



Cannabinoids and Autism

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EVEN THOUGH I AM:

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I AM NOT HERE TO REPRESENT THE UNIVERSITY OF UTAH

Disclosures

- Consultant, Advisory Board and Steering Committee member for BioMarin Pharmaceuticals
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- ▶ In Utah, you can legally get a prescription for marijuana to treat autism
 - ▶ This was NOT the recommendation of the Utah Medical Association
 - ▶ I can explain...

Autism Spectrum Disorder (ASD)

- ▶ Impairment in social communication/interaction
- ▶ Utah, you can legally get a prescription for marijuana to treat autism
- ▶ Restricted, repetitive interests or behaviors
- ▶ Onset during childhood

Agitation is not a core feature of ASD

Evidence-based Treatment for ASD

- ▶ **Skills-based Intervention – the earlier the better!**
- ▶ Applied Behavioral Analysis (ABA) – strongest evidence-basis
- ▶ PECS (picture exchange communication)
- ▶ Augmentative communication

Evidenced-based Medication Treatment of ASD:



“Evidence-based” treatment for agitation

- ▶ FDA has approved two antipsychotic medications for the **short term** treatment of agitation/irritability
- ▶ Medical prescribers’ knee jerk reaction to agitation in this patient population is to prescribe antipsychotics.
- ▶ Prescribing antipsychotics may be fast and easy, but it is plagued with serious long-term side effects and complications

...and it often doesn’t fix **the problem.**

Pain

Sleep disturbance

Other medical conditions

Psychiatric disorder

Psychosocial stressors

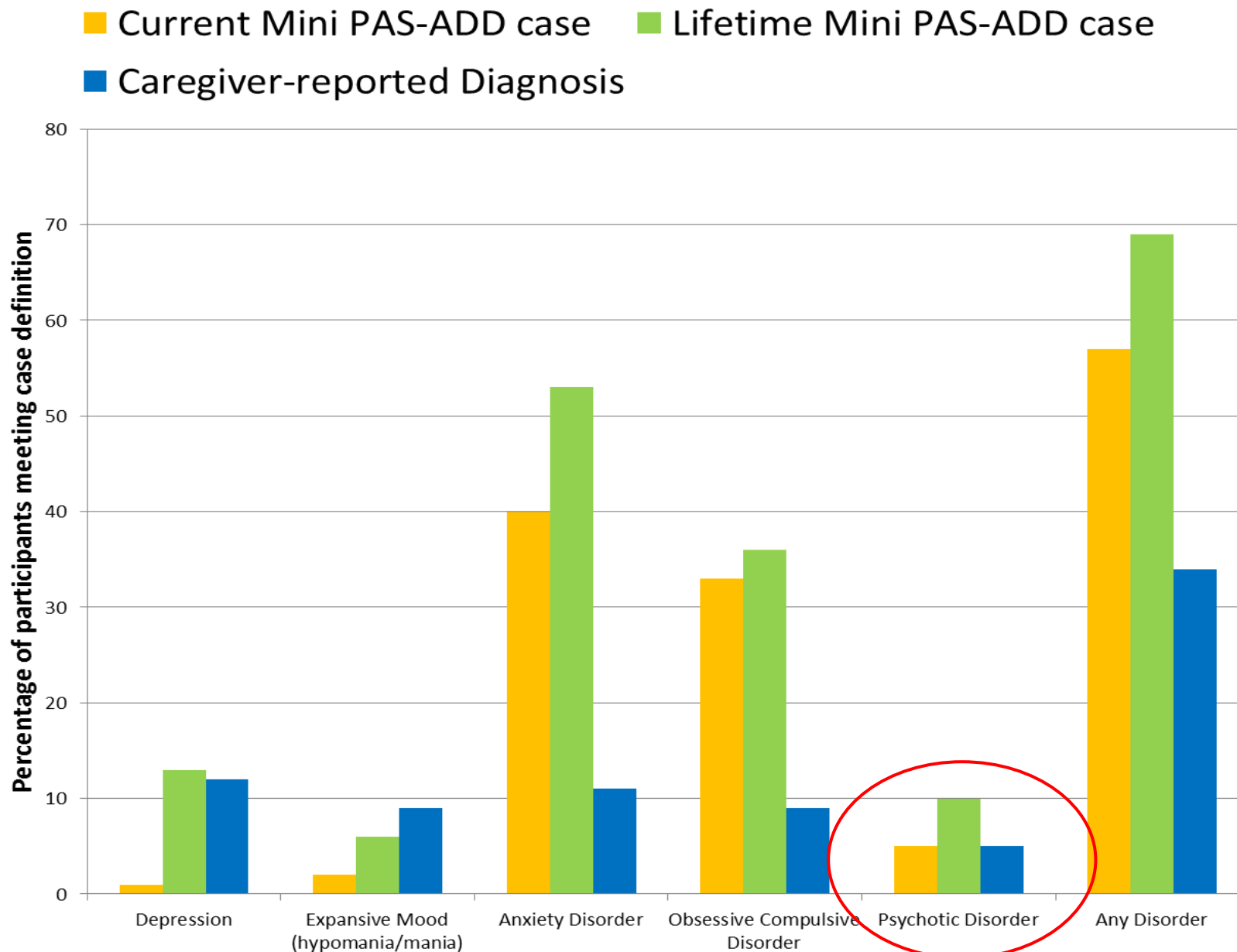
Inadvertently reinforced
behaviors

Communication challenges

Agitation

Psychiatric Comorbidity: Children with ASD

- ▶ At least 72% had at least one additional psychiatric diagnosis
- ▶ specific phobia (44%),
- ▶ Obsessive Compulsive Disorder (37%)
- ▶ ADHD (31%)
- ▶ Major Depressive Disorder (10%)
- ▶ Oppositional Defiant Disorder (7%)
- ▶ > 1 was common



Underlying causes of agitation are not routinely identified and treated

Because:

1. Most medical providers do not have the expertise to know what to ask to identify the underlying condition
2. Even if they did have the expertise, they do not have the time to ask all of these questions

Parents look elsewhere for answers

Which is why...

- ▶ In Utah, you can legally get a prescription of marijuana if you have autism

Yet...

- ▶ This was NOT the recommendation of the Utah Medical Association


Marijuana:

- ▶ Plant-derived cannabinoids:
 - ▶ δ -9 tetrahydrocannabinol (THC) -- the main psychoactive component
 - ▶ Cannabidiol (CBD) – the FDA-approved treatment for severe seizure disorders

CBD

- ▶ Reduces neural excitation
- ▶ FDA-approved for severe seizure disorders (Epidiolex)
- ▶ *Potential* benefits are being investigated for addiction, anxiety, psychosis, autism
- ▶ Anxiolytic effects may have a U-shaped curve with a therapeutic window of response

Dharmapuri S, Miller K, Klein JD. Marijuana and the Pediatric Population. *Pediatrics*. 2020 Aug;146(2):e20192629; Premoli M et al Cannabidiol: Recent advances and new insights for neuropsychiatric disorders treatment. *Life Sciences* 224 (2019) 120-127



CBD **without** THC may have therapeutic value for psychiatric disorders with relatively minimal side effects

Although efficacy has not been proven, CBD is a reasonable option if proven treatments have failed and cost is not prohibitory

THC

- ▶ The main psychoactive component
- ▶ Causes the high
- ▶ Neurologically activating
- ▶ Responsible for the analgesic, antiemetic, and appetite stimulation properties of marijuana
- ▶ Also responsible for the perceptual alterations, paranoia/psychosis, impaired learning, memory, attention

Dharmapuri S, Miller K, Klein JD. Marijuana and the Pediatric Population. *Pediatrics*. 2020 Aug;146(2):e20192629; Premoli M et al Cannabidiol: Recent advances and new insights for neuropsychiatric disorders treatment. *Life Sciences* 224 (2019) 120-127

The Ugly: THC causes psychosis

- ▶ Likelihood of developing psychosis among daily THC users increases with THC potency
- ▶ In a recent study by Di Forti et al, “daily marijuana use and high-potency marijuana (THC content >10%) are the strongest independent predictors of whether an individual will have a psychotic episode. “
- ▶ THC use associated with antipsychotic treatment failure and relapse
- ▶ Patients with schizophrenia and a history of cannabis use have longer durations of their first hospitalization (59 days v. 30 days) and a higher rate of readmission (10 times v. four times).

Di Forti M, et al. The contribution of cannabis use to variation in the incidence of psychotic disorder across Europe (EU-GEI): a multicentre case-control study. *Lancet Psychiatry*. 2019 May;6(5):427-436.; Manrique-Garcia E, et al. Prognosis of schizophrenia in persons with and without a history of cannabis use. *Psychol Med*. 2014;44(12):2513–2521

Autism and psychosis

- ▶ Individuals with autism are at higher risk for developing psychosis
- ▶ The propensity towards psychosis in autism is unmasked by FDA-approved drugs that demonstrated during clinical trials to cause psychosis: stimulants, atomoxetine, and amantadine
- ▶ It can take months, sometimes years, to see this complication emerge
- ▶ A core feature of autism is the ability to communicate ones thoughts and feelings – this is problem when trying to monitor a patient for the emergence of early psychotic symptoms
- ▶ Because psychosis is something that often emerges over time, patients and their families, do not attribute agitation caused by psychosis to the medication that was started months or years ago.

I have seen this over and over again

Where is the Evidence?

- ▶ In support of THC use for autism:
 - ▶ Testimonials
 - ▶ A few published case reports
 - ▶ One retrospective study demonstrated reduced agitation in 44 of 60 children (except one girl developed psychosis after 6 months and two other children experienced an escalation of their agitation).
 - ▶ ...but a subsequently double blinded placebo-controlled trial failed to show treatment efficacy in its primary endpoint

Where is the Evidence?

- ▶ Against THC use for autism:
 - ▶ Psychosis is a real problem
 - ▶ I can share several patient stories, where new onset psychosis occurred months after starting THC

Standard of Proof: FDA approval

- ▶ Despite the promising testimonials, there is no evidence meeting the standard of proof in medicine to support THC's efficacy in treating ASD.
- ▶ Yet, there are mountains of strong evidence demonstrating that (1) individuals with autism experience greater vulnerability to developing psychosis *and* (2) THC causes psychosis in vulnerable individuals.

Big Picture

Those who treat autism with THC do so at their peril

Those who use THC to treat agitation associated with autism
can be creating a much bigger problem

- ▶ CBD **without** THC may have therapeutic value for psychiatric disorders with relatively minimal side effects, though strong evidence for efficacy is still lacking
- ▶ Although evidence for efficacy of CBD on psychiatric disorders has not yet met the standard of proof set in medicine, CBD **without** THC is a reasonable option if proven treatments have failed and cost is not prohibitory