



CBD, Seizures & SynGAP: Parents Experience

By Walther Otto Müller - From Franz Eugen Köhler's *Medizinal-Pflanzen*. Published and copyrighted by Gera-Untermhaus, FE Köhler in 1887 (1883–1914). Obtained from <http://caliban.mpiz-koeln.mpg.de/~stueber/koehler/>. Originally uploaded to wikipedia by w:User:Chmod007 on 19:57, 14 November 2004. An enhanced version was uploaded to wikipedia by w:User:DarkEvil on 17:39, 14 December 2006, Public Domain, <https://commons.wikimedia.org/w/index.php?curid=1739269>

Three important notes before we start:



This presentation is available at:

www.syngapresearchfund.com/knowledge

If you are new to this, it will feel like tons of information, hang in there, it all comes together.

Neither SRF nor any parent here is in anyway compensated for the brands mentioned or this webinar, we are just sharing what worked in the hopes that you can learn from our efforts.

Parents sharing their story today

- Aaron Harding – California – bit.ly/SRFWW_Jaxon
- Fraser Chatterton – Australia – Abi
- Jo Ashline – California – bit.ly/SRFWW_Andrew
- Ray Holden – UK – Miles
- Virginie McNamar – Indiana – bit.ly/SRFWW_Ty
- Mike Graglia – California – bit.ly/SRFWW_Tony
- Peter Halliburton – Texas – bit.ly/SRFWW_Carter

Nobody here is a doctor, this is not medical advice, consult a physician before changing meds.

If your physician is not willing to try CBD, find a new one.

Monica & Aaron - California



Jaxon's Seizure Treatment History

- Keppra
- Topomax; stopped due to behaviors
- Depakote (Valproic Acid)
- Tegretol; oral aversion
- Zonegran; oral aversion
- Clobazam
- Lamotrigine (the cocktail); didn't work
- Clobazam (currently 40mg)
- CBD:THC (currently 84mg)



Clobazam (Onfi®) and CBD potentiate each other



We will get into this more at the end, but since so many Syngap patients in the US try Onfi it is worth noting that the two drugs make each other more potent and so less of each may be needed.

For more see this article:



Full-Length Original Research | [Free Access](#)

Drug-drug interaction between clobazam and cannabidiol in children with refractory epilepsy

Alexandra L. Geffrey, Sarah F. Pollack, Patricia L. Bruno, Elizabeth A. Thiele [✉](#)

First published: 26 June 2015 | <https://doi.org/10.1111/epi.13060> | Citations: 139

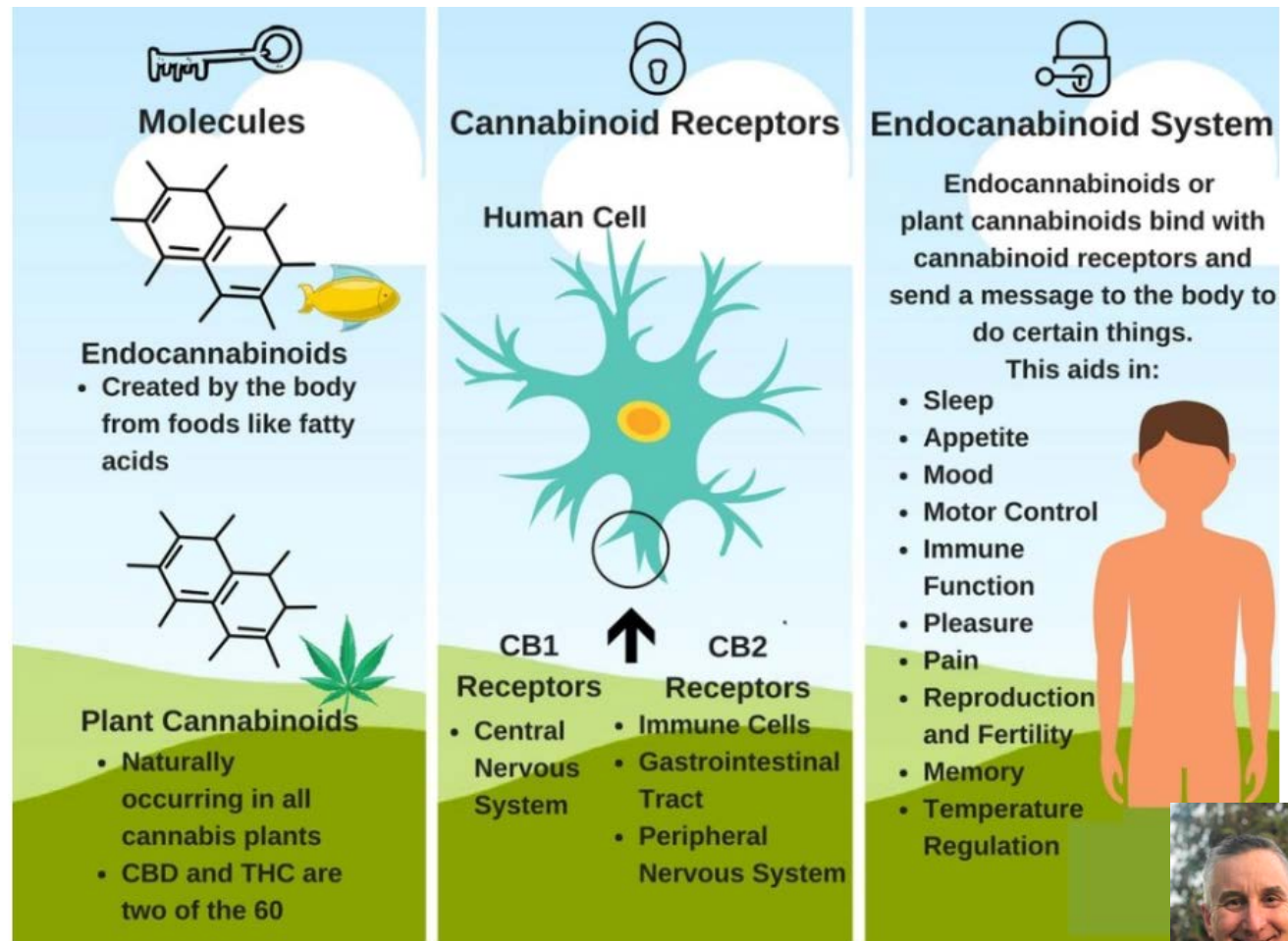
<https://onlinelibrary.wiley.com/doi/full/10.1111/epi.13060>



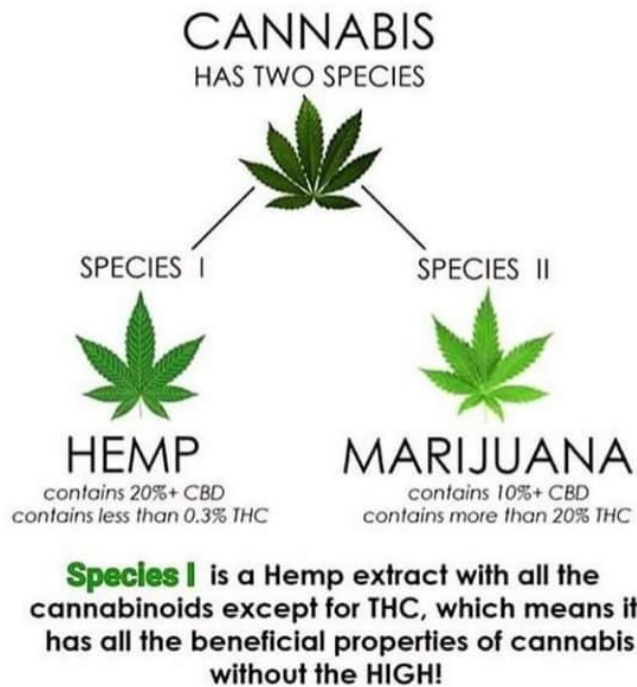
Endocannabinoid System (ECS)

“The precise mechanisms by which CBD, including EPIDIOLEX, exerts its anticonvulsant effect in humans are unknown. Cannabidiol does not appear to exert its anticonvulsant effects through interaction with cannabinoid receptors”
-- Epidiolex package insert

Image: hawaiimedical.com/2017/09/21/what-is-cbd/



All CBD oils are not the same



	HEMP-based Cannabis Sativa All CBD	MARIJUANA- based Cannabis Indica CBD & THC
Over the counter	<ul style="list-style-type: none"> Charlette's Web 	Not available for kids
Rx Req'd	<ul style="list-style-type: none"> Epidiolex 	<ul style="list-style-type: none"> Jayden's Juice (CA) Hayleigh's Hope (CO) State Specific due to Federal/State Law



Graphic by NM Brief Relief at nmbriefrelief.com

1,350+ articles on CBD Epilepsy in 2019!



FULL-LENGTH ORIGINAL RESEARCH | Open Access |

Long-term cannabidiol treatment in patients with Dravet syndrome: An open-label extension trial

Orrin Devinsky , Rima Nabhout, Ian Miller, Linda Laux, Marta Zolnowska, Stephen Wright, Claire Roberts

First published: 23 December 2018 | <https://doi.org/10.1111/epi.14628> | Citations: 16

<https://onlinelibrary.wiley.com/doi/epdf/10.1111/epi.14628>



Invited Review | Free Access

Efficacy of cannabinoids in paediatric epilepsy

Shayma Ali, Ingrid E Scheffer , Lynette G Sadleir

First published: 06 November 2018 | <https://doi.org/10.1111/dmcn.14087> | Citations: 4

<https://onlinelibrary.wiley.com/doi/full/10.1111/dmcn.14087>

Google Scholar search results for "cbd epilepsy" (1,350 results, 0.07 sec).

Articles

Any time
Since 2019
Since 2018
Since 2015
Custom range...

Sort by relevance
Sort by date

☒ include patents
☐ include citations

Create alert

The proposed multimodal mechanism of action of cannabidiol (CBD) in epilepsy: modulation of intracellular calcium and adenosine-mediated signaling (P5. 5-007)
K Nichol, C Stott, N Jones, RA Gray, M Bazetou... - 2019 - AAN Enterprises
Objective: We present preclinical evidence summarizing CBD's leading mechanisms of action in epilepsy. Background: Although commonly misrepresented, CBD does not act through cannabinoid receptors at physiologically achievable concentrations. CBD has ...
☆

Quality of life in adults enrolled in an open-label study of cannabidiol (CBD) for treatment-resistant epilepsy
TE Gaston, M Szaflarski, B Hansen, EM Bebin... - Epilepsy & Behavior, 2019 - Elsevier
Abstract Treatment-resistant epilepsy (TRE) is associated with low quality of life (QOL). Cannabidiol (CBD) may improve QOL, but it is unclear if such improvements are independent of improvements in seizure control. Our aim was to compare QOL at baseline ...
☆ Cited by 3 Related articles All 4 versions

... Interaction Studies with Coadministration of Cannabidiol (CBD) and Clobazam, Valproate, Stiripentol or Midazolam in Healthy Volunteers and Adults with Epilepsy
J Szaflarski, P Patsalos, B Gidal... - 2019 - thieme-connect.com
Materials and Methods: Effects of multiple-dose CBD on steady-state pharmacokinetics (PK) of CLB, N-desmethyl clobazam (N-CLB), VPA, 2-propyl-4-pentenoic acid (4-ene-VPA), and STP, and multiple-dose CLB, VPA, and STP on steady-state PK of CBD and metabolites ...
☆

... of Cannabidiol (CBD) and Clobazam (CLB), Valproate (VPA), Stiripentol (STP) or Midazolam (MDZ) in Healthy Volunteers (HVTs) and Adults with Epilepsy (S3. 003)
J Szaflarski, P Patsalos, B Gidal, K VanLandingham... - 2019 - AAN Enterprises
Objective: To summarise current understanding of DDIs when CBD is coadministered with CLB, VPA, STP or CYP3A4 substrate. Background: DDIs between CBD and common antiepileptic drugs (AEDs) is of clinical interest since it is anticipated that CBD will ...
☆

The Modulatory Effects of Cannabidiol on Microglial Function and Expression in Epilepsy
TR Victor, JC Nissen, MW Elmes, DG Deutsch... - The FASEB J, 2019 - fasebj.org
... We postulate that CBD modulates the activation of microglial cells in the brain during experimental epilepsy. In this study, we evaluate the effects of CBD on cell death, microglial receptor expression in vitro and in vivo post seizure ...
☆

Fraser Chatterton – Australia



Abi's Story: The search for seizure reduction using Cannabis.

- Live in Australia under prohibition.
- Travelled to NZ & Japan for access and treatment.
- Tried lots of brands and ratios.
- Endoca, Elixinol, Charlotte's Web, Haleigh's Hope, Tilray, CannEpill, various 'green fairy' oils.
- Now have legal access for a CBD:THC isolate (20:1).
- Looking to purchase land next year and start a Hemp farm.



Lessons Learnt (1 of 2)



- It's all cannabis!
- True Hemp is cannabis sativa bred for fibre and seed.
- Modern growers have focused on breeding low THC cannabis that can be labelled as hemp.
- Not all oils are equal. Two brands may have the same ratios but have different effects.
- Oils made from these varieties have a better terpene and flavonoid profile than true hemp cultivars and should be sought after.
- Linalool, Myrcene, Pinene are the main terpenes to look for.
- Extraction methods produce different results. Look for residues. CO2 extraction most prominent with paediatric patient oils.
- MCT oil excellent base as it is high fat and aids absorption.
- Buy brands that have lab tests.
- Cannabis is used for bioremediation & will take up heavy metals. Buy organic.



Lessons Learnt (2 of 2)



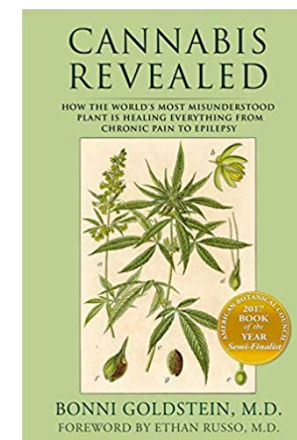
- Pharma cannabis (Epidiolex etc) use isolates for standardisation and precision but lack terpenes and other plant compounds we don't know about yet.
- Entourage effect is not magic! (Dr Shaffer). Thousands of years of empirical data in herbal medicine support the synergy of plant medicines. Scientist are catching up and data is available to support the entourage effect theory.
- Don't be afraid of THC! Better seizure control can be found in ratios with higher THC content. 10:1, 20:1.
- CBD can be stimulating if given too late in the afternoon or evening, low dose THC effective for sleep disturbance especially Indica varieties.
- CBDV cultivars are being bred for seizure control.
- Start low and go slow. Pharma CBD and Hemp Oils dose differently.
- If you're going to try and learn from Facebook, join a brand name support group.



Suggested Reading



- pediatriccannabissupport.com/startingyourchildonmedicalmarijuana/
- www.projectcbd.org/medical-marijuana-seizures-sulak-saneto-goldstein
- www.fundacion-canna.es/en/terpenes
- www.medicinalgenomics.com/wp-content/uploads/2016/05/Bonni-Goldstein-CannMed2016.pdf
- Pediatric CBD dosing Guidelines
www.theroc.us/images/PediatricGuidelines.pdf
- Read Cannabis Revealed by Bonnie Goldstein



Jo Ashline – California



Delayed Development: Low tone, delayed crawling and walking, babbling ceased at 12 months, non-verbal, eye contact ceased at 12 months, first drop attacks and abnormal absence seizures at 2 years of age.

- **Age 2:** Diagnosed with severe form of autism, epilepsy, and global developmental delay.
- **Age 13:** Lennox Gastaut Syndrome confirmed
- **Age 16:** Syngap1

Andrew can have hundreds of seizures per day when not properly treated.



Seizure Treatment History

- Monotherapy
 - Zonegran - Failed
 - Klonopin - Failed
- Polytherapy
 - Klonopin & Depakote – Min. to Mod. control - Daily seizures
 - Klonopin, Depakote & Topomax – Min to Mod control - Daily seizures, anorexia as side effect of Topomax
 - Klonopin, Depakote & Lamictal – Min to Mod control – Daily seizures
 - Depakote, Klonopin & Felbatol – Min to Mod control – Daily seizures
 - Depakote, Felbatol, Onfi – Min to Mod control – Daily seizures
- CBD (along with Depakote, Felbatol & Onfi)
 - Charlottes Web -- Failed
 - CannaKid -- Failed
 - **Epidiolex**
 - **First time nearly 100% seizure control since onset of epilepsy at age 2.**
 - **Seizure control lasted approximately 6 months.**
 - **After removal of Onfi, seizures came back suddenly.**
 - **Currently adjusting to obtain seizure control again.**



Barriers to CBD Treatment



- **Geographical location** – is it legal/accessible where I live? Am I breaking the law? What are my options?
- **The right diagnosis** – for Epidiolex, this means Lennox Gastaut or Dravet
- **Lack of knowledgeable/agreeable physicians** who are on board with CBD treatment
 - Will the doctor support me and my child?
 - Will the hospital prevent me from administering CBD if my child happens to be inpatient?
- **Disruptive/concerning side effects**
 - Andrew lost 32 pounds in 5 months and continues to drop weight at an alarming rate. We are working on this with his team, but it's been scary.
 - Loose stools. For our developmentally delayed son, this has meant many accidents, though a small price to pay for better seizure control.
- **Potentially dangerous interactions with current AEDs**
- **Cost** – Will my insurance cover this? How much is it out of pocket?



Last thoughts...



If you have the right support in place and have done the research, CBD treatment has been shown to dramatically improve quality of life for a significant portion of the epilepsy population.

Every child/adult is different and what works for one may not work for another.

Aside from the side effects I've mentioned, Andrew has finally responded to a treatment protocol and we had months where he was thriving.

He was thinking more clearly, his mood was improved dramatically, behaviors were down significantly, he was able to access his life more meaningfully, and his overall quality of life increased.

We continue to work to lessen side effects while finding that dosing sweet spot again.



Ray Holden – UK



Miles, a boy with Syngap, is now 10. From birth to age 5

- Developed well in the first 6 months of life
- Then development plateaued
- Miles immune system was very poor in his first years
- Miles had poor fine and gross motor skills
- Miles lacked physical and mental energy
- Epilepsy developed fast from a few eye rolls to drop seizures in a very short space of time



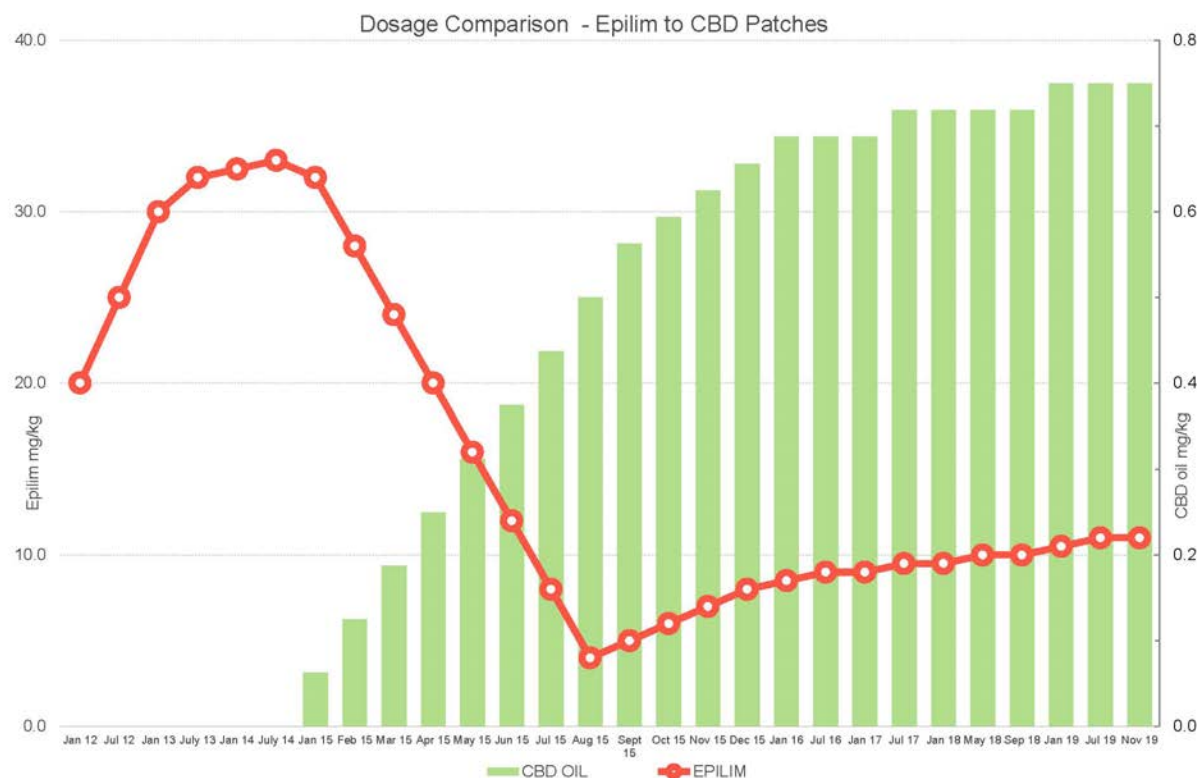
Miles journey to CBD

Years 5-10

- Miles Epilepsy was controlled well with Epilim (Sodium Valproate)
- Epilim dosage was high, high enough to be neurologically sedative
- CBD was introduced to try to get Miles off Epilim
- We moved to topical/transdermal CBD quite quickly
- Control has been achieved for a long period of time
- Missense de novo mutation, diagnosed 2 two years ago
- Miles does have the odd eye roll from time to time
- Both doses of Epilim and CBD are very slowly being raised
- We are considering buying a personal EEG to monitor activity. Such as 'Muse 2'.
 - <https://choosemuse.com/muse-2/>



Epilim - CBD Dosage to maintain general seizure control



Epilim (Sodium Valproate)

- Miles achieved control with his first anti-convulsant
- We achieved general control at over 30mg/kg
- 30mg/kg is very neuroactive and sedating. It controls seizures, but limits development
- We decided to search for something else to help control seizures

CBD

- CBD was first given orally, under the tongue and swallowed
- We used Charlottes Web Oil (8% strength) in tandem with lowering Epilim in steps
- Transdermal patches introduced initially to lower costs and volume administered

Two CBD products

SRF



10mg CBD Oil Patch



40% strength CBD Oil



CBD Patch & Oil Booster



Why transdermal patches?

Why we switched from oil to patches

- Transdermal patches introduced initially to lower costs and volume administered
- Transdermal CBD is up to 10 times more bioavailable than ingested CBD
- We found we could use 1/8th of the oral dose. So the factor of ten was consistent with our experience.

Benefits/Issues

- Transdermal patches are cheaper/easier to administer/evened out the dose entering the bloodstream
- We apply patches twice daily
- We apply them to an area that they cant be removed or less prone to rubbing off (between the shoulders) To further reduce costs, we have found 'boosting' with direct oil drops helps raise CBD levels
- CBD patches cause minor irritation, probably just from the latex patch not allowing the skin to breath/sweat/release oils. But we move each patch slightly from day to night
- We currently use 1 and half patches a day (15mg) =
3/4 of a patch, twice a day, plus 10mk/kg of Epilim



Virginie McNamar – Indiana

bit.ly/SRF_4P_LGS



- Ty's Syngap journey has been in two chapters, both CBD oils.



Charlotte's Web



- First seizure on October 2018 at 3.5 yrs old. Doc recommends Charlotte's Web before we try any other AED
 - Low dose to start: 5mg 3 times a day (15mg total)
 - Great results right away: no seizure/more focused/more language/feels calmer but more awake
 - Teachers and therapists asked what we were doing different
 - Had to increase frequently to stay ahead of seizures
 - Easy to buy but not covered by insurance... \$\$\$
-
- Watch this CNN Special about how this product started:
www.youtube.com/watch?v=oxrKyjeClTk



Epidiolex



- March 2019 EEG - Slow Spike and wave showing LGS
- EEG is terrible but low dose of CBD (30mg/day) helps control seizures
- Doctor prescribes Epidiolex
- Takes a month to be approved and delivered
- Slow titration - 4 months to get to prescribed dose
- More seizures for a week after each increase but seizure control after that. Increase every 3 months with weight gain
- No side effect
- No problem traveling overseas with it.
- Only medication Ty is on
- Good seizure control and continued progress



Mike Graglia - California



Tony's story

- Slow to develop
- Seizures at 3
- Syngap Dx at 4
- Failed on Lamictal (some seizure reduction and 100% side effects) & Onfi
- Keto helped with seizures
- We tried Hemp based CBD (CW) but then went to JJ to see if it would improve results. Got our Rx from 420Recs.com in Cali for \$40.
- Keto and CBD with THC (28:1) with MAD has brought seizures under control!
- Thank you to Aaron for telling us about CBD, our hope is that this webinar helps others consider this option quickly, like we did.
- Good article on Tony & CBD: bit.ly/CBDTony



Peter Halliburton – Texas

bit.ly/SRF_4P_PH



Carter is 2, he was diagnosed with Syngap earlier this year. His story, so far, is one of CBD not always doing the trick.



Carter's journey with CBD



Carter is 2, he was diagnosed with Syngap earlier this year. His story, so far, is one of CBD not always doing the trick.

- Seizures begin at 21 months, 50-100/day within 6 weeks - 60% drops/40% absence
- Keppra – Failed
- Depakote – Effective at top end of therapeutic range, but caused extreme lethargy, lack of appetite, low platelets - weaned off
- Onfi (15mg) – Highly effective while overlapping Depakote for few weeks, lost efficacy as monotherapy
- Requested CBD treatment trial from 4 neurologists, none of which agreed
- Researched, found refractory epileptologist 3hrs from us experienced with CBD
- Initially prescribed 20:1 CBD:THC – increasing to 20mg, 50mg, 80mg, 100mg over 3 weeks - Onfi remained at 15mg
- Moved to Epidiolex 80mg 1 week, 100mg 1 week + 5mg 1:1 CBD:THC
- Still having ~40-50 seizures daily
- Quality of life being affected, currently reverting to traditional AED options
- Weaning down Epidiolex (80mg), Onfi stable (15mg), added low dose Depakote back into the mix (300mg/daily) and seeing significant improvement already
- Haven't written off CBD:THC as option completely – just perhaps not the best option for us to find the most immediate seizure control at this time



The Cytochrome P-450 System in the liver is behind most of drug:CBD interactions



- The cytochrome P-450 system is found within the liver and is responsible for metabolizing over 60% of pharmaceutical drugs available on the market today. Within this system, there are more than 50 enzymes that process and eliminate toxins.
- This means that when consuming CBD products, many other drugs to take longer than normal to be processed by the body. This can result in negative side effects and complications. On the flip side, these interactions can be positive. These interactions can be used to lower dosage requirements, mitigate side effects, and improve the quality of life in some patients.
- See also: cbdoilreview.org/cbd-cannabidiol/cbd-p-450-enzyme/

	CBD May Raise the Blood Level of This Drug	This Drug May Lower the Blood Level of CBD	This Drug May Lower the Blood Level of THC	This Drug May Raise the Blood Level of CBD	This Drug May Raise the Blood Level of THC
Amitriptyline (Elavil®)				*	
Carbamazepine (Tegretol®)		*	*		
Carisoprodol (Soma®)	*				
Citalopram (Celexa®)	*				
Clarithromycin (Biaxin®)				*	*
Clobazam (Onfi®)	*				
Clomipramine (Anafranil®)				*	
Diazepam (Valium®)	*				
Fluconazole (Diflucan®)				*	*
Imipramine (Tofranil®)				*	
Ketoconazole (Nizoral®)				*	*
Lansoprazole (Prevacid®)	*				
Omeprazole (Prilosec®)	*				
Phenobarbital		*	*		
Phenytoin (Dilantin®)	*	*	*		
Rifampin		*	*		
St. John's Wort		*	*		
Telithromycin (Ketek®)				*	*



Any Questions? Resources



- USDA Hemp and Farm Bill Programs: www.farmers.gov/manage/hemp
- FDA: www.fda.gov/news-events/public-health-focus/fda-regulation-cannabis-and-cannabis-derived-products-including-cannabidiol-cbd
- CDC: www.cdc.gov/marijuana/nas/therapeutic-benefits.html
- Minnesota: www.health.state.mn.us/people/cannabis
- Realm of Caring: www.theroc.us
- Project CBD: www.projectcbd.org
- Dr. Bonni Goldstein: www.bonnigoldsteinmd.com
- UC San Diego: www.cmcr.ucsd.edu
- Univ of Alabama: www.uab.edu/medicine/neurology/research/uab-cannabidiol-program

AES - 1st SynGAP Roundtable



- Please tell your Neuro about the Roundtable
- Friday, December 6th at 8 AM
- Baltimore, MD
- Timed to coincide with the annual meeting of the American Epilepsy Society (AES)

bit.ly/SYNGAPAES