revealed no overall improvement, though secondary findings appeared to suggest possible mild improvement in hyperactivity but not inattention:

• Cooper RE, Williams E, Seegobin S, et al. Cannabinoids in attention-deficit/hyperactivity disorder: a randomised-controlled trial. *European Neuropsychopharmacology*. 2017; 27: 795-808.

COOPER-KAHN: How would parents or other individuals distinguish between cannabis use and overuse in their children or loved ones?

GRAY: The term used clinically for problematic use is cannabis use disorder, which involves a constellation of symptoms related to functional impairment. Cannabis use disorder ranges from mild to moderate to severe, depending on the number of symptoms present. Symptoms may include giving up other important activities and dedicating excessive time to use, continued use despite adverse consequences, and evidence of physiological dependence (for example, tolerance and withdrawal). In general, there should be particular concern with adolescents using any amount of cannabis, as it can be cognitively impairing. Additionally, adolescents are known to have about double the risk, compared to adults, of progressing to cannabis use disorder. Overall, if a loved one's cannabis use is adversely impacting school/work performance, affecting relationships, and/or leading to other impairments, this suggests that use has become problematic.

COOPER-KAHN: Can you identify factors within the ADHD population that put individuals at greater risk?

GRAY: As noted above, the core symptoms of ADHD may lead to increased risk for initiating cannabis use, and some individuals with ADHD may perceive the "calming" effect of cannabis as desirable. Additionally, there are shared genetic risks for ADHD and cannabis use.

COOPER-KAHN: On the other hand, are there protective

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factors that decrease the risk of cannabis use in those with ADHD?

GRAY: I'm not aware of specific protective factors among those with ADHD, aside from the potential that adolescents with the inattentive subtype may be at reduced risk for problematic use compared to individuals with the hyperactive/impulsive subtype or combined type, per the findings of Elkins et al., 2007, noted above.

COOPER-KAHN: Are there ways that we can help our youth to build resiliency and reduce the risk?

GRAY: An important message to youth is the importance of ongoing brain development, which continues into the mid-twenties. Substance use during adolescence and young adulthood may have lasting implications for brain functioning, and the message of "protecting the brain while it's under construction" is important to convey. Helping youth with ADHD feel equipped to manage social pressures and stressors with adaptive skills is critically important, avoiding the misperception that substance use is either normative or therapeutic. Some basics can include practical substance refusal skills (such as, how to turn someone down that offers you cannabis or other substances).

COOPER-KAHN: What types of treatment are most effective for cannabis use disorder? Are there specific behavioral and/or pharmacologic advances that people should look for?

GRAY: The best evidence-based treatments for cannabis use disorder include motivational interviewing, cognitive-behavioral therapy, and (for youth) a variety of modalities of family therapy. The good news is that these types of psychosocial treatment can be helpful across a number of conditions, and treatment can address cannabis use while also addressing other presenting symptoms. The not-so-good news is that there is still a lot of room for improvement, as many people struggle to reduce or stop cannabis use even with the best of treatments for cannabis use disorder. Studies in youth and adults have shown that adding contingency management, which involves providing rewards for desired behavior (such as a negative urine cannabinoid test) can enhance outcomes.

There are no FDA-approved medications for treating cannabis use disorder, though a number of ongoing studies are examining promising candidate treatments to complement psychosocial and behavioral interventions. Our team has published findings involving the supplement N-acetylcysteine, which in trials to date showed significant benefit for adolescents, but not adults, with cannabis use disorder:

- Gray KM, Carpenter MJ, Baker NL, et al. A double-blind randomized controlled trial of N-acetylcysteine in cannabis-dependent adolescents. *American Journal of Psychiatry*. 2012; 169:805-812.
- Gray KM, Sonne SC, McClure EA, et al. A randomized placebo-controlled trial of N-acetylcysteine for cannabis use disorder in adults. *Drug and Alcohol Dependence*. 2017:177:249-257.

COOPER-KAHN: Individuals who overuse cannabis or other

substances are not always looking for treatment. How do you work with reluctant clients?

GRAY: Motivational interviewing is an important approach in this regard. This approach meets the client where he or she is and avoids confrontation, which can be counterproductive. While building rapport and gaining an understanding of the context of problematic use, over time there is a shared dialogue regarding potential motivators for change. This approach is important in building a therapeutic alliance and developing shared goals for success.

Contingency management can also be quite helpful. Given that it provides an external reward for behavior change, even when internal rewards are not perceived, it allows access to positive associations with non-use of substances. Over time, with contingent rewards for not using, clients may begin to internalize the benefits of not using (for example, improved school or work performance, improved relationships, money saved due to not purchasing cannabis) and sustain this behavior over time.

COOPER-KAHN: Are there ways that you adapt the treatment for adolescents and young adults?

GRAY: Young people are often brought into treatment because someone else (family, school, law enforcement) perceive a problem, while the individual may not be motivated for change or even perceive a problem. We are sensitive to this, as well as the counterproductive nature of aggressive confrontation. For youth, we are particularly fond of incorporating motivational interviewing and contingency management to complement cognitive-behavioral therapy. We are also focused on incorporating family into treatment in a positive way (working on natural rewards for desired behavior, for example, rather than maintaining a negative/sole focus on punishing unwanted behavior). Ultimately, the hope is that goals between the youth and the family can merge, as that helps create an alliance (in what otherwise might be a conflictual relationship) and predicts success.

COOPER-KAHN: Are there any specific practical considerations to know about when working with individuals with both ADHD and cannabis use disorder?

GRAY: I generally advise working on addressing ADHD and cannabis use disorder in tandem, rather than in sequence. There are, of course, complexities when considering ADHD pharmacotherapy in the context of active substance use, but in general we know that ADHD and cannabis use disorder are related both genetically and behaviorally, and in the end we want to treat the "whole patient" rather than picking one condition or another. This is a more reasonable approach when building a positive therapeutic alliance and seeking longer-term improved functional outcomes. **Q**

Joyce Cooper-Kahn, PhD, is a clinical child psychologist and coauthor of Late, Lost, and Unprepared: A Parent's Guide to Helping Children with Executive Functioning (Woodbine, 2012). She is deputy co-chair of Attention's editorial advisory board.