CANNABIS:
DOES IT HELP OR HURT ADHD?

Beverly Shin, MD, DMA
Addiction Psychiatry Fellow
University of Washington

I have no conflicts of interest to disclose

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Objectives

- Discuss high co-morbidity between ADHD and Substance Use Disorders (SUD's) , including Cannabis Use Disorder
- Discuss neurobiological, developmental, and genetic factors that may contribute to high level of co-morbidity between ADHD and SUD's
- Discuss current hypotheses for high level of co-morbidity
- Review current evidence about benefits/harms of cannabis on ADHD symptoms
- Discuss assessment and treatment considerations for patients with co-morbid ADHD and cannabis use

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CANNABIS USE AND ADHD: SOME NUMBERS

- 6-8% of children ages 2-18 in the US carry ADHD diagnosis
- ADHD is the most common neurobiological disorder presenting in childhood
- ADHD persists into adulthood in 35-50% of cases
- 4-5% of adults diagnosed with ADHD
- Cannabis is most commonly used illicit drug by both adolescents and adults
- Cannabis is the most commonly used illicit drug by adolescents with ADHD

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CANNABIS USE AND ADHD ARE HIGHLY CO-MORBID

ADHD is a risk factor for cannabis use (or any substance use)

- Meta analysis: Children with ADHD were 1.5 times more likely to develop a substance use disorder
- Children with ADHD are more likely than non-ADHD peers to begin smoking cannabis at a young age
- ADHD in adolescents associated with more severe SUD and greater functional impairment
- Among adults in SUD treatment, ADHD associated with
  longer duration of SUD and slower remission

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Cannabis Use and ADHD are Highly Co-Morbid

ADHD is over-represented among adolescents and adults with substance use disorders

- Cannabis Youth Treatment Study
  - 600 adolescents who met DSM-IV criteria for cannabis use disorder
  - **38%** also met criteria DSM-IV criteria for ADHD
- Large meta-analysis of adults in substance use treatmen
  - **Nearly 1 in 4** met DSM-IV criteria for ADHD

Associations Between ADHD and SUD

Neurobiological factors

- Overlapping brain abnormalities in ADHD and SUD
  - Changes in dopaminergic **syst**em and **striatal** involvement found in both
  - **Genetic aberrations in** dopamine transporters found in bo
- Impaired pre-frontal cortex oversight of limbic motivation-reward structures in ADHD → Difficulties with **behavior inhib**ition and **reward modulation**
  - Could lead to **greater risky substance use**

Associations Between ADHD and SUD

Developmental vulnerabilities in ADHD might increase risk of SUD

- Low academic achievement
  - Kids with ADHD often have poor academic performance even with adequate intellectual capabilities
  - Academic under-achievement is risk factor for SUD
- Risky decision making
- Social dysfunction

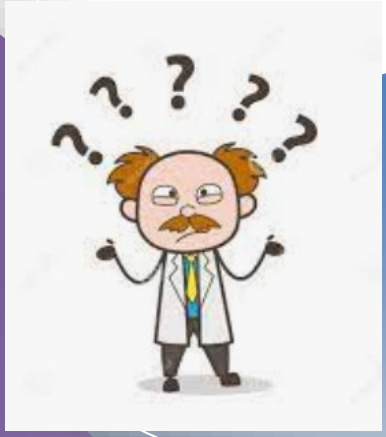
Associations Between ADHD and SUD

Genetic factors

- Both are heritable
- Several studies support a shared genetic background between ADHD and SUD
- Some evidence that aberrations in dopamine transporters are involved in both

So does cannabis help or hurt ADHD?

As usual with cannabis…it is complicated!



- ADHD is a disorder with a variety of different symptoms
  - Cannabis may have different effects on different symptoms, i.e. help hyperactivity but hurt inattention
- Cannabis plant is very complex, with over 500 biologically active compounds, very few of which have been well-studied in humans
- Schedule I status of cannabis continues to create significant regulatory and financial barriers to research
- **So…Not a lot of data currently**
- **NO randomized controlled trials looking at whole plant cannabis and ADHD**

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What do patients with ADHD who use cannabis say?

- Majority of patients with ADHD in online forums and in survey studies endorse IMPROVEMENT in ADHD symptoms from acute cannabis use, especially for:
  - Hyperactivity
  - Impulsivity
  - Restlessness
  - Mental frustration
- Responses about affects on attention and memory more mixed
  - Equal proportions of people report improvement and worsening of attention
  - Majority of people report worsening memory

What does clinical research tell us?

- Very little data currently
- One randomized placebo-controlled trial of synthetic THC/CBD oromucosal spray (nabiximol) in adults with ADHD
  - 30 adults diagnosed with ADHD
  - Dosed with nabiximol daily over 6-week period
  - Primary outcomes were cognitive performance and and activity level using Qb test
  - Secondary outcomes were behavioral and emotional lability symptoms of ADHD
  - No difference in primary or secondary outcomes between treatment and placebo
    - But one dose nabiximol has 2.7mg THC, and one "dose" of smoked cannabis has 10-30mg THC
  - Authors noted no impaired cognition with nabiximol

What does clinical research tell us?

One small study of cognitive effects of cannabis specifically on patients with ADHD

- **Small cross-sectional study (N=128)**
- **Neuropsychological testing to assess cognitive performance in young adults**
  - **ADHD and using cannabis regularly**
  - **ADHD and not using cannabis regularly**
  - **Matched peers with no ADHD and using cannabis regularly**
  - **Matched peers with no ADHD and not using cannabis regularly**
- **ADHD groups performed worse than controls on executive function tasks, but interactions between ADHD and cannabis were NOT significant**
- **Childhood diagnosis of ADHD, not cannabis use, was associated with executive dysfunction**

Cognitive effects of cannabis in general

Good reasons to worry about this in adolescents!

- Sensitive developmental period
  - Executive function
  - Emotion regulation
- Endocannabinoid system highly involved
  - Regulates appetite, sleep, emotion, memory, moveme
  - Big changes in endocannabinoid levels during teen y

Studies consistent in showing that acute cannabis intoxication impairs:

- Attention
- Memory
- Learning

Cognitive effects of cannabis in general

But data about LONG-TERM effects of cannabis on cognition is mixed

- **Several studies report associations between frequent and early-onset cannabis use and executive function deficits**
  - **These studies have been widely criticized for having many confounding variables**
    - **Co-morbid psychiatric illness (such as ADHD!)**
    - **Co-morbid substance use disorders (in addition to cannabis)**
- **Frequency of use often not accounted for in many studies**
- **Length of abstinence not taken into consideration in many studies**
  - **Cognitive dysfunction may have been due to residual effects of recent use o withdrawal rather than from persistent changes from chronic cannabis use**

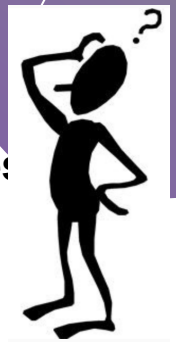
Cognitive effects of cannabis in general

2018 JAMA meta-analysis of association between cannabis use and cognitive functioning in adolescents and young adults

- Found statistically significant but SMALL cognitive effects associated with heavy or frequent cannabis use in adolescents—might not be clinically meaningful
- Increased abstinence time associated with decreased effect sizes
  - Studies with abstinence periods < 72 hours had small, non-significant effect sizes
- Concluded that there is a detectable but limited association between chronic cannabis use and cognitive functioning in adolescents and young adults
- Consistent with 3 prior meta-analyses of adult chronic cannabis users
  - Small negative associations between attention/executive functioning with frequent or heavy cannabis use
  - Effects almost undetectable in studies that required several days/weeks of abstinence prior to assessment

Many Unanswered Questions…

- **What are the long-term cognitive effects of cannabis on adolescents and adults?**
- **Does cannabis affect executive functioning in patients with ADHD differently or more dramatically?**
- **Is there a threshold of a particular amount or frequency that tips the scales for cognitive effects?**
- **Is there a critical developmental window when cannabis more severely affects executive function?**
  - Some animal and human data suggests that starting at younger age may worsen long-term cognitive outcomes
    - But again, results are mixed…



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Future Directions

Difficult to draw conclusions about causal relationship between cannabis and cognitive functioning because current studies do not account for cognitive deficits that may have existed PRIOR to cannabis use

- Need longitudinal studies that begin prior to cannabis initiation

Adolescent Brain Cognitive Development Study

- Will follow 10,000 children ages 9-10 over ten-year period
- Neuro-imaging
- Neuropsychological testing
- Genetic analysis
- Academic records
- Extensive assessment of psychiatric, social, and cultural dimensions

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So does cannabis help or hurt ADHD?

A better question might be: What is the interaction between ADHD and cannabis use?

And what does this mean clinically?

CANNABIS USE AND ADHD ARE HIGHLY CO-MORBID

MUST assess carefully for ADHD with cannabis use and vice versa!

- But assessment of ADHD with cannabis use can be tricky
  - ADHD symptoms can be disguised or mimicked by influence of cannabis use or withdrawal
    - Ideal to do assessment during period of abstinence if possible
  - Longitudinal history of cognitive function, academic performance, and overall function
  - Collateral and objective measures especially important
    - History from family, partner/spouse, friends
    - Assessment scales

PATIENTS WITH ADHD AND CANNABIS USE DISORDER ARE MORE LIKELY TO PRESENT WITH CO-OCCURRING MOOD OR PERSONALITY DISORDERS

Must also do thorough psychiatric assessment

- Mood and anxiety disorders especially common
- Rates of conduct disorder in boys diagnosed with ADHD estimated to be 25-30%
- **Conduct disorder + ADHD confers additive risk for substance use** than with either one alone

Providers are often hesitant to treat ADHD with stimulant medications if they have cannabis use disorder

- **BUT STIMULANT TREATMENT FOR ADHD REDUCES RISK OF DEVELOPING SUBSTANCE USE DISORDER**
- **Stimulant treatment of ADHD initiated at early age and continued long-term may be particularly beneficial**
  - **Youth with ADHD treated before age 9 who remained on long-term stimulant medications had similar levels of substance use as healthy controls**

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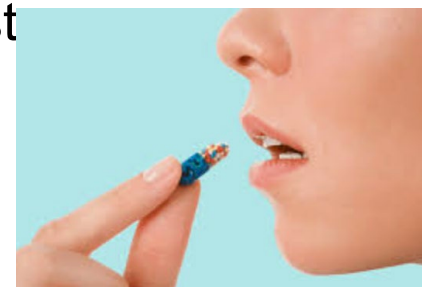
ADHD PHARMACOTHERAPY AT STANDARD DOSES MAY BE LESS EFFECTIVE IN PATIENTS WITH CO-MORBID CANNABIS USE DISORDER

- **But still some benefit both to ADHD and to SUD, especially if ADHD symptoms are significant driver of cannabis use**
- **In adults, pharmacotherapy outcomes are better if ADHD more severe**
- **May require higher doses**
  - Anecdotal evidence
  - Recent methylphenidate and amphetamine trials using higher doses had better treatment results than prior trials with standard dosing

EVEN WITH THESE LIMITATIONS, SHOULD STILL TRY TO TREAT ADHD IN CANNABIS USE DISORDER!

- Manage expectations for treatment results and partner with patient to improve chances of success
- Success in treating ADHD may motivate abstinence and improve engagement in SUD treatment
- Heavy cannabis use may interfere with pharmacotherapy for ADHD, so may need to target this first



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THANK YOU!

Questions?
shinbev@uw.edu

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Resources

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