## Cannabis and CBD use in ASD and SIB

MATTHEW TESTER BSC, MD CANDIDATE (2024) FAMILY SUPPORT INSTITUTE NOVEMBER 8<sup>TH</sup>, 2021

### Land Acknowledgement



I would like to acknowledge that I am coming to you today from the traditional, ancestral, and unceded territory of the Coast Salish Peoples, including the territories of the Musqueam, Squamish, Stó:lō and Tsleil- Waututh Nations

### Outline

- Introduction and background
- •What are people saying?

- •What does the science say?
- •What's next, practical considerations, and helpful resources

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### Learning Objectives

- Understand some of the cultural context around use of medical cannabis and CBD, especially for severe childhood epilepsy
- 2. Gain a basic understanding of the endocannabinoid system
- 3. Define what phytocannabinoids are and appreciate the differences between THC and CBD
- 4. Review the methods, results, strengths, and weaknesses of three recent studies of CBD-rich cannabis for autism spectrum disorder and behaviours like SIB
- 5. Briefly review the current trend in cannabis research in ASD

### About Me

- Graduated with a BSc from UBC in 2019
- Research assistant at BC Children's Hospital 2017 – 2018, and 2019 – 2020
- Started MD journey in 2020









### Why CBD, and why now?

- The story of Charlotte Figi, a then 6 year old girl with Dravet syndrome, a severe childhood epilepsy syndrome that is resistant to most known seizure medications
- Paige, Charlotte's mom, found previous research suggesting cannabidiol (CBD) in cannabis could help control Charlotte's seizures
- Paige found the cannabis strain "Hippie's Disappointment", high in CBD and very low in THC
- After taking oil from Hippie's Disappointment, there was a drastic reduction in Charlotte's seizures



### Why CBD, and why now?

- The Stanley Brothers renamed Hippie's Disappointment to Charlotte's Web
- The story of Charlotte Figi spread, and demand for Charlotte's Web skyrocketed
- In 2018, Epidiolex (CBD) was FDA approved for use in children with the severe epilepsy syndromes Lennox-Gastaut and Dravet



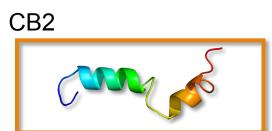


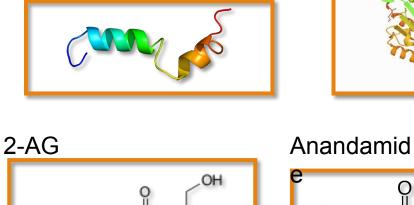
# So, what does cannabis do?

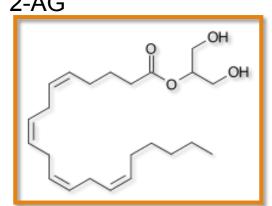


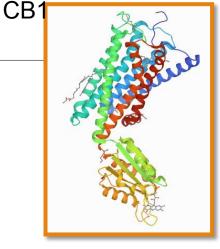
### The Endocannabinoid System

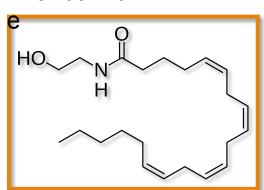
- Widespread system in the body, made of lipid (fats) messenger molecules, their receptors, and various enzymes
- Cannabinoid receptors (CB) 1 and 2 only discovered in the early 1990s
- May be involved in pleasure, memory, thought, concentration, movement, anti-inflammation, but not well understood











### Phytocannabinoids

 80+ cannabinoid molecules present in cannabis plant!

### Δ9-tetrahydrocannabinol (THC)

- Causes the "high" of cannabis use
- Currently accepted use in chronic pain, MS spasticity, chemo-related nausea

### Cannabidiol (CBD)

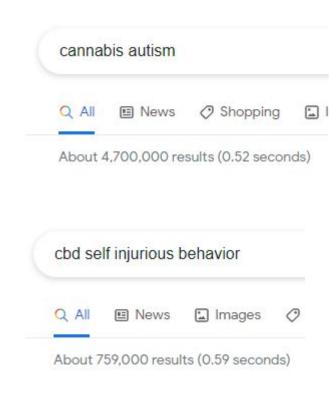
- Does not cause a high, modulates endocannabinoid system indirectly
- Proven anticonvulsant effects, potential antianxiety properties

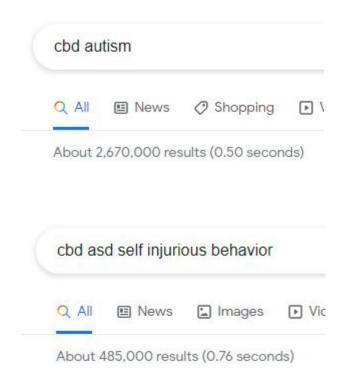
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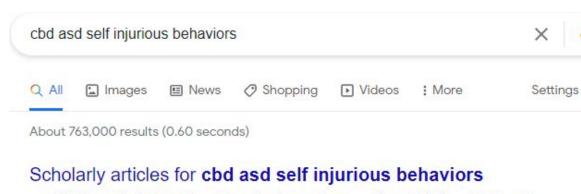
# So, what are people saying?



### Just a simple Google search...







... of CBD-enriched Cannabis sativa extract on autism ... - Fleury-Teixeira - Cited by 20

... regarding cannabis use in children with autism ... - Duvall - Cited by 8

... with autism spectrum disorder and severe behavioral ... - Aran - Cited by 70

pediatrics.aappublications.org > peds.2018-0558.full.pdf

### Ethical Implications for Providers Regarding Cannabis Use in ...

by SW Duvall · 2019 · Cited by 8 — Children with **autism** spectrum disorder (**ASD**) are at risk for **self-injurious behaviors** that can be difficult to treat in the context of co-occurring low ...

clinicaltrials.gov > show > NCT04517799 ▼

### Trial of Cannabidiol to Treat Severe Behavior Problems in ...

Aug. 18, 2020 — Children with autism spectrum disorders (ASD) may have severe behavior problems, including aggression, self-injurious behaviors, severe and ...

www.ncbi.nlm.nih.gov > pmc > articles > PMC6333745

### Oral Cannabidiol Use in Children With Autism Spectrum ...

by D Barchel · 2018 · Cited by 63 — Objective: Children with **autism** spectrum disorder (**ASD**) commonly exhibit comorbid symptoms such as aggression, hyperactivity and anxiety. Introduction · Materials and Methods · Results · Discussion

bmcpsychiatry.biomedcentral.com > articles \*

### Current state of evidence of cannabis utilization for treatment ...

by R Agarwal  $\cdot$  2019  $\cdot$  Cited by 16 — The core symptoms and co-morbidities associated with **autism** spectrum disorders (**ASD**) affect daily living and quality of life. Existing ...

### CBD Oil and Autism: What Parents Need to Know

CBD oil is becoming an increasingly popular treatment option for a variety of health conditions – including autism. But is CBD oil a safe autism treatment for kids?



### Can Medical Marijuana Help Kids With Autism?

BRAIN & NERVOUS SYSTEM > AUTISM > TREATMENT/THERAPY

### CBD Oil as a Treatment for Autism

By Lisa Jo Rudy Medically reviewed by Arno Kroner, DAOM, LAC Updated on May 14,

## The Verywells and WebMDs

- Other top hits online are from common sources like Verywell, WebMD, Autism Parenting Magazine, Spectrum news, etc.
- In generally, they report that CBD can help with:
  - Anxiety and stress
  - Sleep
  - Problem behaviours, like aggression and self-injurious behaviours
  - Improves social ability
  - Seizures
- They say in some, CBD may have side effects like nausea, vomiting, and drowsiness

### What are parent's experiences?



### Advocacy Groups

 The promise and optimism of medical cannabis and CBD treatment for ASD has led to the formation of parent-led advocacy groups







## What Does the Science Say?

Brief Report: Cannabidiol-Rich Cannabis in Children with Autism Spectrum Disorder and Severe Behavioral Problems—A Retrospective Feasibility Study

Adi Aran<sup>1</sup> · Hanoch Cassuto<sup>2</sup> · Asael Lubotzky<sup>1</sup> · Nadia Wattad<sup>1</sup> · Esther Hazan<sup>1</sup>

### Aran et al. 2019

- Methods: Restrospective chart review study of 60 kids with ASD disruptive behaviours. Treated with CBD-rich cannabis extract
- **Results:** 61% children reported to have considerable *improvement* in behaviour problems, 39% reported *improved* anxiety, 47% reported *improvement* in communication
- Side effects: aggravated sleep disturbance, restlessness, irritability, loss of appetite
- Limitations: Small sample, reliance on self-report, not blinded or controlled

# Oral Cannabidiol Use in Children With Autism Spectrum Disorder to Treat Related Symptoms and Co-morbidities

Dana Barchel<sup>1†</sup>, Orit Stolar<sup>2†</sup>, Tal De-Haan<sup>1</sup>, Tomer Ziv-Baran<sup>3</sup>, Naama Saban<sup>4</sup>, Danny Or Fuchs<sup>1</sup>, Gideon Koren<sup>1,5</sup> and Matitiahu Berkovitch<sup>1\*</sup>

### Barchel et al. 2019

 Methods: 53 kids recruited with ASD and administered cannabis extract at a ratio of 20:1 CBD to THC, followed-up for at least 30 days

### Results:

Domain	% of participants improved	% of participants with no change	% of participants with worsening
Hyperactivity (N=38)	68.4%	28.9%	2.6%
SIB/rage attacks (N=34)	67.6%	23.5%	8.8%
Sleep problems (N=21)	47.1%	29.4%	23.5%
Anxiety (N=17)	47.1%	29.4%	23.5%

- Side effects: most common reported were sleepiness and decreased appetite
- Limitations: Small sample size, short follow-up period, lack of blinding

### RESEARCH Open Access

### Check for updates

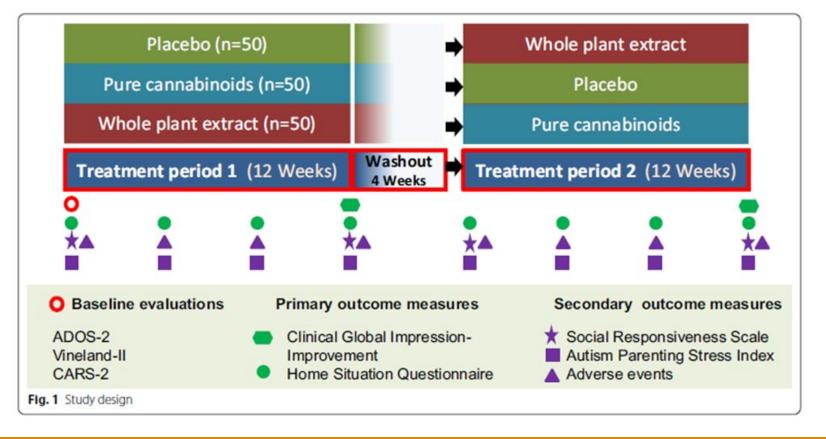
## Cannabinoid treatment for autism: a proof-of-concept randomized trial

Adi Aran<sup>1</sup>\*©, Moria Harel<sup>1</sup>, Hanoch Cassuto<sup>1</sup>, Lola Polyansky<sup>1</sup>, Aviad Schnapp<sup>1</sup>, Nadia Wattad<sup>1</sup>, Dorit Shmueli<sup>2</sup>, Daphna Golan<sup>3</sup> and F. Xavier Castellanos<sup>4</sup>

### Aran et al. 2021

• Methods: Randomized, double-blind, placebo-controlled trial with kids and teens with

ASD



### Aran et al. 2021

### Results:

- 150 children, average age 11.8 years, were recruited and randomly assigned to one of the three groups
- No severe or serious adverse events
- Significantly more participants had behaviour improvement in the whole plant extract group than the placebo group, according to CGI-I
- No significant differences between groups on the HSQ-ASD
- Significant improvement in social communication in whole plant extract group compared to placebo

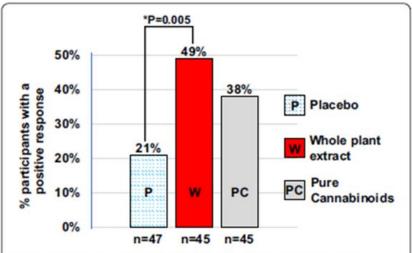


Fig. 3 Participants (%) whose behavioral problems either much improved or very much improved on the CGI-I scale following treatment. Response to 12-week treatment using the Clinical Global Impression-Improvement (CGI-I). Positive response in this scale is defined as a rating of 'much improved' or 'very much improved' [34]. Outcome was analyzed using Likelihood ratio chi-square test. P value is unadjusted. \*Remains significant after Bonferroni-correction for multiple comparisons

## Aran et al. 2021: Progress, with limits

In this study, we have demonstrated for the first time in a placebo-controlled trial that cannabinoid treatment has the potential to decrease disruptive behaviors associated with ASD, with acceptable tolerability. This is specifi-

### Aran et al. 2021: A Word of Caution

### Funding

The study was funded by BOL Pharma, Revadim, Israel and the National Institute for Psychobiology in Israel (#203-17-18). The funding bodies were not involved in any way in the study design, collection, analysis and interpretation of data or in the writing of the manuscript.



### What's Next?

### RCTs, RCTs, RCTs...

Row	Saved	Status	Study Title
1		Recruiting	CAnnabidiol Study in Children With Autism Spectrum DisordEr
2		Not yet recruiting	Trial to Investigate the Safety and Efficacy of Cannabidiol Oral Solution (GWP42003-P; CBD-OS) in Children and Adolescents With Autism Spectrum Disorder
3		Recruiting	Cannabidiol for ASD Open Trial
4		Unknown †	Shifting Brain Excitation-Inhibition Balance in Autism Spectrum Disorder
5		Recruiting	Trial of Cannabidiol to Treat Severe Behavior Problems in Children With Autism
6		Completed	Cannabinoids for Behavioral Problems in Children With ASD

### Resources

How to Evaluate Health Information on the Internet: Questions and Answers - How To Evaluate Health Information on the Internet: Questions and Answers (nih.gov)

Cannabis and autism, explained - Cannabis and autism, explained | Spectrum | Autism Research News (spectrumnews.org)

Agarwal R, Burke SL, Maddux M. Current state of evidence of cannabis utilization for treatment of autism spectrum disorders. BMC Psychiatry. 2019 Dec;19(1):328.

MacCallum CA, Russo EB. Practical considerations in medical cannabis administration and dosing. Eur J Intern Med. 2018 Mar 1;49:12–9.

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All the research participants, their families, and everyone else driving this conversation forwards!









Thank you!
Questions? Email: sstephens@fsibc.com

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- 2. <u>Charlotte's Web (cannabis) Wikipedia</u>
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- Can Medical Marijuana Help Kids With Autism? (webmd.com)
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