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This doc is still woefully outdated

See my [Disclaimer](#) below for more details on how outdated this doc is. However there is one article that is so informative and well written about the current (as of 2020) state of Dravet syndrome genetic research (and the genetic background about how Dravet syndrome works) that I wanted to share it here in case anyone accidentally stumbles upon this ancient doc. So stop reading this doc now and instead go read this:

[Gene Therapy for Dravet Syndrome](#)

This is another good article to read regarding COVID vaccines and Dravet gene therapies (as of March 2021):

Disclaimer

Note that I've been out of my "extreme Dravet research mode" since early 2014. I've only made a few minor updates since then (the biggest being our experience with Diamox). Any exciting Dravet developments since 2014 probably aren't mentioned here.

I am no Dravet syndrome (DS) expert. I have no medical background. I certainly don't know everything about Dravet syndrome. What's written here is primarily my opinion, so take it with a grain of salt. **I could be completely wrong about everything I write here**, but I thought others may be interested in what I believe and why. **Don't make any medical treatment changes based on my writings (or anything else you read on the Internet), always consult your doctor/neurologist first.** Any change in treatment for a Dravet syndrome patient entails some risk.

Verbose Author Description

- I am LJ's dad (LJ = my Dravet syndrome daughter)
- I live in the United States, so keep in mind I write from that point of view. Treatments in other countries may have different names. Other countries have treatments available that we don't and vice-versa.
- I can be reached at "dsthoughts DOT jim-j AT mamber DOT net"
- I (try to) keep [this document](#) up to date with my daughter's current status
- If you're looking for more optimistic and hopeful info try [this document](#)
- <http://littleluella.blogspot.com/> is my wife's blog about our Dravet journey. She outdoes me in in both word and picture count.
- You can access this document via either of these URLs (the first one being the direct preferred method):
 - <https://docs.google.com/document/d/1dE62qZ-zt6Vty4Q8FfMA4ZdUXH0Ti8DA67QLzL01y4c/edit#heading=h.r970t4a6f0qs>
 - <http://tiny.cc/dsthoughts>

First Get Some Help!

- Dealing with Dravet syndrome can take a lot of time and effort. It can be mentally, emotionally and physically exhausting. Hopefully you've got friends and family that can help out.
- Reach out to other Dravet parents that know what you're going through
 - For most of that it means using the Internet
 - Most peer support and information is now found in the Dravet syndrome groups on Facebook:
 - [Dravet Support Group](#)
 - [Dravet.org](#)
- There are several Dravet syndrome websites that have lots of useful info. A few I'm

aware of:

- <http://www.dravetfoundation.org/>
- <http://www.ice-epilepsy.org/>
 - ["My Child Has Dravet – Now What?"](#) is also a good read
- ["Comprehensive care of children with Dravet syndrome"](#) was written to help healthcare professionals effectively assist Dravet syndrome patients and their families, but it contains lots of good information for Dravet parents to read as well.
- Go to <http://www.diseasemaps.org/en/dravet-syndrome/> to sign up your child and see who else in your area has Dravet syndrome. You can contact others through this map, maybe there's someone in your area that has a child with Dravet syndrome?
- Do you have access to someone with experience treating Dravet syndrome? An epileptologist should be better than a neurologist. A pediatric epileptologist/neurologist is even better.

A Good Overview of Dravet Syndrome

Both of the links below take you to the same video of the "Special Lecture on Dravet Syndrome at the European Paediatric Neurology Society Congress in Brussels" from 25SEP2013. I believe this presentation's target audience is neurologists, but there's still lots of good information in there for laypeople like myself.

<http://www.brabantpharma.com/brabant-pharma-hosts-special-lecture-on-dravet-syndrome-at-the-european-paediatric-neurology-society-congress-in-brussels/>
<http://youtu.be/4w9TP1zKg4M>

A Few Discouraging Dravet Facts

I don't believe these are mentioned elsewhere in this document, so in the interest of full disclosure let's get them out of the way now:

1. Dravet syndrome (almost) always causes mental and physical handicaps, and can include regression (losing already acquired skills)
2. Dravet syndrome patients have a high mortality rate ([SUDEP](#) is common with Dravet syndrome)
3. Dravet syndrome seizures are difficult to control with [AEDs](#) (antiepileptic drugs)
4. Dravet syndrome is caused by a genetic mutation in the SCN1a gene. Treatments for genetic mutations aren't commonly available (yet).
 - a. Yes I realize there are Dravet patients that tested negative for a SCN1a mutation. These patients could still have a SCN1a mutation that the test missed or have another gene mutation that causes the same symptoms as Dravet syndrome. Is Dravet syndrome caused by another gene still Dravet syndrome?
5. Since Dravet syndrome has a genetic cause you will never outgrow it, it will always be with you

My Dravet Syndrome Philosophies

Like most Dravet syndrome parents I had zero Dravet syndrome knowledge (or even general epilepsy knowledge) prior to getting the DS diagnosis. After learning about DS for a couple years now I think we handled it pretty well in the beginning, but there are several things I wish we had done differently. In this paper I'll present what I've come to believe about Dravet syndrome along some of the treatment options and considerations.

Much of what I write here is not necessarily the most uplifting. [I am generally an optimist](#), but I also believe that DS parents should be fully informed regardless of if that information is positive or negative. There are reasons to be hopeful even without ignoring all the negative aspects of DS.

Note that while not everyone will agree with my opinions and philosophies, I'm also not the first or only person to come up with these ideas. In addition to reading a lot of Dravet related research articles I also rely on anecdotal reports and opinions from other parents as well. If you see something here that echoes your view then maybe I plagiarized it from you. I haven't listed any of my other parental sources. If you want credit for something in this paper then let me know and I'll try to give credit where credit is due.

There's Almost Always More than One Option

In many aspects of Dravet syndrome patient care some parents assume that there's only one right way. In reality there's almost always several options. This document is just another option for Dravet treatment/ideas you can consider. I think everyone should be aware of different options so they can make their own informed decision.

I may not even be aware of all the options. Don't assume that by reading this paper you'll know all the options that are available. I do know that all the options you have will almost always be bad ones. I.e. it's not a matter of choosing the "obviously right answer", but trying to choose the one that is the "least bad".

I'm Pro "Anything That Has a Good Chance of Helping My Daughter"

Over the years I've noticed a few DS parents that fall into one of two categories:

1. Pro-alternative treatment/anti-pharmaceuticals
2. Pro-pharmaceuticals/anti-alternative treatments

I have friends in both groups. I respect both groups. I believe the individual stories of success and failures from both groups. I've tried treatments from both groups and will continue to evaluate and try treatments from both groups. I'm willing to try anything to help my daughter as long as it's safe and has a good chance of helping her. I think the majority of DS parents feel this way.

I don't believe this paper is biased either way. I've tried to go where the research, anecdotal reports and my own experience have led me. I haven't intentionally left out any great DS treatment options. If you feel that I have, then send me an email and I'll be happy to plagiarize

your research. :)

When evaluating new treatment options I consider these factors:

- Cost of the treatment (time, resources, money)
- Risk of the new treatment
- Success rate of the new treatment

Some (but certainly not all) mainstream treatments have the advantage of large trials and reports on their risks and success rates. With alternative treatments (and new mainstream treatments) it's more difficult to objectively determine how effective or risky a treatment is. Anecdotal reports from other parents are helpful, but sometimes parents may accidentally omit relevant info (like other treatment changes that occurred at or near the same time). So while I'm happy to see another parent report that a new treatment worked great for them, I don't get too excited until the same success can be repeated by more families.

Dravet Syndrome is not Just Seizures

The majority of neurologists, researchers and parents tend to focus on Dravet syndrome's seizures. For many, how well their Dravet syndrome child/patient is doing is measured by how many seizures they're having. I can understand the seizure fixation since seizures are:

- The first Dravet syndrome symptom you notice
- The most dangerous aspect of Dravet syndrome
- The most visible and prominent feature of Dravet syndrome

If seizures were all that Dravet syndrome entailed then I wouldn't even see the need for it to have its own name, we could all just refer to our kids having refractory epilepsy. Instead Dravet syndrome has many comorbidities like:

- Autistic traits
- ADHD
- Other behavioral issues
- Cognitive deficits
- Sleep problems
- Autonomic problems (body temperature control, sweating, heart rate, etc.)
- Coordination problems
- Orthopedic disorders

If you don't have seizure control, than seizures are the only thing you worry about. I understand that, I've been there. We are fortunate in that we do have seizure control. Seizure control (which is a very relative term), a good rescue med (intranasal midazolam) and a few years of DS experience have gotten me to the point where my primary concern is no longer my daughter's seizures. Instead I'm more concerned about her present ADHD and her future cognition (which isn't impaired yet).

Instead of describing Dravet syndrome as simply a severe "seizure disorder" I think it's more

accurate to concisely describe it as a combination of refractory epilepsy, autism and ADHD. Epilepsy is always present in Dravet syndrome, the autistic and ADHD traits range from nonexistent to severe. Many of the more severe DS cases I've read about are severe because they have severe autistic traits.

So if your child has epilepsy and ADHD why would you treat the epilepsy and not the ADHD? If your child has epilepsy and autism why would you use their seizure count as the only metric of how well they're doing? Does it make sense only to search for cures to the seizures? I don't think so and fortunately more research is being done on the non-epileptic features of Dravet syndrome.

You (Currently) Have Minimal Control Over Your Child's Outcome

Probably not what you wanted to read. I'm sure some will disagree with me (and I hope I'm wrong), but it appears that (to a large degree) we can't control the outcome of Dravet syndrome. For reasons we don't fully understand yet some kids have milder cases of Dravet syndrome and other kids have much more severe cases (we do know that individual genetic mutations do not tell the whole story). Despite our best efforts we can make very little difference in the outcome of Dravet syndrome. For example I know several Dravet parents who are a lot smarter than me, who do all the right things for their kids and yet are unable to make big improvements in their kids' outcome. I believe the biggest effect we can have on our kids' outcome is to basically try to [balance two conflicting goals](#):

1. Prevent status epilepticus
2. Don't over-medicate

Now let me balance the negative paragraph above with a few more positive thoughts:

- I haven't yet found a single treatment that produces the best outcome, but that doesn't mean it's not out there. I'm always looking for new ways to help my daughter (but I keep my expectations in check too).
- I said "minimal control", not "no control". You can make a difference in your child's outcome. Hopefully some of the ideas presented here will help you maximize your child's potential.
- I have compiled my more [hopeful DS info in this document](#)

The Dravet Parent Should Lead the Team

I believe that as the parent you should be the one making the decisions for your child's Dravet syndrome treatment. This does not mean I'm anti-doctor or anti-medical establishment (although I am certainly open to learning more about alternative treatments). On the contrary I value our neurologist's advice more than any other advice or info that I get. However I do take into account information I get from sources other than my neurologist. Fortunately when I do bring up questions and ideas about other treatment options my neurologists have always been supportive and receptive. I've never gone against any of our neurologists' instructions, but they have agreed to try some of my ideas. Our neurologist is the expert on Dravet syndrome, but my wife and I are the experts on LJ.

Basically I think proper treatment of my daughter's Dravet syndrome requires a team. The two most important members of "Team LJ" are my wife and me. The next most important person on the team is our neurologist. After that there are other parents, Internet groups, etc. who are all valuable members of "Team LJ", but ultimately it's up to us (LJ's parents) to make the final call on what we're going to try next for LJ's Dravet treatment.

I don't want the responsibility of coaching the team for your Dravet child. You as the parent/guardian need to fulfill that role. I'm always happy to give advice (I try to to minimize my unsolicited advice :), but I won't give out decisions. I don't want to be responsible for someone else's child. Caring for my own Dravet kid is a big enough responsibility.

In summary I just used a lot of words to say that I hope the info I present here can help you make better more informed decisions, but I don't intend to make the decisions for you.

Document Medicine/Treatment Changes and Seizures

You don't have to go overboard with documentation (like I do), but you should at least record every medicine/treatment change you make. This is very important, in case you see changes you'll want to know if you can correlate it to a medicine/dose/treatment change. I was shocked to discover even a very small dose of clobazam caused insomnia in my daughter. I would've never found this without my "treatment changes" documentation.

It's also very helpful (at least initially) to document your seizures. Even something as simple as date, time and duration is helpful. If the seizure is strange or different you may want more notes so you can better describe it to your neurologist. If you have a camera or smartphone that can take a video of the seizure then you can show your neurologist exactly what you saw.

I personally [use a spreadsheet](#) and [a document](#) to track LJ's seizures and a separate spreadsheet for treatment changes. My method of tracking is overkill, but old habits are hard to break. I know there's a <https://www.seizuretracker.com/> website, but I've never used this so I can't vouch for it. If I had known about <https://www.seizuretracker.com/> before I created my spreadsheet I would have tried seizure tracker first.

Be Aware of Seizure Triggers

If your child has frequent seizures you may be able to identify seizure triggers. For some parents they can be certain that if their child experiences the trigger they will have a seizure. For us LJ's seizure triggers are more like seizure risks. Exposing her to one of her seizure triggers does not guarantee she'll have a seizure, but it does increase the risk. If you choose to keep detailed notes about your DS child's seizures that may help you identify triggers. Of course DS seizures can come without any trigger at all.

I don't have a comprehensive list of what can trigger a seizure, but it's pretty safe to say just

about anything can be a trigger (foods, lights, emotions, temperatures, etc.). Each DS kid is unique and has their own set of triggers (or maybe none at all). LJ's list of triggers is [here](#).

Only Make One Change at a Time and Go Slow

Sometimes you're in emergency mode, when things are very bad and you need to take a shotgun approach to fix whatever crisis you're facing. For example maybe you've lost seizure control and you need to throw several AED (antiepileptic drug) changes at the problem all at once. While this can and does happen, it's always best to make only one change at a time if possible.

By making one treatment change at a time you'll have a better chance at knowing what specific thing you changed that helped or hurt your child. I try not to limit my "only change one thing at a time rule" to just AEDs either. Any other medicine changes, treatment changes, dietary changes, etc. should (ideally) be done in isolation from any other changes. If you are forced to make several changes at once then you'll be left guessing what change had what side effect (good or bad). The only chance of determining this after the fact is to begin undoing your changes one by one.

One more thing to consider with AEDs is how quickly you go up or down when changing your dose. I.e. how long do you take to titrate your AED. Unless you need to quickly change your AED (for example you've lost all seizure control) I always prefer to slow titration down. I feel this helps decrease AED side effects from the dose level change. A slow titration schedule will also help you know what change (or what dose level) caused what effects in your child.

In summary (whenever possible) change only one thing at a time and take it slow.

Dravet Syndrome Effects Change Over Time

And just to keep things from being too simple another Dravet syndrome complication is that the way Dravet syndrome presents itself usually changes over time. So even if you don't make any changes your child's seizures may change (in features and/or frequency). Even with detailed records of all your changes it's impossible to be truly certain that any specific treatment change caused a specific outcome (seizure change, side effect change, etc.).

Sometimes if you're not certain if a specific change caused a specific outcome it may be worthwhile to undo and redo the change so you can be (fairly) confident the variable you changed really was the cause (aka perform your own "[N of 1 trial](#)"). This is how I discovered that even 1.25 mg/d (0.09 mg/kg/d) of clobazam caused insomnia in my daughter. I didn't believe that such a small dose could have that effect until I added and removed clobazam a second time and saw the same results. Note that she was also on stiripentol at the same time and stiripentol amplifies the effects of clobazam. I.e. I wouldn't expect 1.25 mg/day of clobazam to cause insomnia if you're not also taking stiripentol.

Try to Minimize the Number of AEDs (Shoot for Three or Less)

Another goal for AED (antiepileptic drug) use is to try to minimize the number of AEDs you need to use concurrently. Ideally we'd only need to give our kids one AED (aka monotherapy). But with Dravet syndrome the reality is that almost everyone needs to use multiple drugs (polytherapy). However the consensus is the less drugs you need to use the better.

The general rule of thumb I've seen is that you should try to keep the number concurrent of AEDs used to three or less. Of course there are exceptions to this rule. I know kids that need to take four or five AEDs, but this is the exception, not the norm. I.e. I would think twice about using more than three concurrent AEDs. You're in charge of your kid's treatment though, do whatever you (and your neurologist) think is best.

Use Good AEDs

You've probably been using AEDs (antiepileptic drugs) since before you got the Dravet diagnosis. Hopefully the Dravet diagnosis has given you better clarity on what drugs to try. AED choice really comes down to just playing the odds.

Although an experienced neurologist can make a better informed guess than we can, ultimately they're just playing the odds too. Every Dravet kid is different. Once kid's wonder drug could be horrible for the next. The neurologist can't be certain in advance which drug is going to be the right one for your kid, so it probably doesn't do any good to get mad at them if they don't pick the best drug the first time.

As of 2012 we already have a pretty good list of which drugs are better at controlling Dravet syndrome seizures and which actually make them worse. My personal list o' Dravet syndrome drugs with the best odds of controlling seizures (we haven't tried most of these):

- **Stiripentol (STP)**: Not approved by the FDA, so you have to import it (in the US). Many insurance companies won't cover it. It's also expensive, but cost effective (for insurance) if you consider the medical costs from uncontrolled seizures. Studies have shown that it's the most effective DS drug that's currently available (as of 2010?). Normally used with Depakote and/or clobazam. Some also add Topiramate.
- **Clobazam (CLB, Onfi)**: Caused insomnia in my daughter, even at very low doses. As with all benzodiazepines you need to watch out for tolerance. I personally would only use benzo's as a last resort as a daily med (try googling "benzo withdrawal syndrome").
- **Depakote (VPA)**: The standard Dravet syndrome drug. Not great for your liver. Can cause or worsen ataxia. May take a cognitive hit too. We used this one for years.
- **Topiramate (TPM)**: Some think this is even better than STP at controlling seizures, but it's also supposed have some of the worst cognitive side effects
- **Zonisamide (ZNS)**: Chemically different, but side effects are almost identical to TPM
- **Keppra**: Didn't work for us, but many do report good results with it. Just watch out for

the behavior issues. One of the safer AEDs.

- **Felbatol**: Has rare, but harsh side effects. Consensus seems to be that this drug is underutilized and the worst side effects can be monitored and managed or avoided.
- **Acetazolamide (Diamox)**: Good drug with minimal side effects. Biggest concern would be loss of appetite. This hasn't been normally used as a Dravet drug, but it shows a lot of promise. One of the safer AEDs. I have a few more notes on it in my [March 2016 acetazolamide/Diamox notes](#) section below.
- **Verapamil**: Promising calcium channel blocker drug in a clinical trial as of August 2012
- **Bromides**: Old drug. Hard to get (in the U.S.). Must titrate very slowly.
- **Fenfluramine (Belviq, Pondimin, Brabafen, ZX008)**: Fenfluramine was withdrawn from the market in 2001 due to the risk of cardiac effects. Too bad since it may be the most effective DS drug.
 - In the US as of Feb 2016 this is now in [Phase 3 clinical trials](#). So if you want access to this in the US see if you can join the clinical trial.
- **N-acetylcysteine (N-AC, NAC)**: A supplement that appears to be safe. As of Feb 2013 parents are just starting to use this for DS, but it appears to have a decent response rate (my wild guess would be that it helps about a third). Does prolonged use deplete copper, zinc, selenium and/or other trace minerals?
 - NAC degrades quickly after its opened, so it's best to use individually sealed tablets like [PharmaNac](#)
- **CBD (MMJ)**: Several Dravet parents swear by medical marijuana. The CBD controls seizures, but it doesn't give you a high. For pediatric use it's normally delivered via oral drops. That's right, it's just another boring treatment option, but it's reportedly much safer than standard AEDs (with less side effects too). Too bad it's not a legal option everywhere yet.
 - The Facebook "[Pediatric Cannabis Therapy](#)" is probably the best resource for MMJ info.
 - The founders of this facebook group have created a website: <http://pediatriccannabistherapy.com> This FB post from 12DEC2013 describes the change (note that as of 03JAN2014 the FB group is open to comments again):

Note that this isn't an exhaustive list of every Dravet syndrome drug out there. Just the ones I happened to come across that appear have a good chance of helping seizure control.

At <http://dravet.org/about-dravet/treatment-options> they list the good Dravet drugs and the bad ones (the contraindicated ones). As of 21OCT2012 they list these drugs as being contraindicated for Dravet syndrome (**be sure you don't use any of these unless your neuro has a good reason to use them with Dravet syndrome**):

- carbamazepine (Tegretol, Calepsin, Cargagen, Barbatrol, Epitol Finlepsin, Sirtal, Stazepine)
- fosphenytoin (Cerebyx, Prodilantin)
 - Note that while this is contraindicated for Dravet syndrome, it actually does help

status epilepticus for many Dravet kids. Most think it's ok to use short term (to stop status epilepticus), but should be avoided for long term use with Dravet syndrome.

- lamotrigine (Lamictal)
- oxcarbazepine (Trileptal)
- phenytoin (Dilantin, Epanutin)
- vigabatrin (Sabril, Sabrilan, Sabrillex)

Lastly, don't be afraid to double check your neurologist's treatment choices. They're only human and can make mistakes too. For example a 2013 study found that [newly discovered safety risks related to antiepileptic drugs are often not passed to neurologists](#).

March 2016 acetazolamide/Diamox notes

I believe the normal target range with acetazolamide/Diamox for Dravet kids is 5-15 mg/kg/d. LJ is 6, weighs 24 kg and takes 62.5 mg BID (i.e. a half tablet at breakfast and supper). This works out to 5 mg/kg/d for her.

Like most Dravet treatments, I don't think it works for the majority Dravet kids. My informal guesstimate is that Diamox only helps about a third of Dravet kids. For those it does help, however, it can make a big improvement in seizure control.

Prior to Diamox LJ was averaging a seizure/week (while taking STP and VPA). With Diamox she's averaging a seizure every two months and it's the only AED she takes. The first two seizures she had after taking Diamox were longer, 20 and then 11 minutes each. I suspect that was just a coincidence because if you ignore those two seizures while on Diamox she's had 23 other seizures, 5 of which have lasted 5 minutes or longer, her longest seizure being 13 minutes.

Diamox doesn't appear to protect her from fever induced seizures. While sick she's had as many as 3 seizures in a day, but these fever seizures have all been short, 2 minutes or less. For these 23 seizures we've used her midazolam rescue med 7 times. It's possible some of these seizures would have self-resolved without midazolam since we use it fairly aggressively (at the 3 minute mark of her seizure). These 23 seizures occurred over an approximate 15 month time period.

For comparison during her 23 seizures prior to Diamox she had 10 seizures which lasted 5 minutes or longer. Her longest was 40 minutes, but that was exceptional, her second longest seizure was more typical at 15 minutes. For these 23 seizures we used her midazolam rescue med 12 times. These 23 seizures occurred over approximately 4 months.

Luella's been on a Diamox monotherapy for about 1.5 years now.

Unlike most Dravet drugs the side effects of Diamox are usually mild (suppressed appetite being

the most common negative side effect, and lowering the dose can help this). As others have pointed out [here](#) there's always the outside chance of a more severe reaction, but IMHO it's one of the safest Dravet drugs.

The other common (manageable) side effect with Diamox is that it increases your acidity. To counter this LJ takes 1/4 tsp baking soda diluted in a small glass of water BID (at breakfast and supper). This keeps her CO2 level up in a safe range.

For me, Diamox has a good risk/reward ratio. If I could go back in time I'd have certainly tried it sooner. I don't think you have much to lose in trying it, but I'm no doctor so get your neuro's buy in first (and if you can't do that get a new neuro :).

Aim for Good Quality of Life (Not Just Seizure Control)

Many neurologists equate "quality of life" with seizure control. I.e. they focus almost exclusively on seizure control. Seizure control is great and it's certainly a big part of your quality of life. However, seizure control is not the only thing that determines your quality of life. Other things like behavior, cognition, sleep (or lack thereof), etc. all affect your quality of life. Be vigilant for changes in any of these areas when you make any treatment changes. For example if you find that a treatment change improves seizure control but has negative side effects then you need way to weigh the benefit of improved seizure control vs the negative side effects.

I'm Certain Making an AED Change will Help, Hurt or Not Change Your Child's Cognition

There are few DS things I'm certain about, but the statement above is one of them. :) Cognition is a major concern for all Dravet syndrome parents. The thinking used to be that the only way to help cognition was to avoid seizures at all costs. That opinion is slowly changing. The way I understand it is:

1. Dravet syndrome itself (independently of seizures) can impair cognition
 - a. From the research I've read this sounds like a more common cause of cognitive impairment than seizures
2. Status epilepticus can cause brain damage which impairs cognition.
 - a. Note that many Dravet kids (my daughter included) have had multiple status seizures with no impact on cognition. So while status is a cognitive risk, [it's not certain to cause permanent problems](#). I think the longer it goes (i.e. several hours or more) the more likely you are to have a bad outcome.
3. Frequent seizures (multiple per day) can impair cognition
4. [Interictal discharges can impair cognition](#)
5. (Most) [AEDs can impair cognition/behavior](#)

If you want to improve cognition you can't currently do anything about reason 1 (but I'm hopeful that will change soon). With proper treatment selection (and rescue med use) hopefully you can avoid cognitive impairment reasons 2-4. Reason 5 (AEDs) is the cognitive/behavioral risk factor

we have the most direct control over. The problem is that to avoid cognitive complication reasons 2-4 most neurologists are more than willing to increase your AED dose, but this also increases the odds that the AEDs themselves will cause cognitive impairment (reason 5).

In my opinion, to optimize cognition and behavior you only want to use enough AEDs to gain reasonable seizure control. After that it's a delicate and personal balancing act of "how good of seizure control do you want" vs. "how big of a cognitive/behavioral hit" are you willing to take?

For example with my daughter on high levels of Depakote and stiripentol we were able to go over two months seizure free, but the severe negative side effects from the drugs wasn't worth the seizure freedom. Instead we chose to lower our AED doses and accept a seizure a week in exchange for the return of our daughter (she was a zombie at high doses of VPA and STP).

I'm not alone in noticing the negative cognitive side effects from AEDs. I know several other parents that have improved cognition by lowering their AED doses. Of course you don't want to just blindly lower your AEDs. This can cause more seizures and even the dreaded status epilepticus. **To scare you even more, other parents have reported that when they tried lowering AEDs they lost seizure control and were never able to regain seizure control (even after going back to their original AED dose).** Don't even think about lowering AEDs if you're not willing to accept the risk of more seizures! This is probably a good place to remind you that **this paper is NOT a guide of what you should do.** This file merely documents my thoughts on several aspects of Dravet syndrome, so that you can have another perspective to keep in mind as you make your own decisions for your unique Dravet patient. Do not make any changes to your child's care based on anything I write!

Although I'm sure some have achieved good seizure control with minimal side effects, it seems to me like most Dravet parents undertake a delicate balancing act between AED seizure control and AED side effects. I think even the best neurologists naturally want to focus more on seizure control than AED side effects. Because of the focus on seizure control many Dravet kids could probably lower their AED doses and/or the number of AEDs they take and receive a cognitive and/or behavior boost with minimal seizure frequency increase. However this is obviously a very personal, important and **possibly dangerous decision** each parent needs to make for their own child (after consulting their neurologist of course).

Consider Dietary Treatment Before Trying AEDs

Note that I'm not anti-drug. LJ's been using AEDs ever since her second or third seizure. AEDs have given us ok seizure control and kept us status epilepticus free for over a year. I probably owe my daughter's life to AEDs. However, I now question if trying AEDs first (before dietary treatment) was the right choice.

If you want seizure control without the negative cognitive/behavioral drug side effects then the Ketogenic Diet has a good proven success rate with Dravet syndrome kids. If I had it to do over again, I would try the [Ketogenic Diet](#) first before dealing with all the drugs and side effects.

There are also two less restrictive forms of the Ketogenic Diet that show promise:

- Low Glycemic Index Treatment (LGIT)
- Modified Atkins Diet (MAD)

The Ketogenic Diet is not for the faint of heart and it entails its own risks (you even have to be hospitalized when you start it). However, assuming your body can safely tolerate it, I'm not aware of any major cognitive/behavioral negative side effects from the Ketogenic Diet (like you get with so many AEDs).

Note that we haven't tried the full Ketogenic Diet ourselves, so I'm not the best spokesperson for it. We have tried the LGIT and GAPS diets though, so we're not complete strangers to restrictive dietary treatments.

Update March 2016: Actually I'd probably try Diamox first since that has worked so well with virtually no side effects for us, before I'd move on to the Ketogenic Diet. Additionally Fenfluramine and medical marijuana also have such great reported effectiveness to side effect ratios that they'd be worth considering first too if you can get access to them.

Get a Good Rescue Drug (aka Replace Diastat with Intranasal Midazolam)

A rescue drug is what you use to stop a seizure. We used to use Diastat (rectal valium). For us, the decision to switch to midazolam (aka Versed) was easy, Diastat quit working for my daughter. However back when Diastat did work it would negatively affect my daughter for 2-4 days (cranky, coordination issues, etc.) after using it. Midazolam only negatively affects my daughter for 2-4 hours. This is what I like best about midazolam (minimal short lived negative side effects). Some other things I like about midazolam (vs Diastat):

- Administration of intranasal midazolam is easier and quicker than rectal Diastat
- Midazolam works more quickly than Diastat
- Midazolam is more effective than Diastat
- Midazolam is cheaper (costs tens of dollars vs hundreds of dollars for Diastat)

If you want a longer more detailed argument for intranasal midazolam you should read <http://intranasal.net/SeizureRx/default.htm> The whole page is a good read, but here's one relevant quote:

"All these authors conclude that transmucosal midazolam is more convenient, easier to use, just as safe, and is more socially acceptable than rectal diazepam. Furthermore, **when given via the intranasal route, midazolam is more effective than rectal diazepam.**"

As usual, nothing's perfect. There are a few disadvantages to intranasal midazolam since it isn't as common as Diastat:

- It's more difficult to buy (you need both the midazolam and the atomizer)
- It can be more difficult to find another caregiver that's familiar with intranasal midazolam

- Laws and/or policies may prevent others (like school nurses, aides, etc.) from administering intranasal midazolam
- If your neuro isn't familiar with intranasal midazolam they may be reluctant to step out of their comfort zone by prescribing it to you.

Note that [Upsher-Smith is working on addressing all of these disadvantages](#). On 23SEP2015 the epilepsy foundation wrote:

"Over the last couple of years, there has been rising interest in developing an FDA-approved benzodiazepine nasal spray. Currently, there are benzodiazepine nasal spray clinical trials underway for people with seizures. These trials are typically enrolling people with "seizure clusters" (i.e., people who typically have multiple seizures in a row). Over the next year or two, there is an expectation that a benzodiazepine nasal spray will be approved by the FDA and made available to people with epilepsy."

- [26APR2017 update](#):
 - Midazolam Nasal Spray (USL261) Phase 3 Trial Meets Primary Efficacy Endpoint In Patients With Seizure Clusters
 - CAMBRIDGE, England, April 26, 2017 /PRNewswire/ -- Proximagen Limited (Proximagen) today announced that **its pivotal Phase 3 trial of intranasal midazolam (USL261) for the rescue treatment of seizure clusters, met its primary efficacy endpoint in a top-level analysis of the data.** Based on these findings, Proximagen will approach the U.S. Food and Drug Administration (FDA) regarding its proposal to submit a 505(b)(2) New Drug Application (NDA) in the second half of this year. **USL261 has been granted orphan drug designation and fast track designation for this use by the FDA.** Findings from the trial will be presented at the upcoming Antiepileptic Drug and Device Trials (AEDD) meeting, May 17-19, 2017 in Adventura, Florida.

So hopefully intranasal midazolam usage will become more mainstream soon. Of course once it's FDA approved it will certainly become much more expensive. Therefore if you don't have good insurance you may want to learn how to use the cheap intranasal midazolam solution now while it's still somewhat common.

Earlier I listed midazolam's short lived side effects as a positive (which it is). However on the other side of that coin is the fact that midazolam's protection is also short lived. If your child clusters and needs extra protection for an extended period than midazolam is not for you. In that case Diastat (or another rescue medication) may be a better choice.

Below is a link to a short video about intranasal midazolam:

<http://www.howcast.com/videos/502068-Epilepsy-Medication-Midazolam-Nasal-Spray-Epilepsy-and-Seizure-Disorders>

[Treatment of Acute Seizures: Is Intranasal Midazolam a Viable Option?]

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3668946/>

This 2013 article concluded:

Intranasal midazolam was found to be efficacious and reasonably safe for treatment of acute seizures in the pediatric population. Various studies have demonstrated a shorter time to seizure cessation with intranasal midazolam versus rectal diazepam in children in the community, prehospital, and ED settings. Many first responders, including caregivers, prefer intranasal midazolam and deem it less invasive for patients. A good safety profile also supports the use of intranasal midazolam, with fewer patients experiencing respiratory depression and oxygen desaturation compared with rectal diazepam. Although intranasal midazolam is less expensive on a direct cost basis, future cost analysis that considers dose, recurrence of seizures, emergency medical technician calls, ED admissions, and treatment of complications should be performed. Optimal dosing of intranasal midazolam for all patients, including those with rhinitis and other nasal abnormalities, needs to be defined, although the **studies presented primarily used 0.2 mg/kg per dose**. Intranasal midazolam should be considered as an anticonvulsant agent for community, prehospital, and ED use in children when intravenous access is not available and the rectal route is not desirable.

How We Buy Midazolam

We buy midazolam in vials, 5 mg/ml in one or two ml vials. Then we draw up the correct amount in the syringe like you would any other med. We do this in advance, so we basically create our own pre-filled syringes. Technically we don't buy them directly, our insurance company does it for us. It's difficult for a non-medical professional to buy medical devices like atomizers, so if you can get your insurance company to buy them for you that's the best route to go.

We keep our pre-filled syringes in a plastic travel toothbrush holder and then put that in a small bag to keep it out of sunlight. I seen others report these homemade pre-filled syringes should last a month or two. In my experience they seem to work fine even at the two month mark (I've never tested anything older than that). Note that intranasal midazolam doesn't need to be sterile since it's sprayed into the nose (not injected with a needle).

The hardest part of using midazolam was finding the correct syringe and atomizer to order. My wife figured this out on her own with the help of Google. We used to get the "MAD130" syringe/atomizer combo (includes plastic tip for drawing the midazolam out of the vial) made by LMA, but it doesn't look like they make this 1 ml syringe/atomizer combo anymore (as of JAN2017). I only see 3 ml syringes here now, but you could just buy the MAD300 atomization device and use it with any luer lock syringe. This website has more details:

<http://www.teleflex.com/en/usa/productAreas/ems/productGroups/atomizationDevices/products/>

When we started this our insurance didn't even know what an atomizer was, but now they pay for everything (which they should be happy to do, since it's about 80 times cheaper than Diastat).

Midazolam can also be given buccally (cheek pocket) or intramuscular (IM)

Midazolam (Versed) can be given buccally (cheek pocket) or intramuscular (IM, needle into leg

muscle). We've done the IM method once (just to test it), I've never personally given it buccally. These alternative delivery methods can be useful to have in case you can't give it via the nose (extremely stuffy nose, etc.)

[Training video for administration - YouTube]

https://www.youtube.com/watch?v=mg2S5V_EjUA

Buccolam administration starts at about 4:30

[ViroPharma - YouTube]

<https://www.youtube.com/watch?v=m5OQhTOoLLM>

2:45 Europe now recommends buccal midazolam for first line treatment (instead of Diazepam)

How to Tell If a Seizure Has Stopped?

Fortunately for us our daughter's seizures are almost always easy to stop with midazolam. A bigger problem for us is determining when her seizure really has stopped. Most of LJ's seizures are non-convulsive. I.e. the primary symptom of most of her seizures is that she's unresponsive. To stop these "unresponsive seizures" we give her a rescue drug which makes her unresponsive. So after administering her rescue drug is she having seizure induced unresponsiveness or rescue drug induced unresponsiveness?

Most time's it's actually pretty easy to tell the difference. She'll let out a big sigh and close her eyes when her seizure stops. In the best case she'll actually respond to simple questions (like "are you ok?"). If it's not obvious here are some things we check:

- Does she make "purposeful movements" like scratching an itch, pushing away an annoying parent that's checking on her, etc. If she makes purposeful movements then her seizure is probably done.
- Does a cold washcloth on face get reaction? If so then the seizure is probably done.
 - If a cold washcloth doesn't work (or you don't have one handy) you could be mean and see if pinching her gets a reaction. If pinching gets a reaction the seizure is probably done.
- If you pry open her eyes and they're shifting back and forth, that's probably a seizure.
- Pry open her eyes and roll her head back and forth. If her eyes move, then the seizure is probably done. If her eyes stay fixed in one position (like staring off left, or straight ahead) then she's probably still seizing.
- If she gets chilled (goosebumps, shivering) her seizure is almost certainly done. She usually gets chilled within 10 minutes of the seizure stopping.
 - While this is a very reliable indicator, the problem is that shivering can look like seizure convulsions (and small convulsions can look like shivering). Seeing goosebumps is the easiest way to verify she's just chilled and not seizing.
- If her O2 stays low (<90%) for more than 10 minutes she's probably still seizing

Note that in the list above none of the things we check can tell us for certain if seizure is done or still ongoing. Basically if her O2 comes back up within 10 minutes we then leave her pulse ox

on her until she wakes up. If her O2 drops after 10 minutes we'll get alerted and can check (and suspect) she's either still seizing or another seizure has started.

Have a Rescue Protocol Letter

In my experience Emergency Room (ER) doctors aren't usually seizure experts. Instead of relying on the ER docs to stop my daughter's seizures we now always carry a "Rescue Protocol" letter with us. Our neurologist wrote our Rescue Protocol letter. We give it to the ER when we need help stopping a seizure (which we've only had to do once since we started using STP and midazolam over a year ago). Basically our letter says:

1. Give midazolam at home
2. ER can give more midazolam (IV or intramuscularly if IV can't be started quickly)
3. Additional doses of more benzodiazepines
4. Depacon (IV form of valproic acid)
5. Fosphenytoin

The ER docs I've worked with have always been happy to transfer responsibility for my daughter's care to my rescue letter. My letter also has my neuro's on call number in case the local ER docs need more help.

SUDEP

[Nighttime Seizure Detection](#) may help prevent SUDEP.

SUDEP = Sudden Unexpected Death in Epilepsy. From

<http://www.epilepsy.org.uk/info/sudep-sudden-unexpected-death-in-epilepsy>

"If a person with epilepsy dies suddenly and unexpectedly, and no obvious cause of death can be found, it is called sudden unexpected death in epilepsy (SUDEP). Sometimes, it is called sudden unexplained death in epilepsy."

Below are my notes from Srinivasan Tupal's talk at the 2012 Dravet Conference in Minneapolis MN. Hopefully I got these facts right from his presentation:

- SUDEP accounts for 17% of all epileptic deaths
- **SUDEP accounts for 50-60% of Dravet syndrome deaths!**
- In Dravet syndrome mean SUDEP age is 4.6 years
- Usually has a respiratory cause
- Most SUDEP occurs after the seizure (postictal state)
- Fluoxetine (aka Prozac, a SSRI) blocked respiratory arrest in DBA/1 mice
 - In clinical trials now for SUDEP
- Fenfluramine (another SSRI) may also prevent SUDEP and appears to be very effective and reducing the # of seizures Dravet syndrome patients have
- One research study monitored 10+ institutionalized epilepsy patients for over a decade
 - Only 2-3 patients had SUDEP
 - The only time when they had SUDEP is when they went home with family for a

- weekend or holiday
- **The conclusion is that SUDEP only occurred when the patients weren't closely monitored.**
- **Therefore if you can be alerted to the seizure and react, SUDEP probably can be prevented**

[Assessment of a quasi-piezoelectric mattress monitor as a detection system for generalized convulsions]

<https://www.sciencedirect.com/science/article/pii/S1525505013002011?np=y>

Epilepsy & Behavior Volume 28, Issue 2, August 2013, Pages 172–176

The risk of sudden unexpected death in epilepsy (SUDEP) is highest with nocturnal, unattended generalized convulsions, and basic resuscitation may be able to prevent SUDEP.

[Electric Shutdown of the Brain: Is it a Cause of SUDEP? | epilepsy.com] 17JUL2013

<http://www.epilepsy.com/newsletter/jul13/electric>

- Entire article was a good read. At the end they had this advice for preventing SUDEP:
 - “Accordingly, SUDEP may share mechanisms similar to that of Sudden Infant Death syndrome (SIDS), and **SUDEP is possibly preventable by patients avoiding the prone sleeping position, by arousing and turning the patient following a seizure, and by using anti-suffocation pillows.**”

Nighttime Seizure Detection

A concern many DS parents have is missing a seizure that happens at night. I believe this is a valid concern since if you can react to a seizure at night you should be able to decrease the risk of nighttime SUDEP and status epilepticus.

<http://www.dannydid.org/> has more information on SUDEP and seizure detection devices. I believe they can also help families that can't afford a seizure detection device get one at little to no cost. From <http://www.dannydid.org/sudep/devices-technology/emfit/>

“NOTE: Emfit offers a 10 percent referral discount to anyone who mentions Danny Did Foundation when placing an order. If placing the order online, enter the coupon code “dannydid” to receive the referral discount. As a secondary option, you can contact the Danny Did Foundation at tfstanton@dannydid.org for assistance in acquiring an Emfit Movement Monitor if this product seems right for you but dire financial constraints are an impediment. In deference to the best use of our funds, we aim to reserve this option for families who are most in need.”

A no cost seizure detection option is to sleep with your child or at least in the same room as your child. I know some parents have developed a keen sixth seizure sense they use to detect nighttime seizures.

I've also heard of another parent that [pins a jingle bell to their child's socks at night](#) as a low tech seizure detection device. I've never tried this, but it sounds like it'd be a lot better than

nothing (as long as the false alarms don't get too annoying).

The next cheapest option is to use a standard baby monitor in the hopes that you could hear the seizure happening. A video monitor is better since you can visually confirm what your child is doing. This isn't the best at helping you detect a seizure, but sometimes you have to make due with what you have.

A pulse oximeter (aka pulse ox) is very effective if your child's O2 or heart rate changes significantly during a seizure. LJ almost always drops her O2 when she seizes which means our pulse ox has worked very well at detecting her seizures. I don't know which pulse ox is best, but we haven't had any problems with ours. We just took what our local health supply store recommended (and our insurance would pay for). We use the Nonin 7500 pulse ox with the 6000CN sensor (it wraps around her big toe like a band-aid). The sensor is disposable, but we use it about a month before we toss it. More info on these items is available at the websites below:

- <http://www.nonin.com/Tabletop/7500>
- <http://www.nonin.com/PulseOximetry/Sensors/DisposableSensors>

An "[Emfit Movement Monitor](#)" can detect convulsive seizures. I don't have any experience with one of these, but they're supposed to be effective for convulsive seizures. The Pulse Ox and Emfit are probably the two most popular seizure detection devices used for DS kids. Some parents use both together.

I know some Dravet parents use a [SmartWatch](#) for their kids at night. Like the Emfit it alerts on movements it thinks are seizures.

The [SAMi sleep activity monitor](#) is a recent (2013) nighttime seizure detection system. I know that many Dravet parents love their SAMi, some claim that it can detect seizures (some complex partials) the Emfit can't. I never used the SAMi, so I can't personally vouch for it.

The seizure detection device that most kids prefer would have to be a "seizure detection dog." I don't know how they do it, but some dogs can be trained to detect a seizure even before it happens! On the downside seizure detection dogs may be contraindicated for families with a house cat and seizure dogs aren't cheap. <http://4pawsforability.org/seizure-assistance-dog/> has more details.

Sleep

!!! Need to expand this section !!!

Most Dravet kids have poor sleep. These sleep problems can be caused by Dravet syndrome itself and AEDs. Many use melatonin to help their DS kids sleep. Melatonin is most effective at helping DS kids fall asleep, unfortunately it doesn't usually keep them asleep all night.

Some research that shows SCN1a mutations directly impact sleep:

- <http://onlinelibrary.wiley.com/doi/10.1111/epi.12060/abstract>
- <http://www.pnas.org/content/early/2012/01/04/1115729109.abstract>
- <http://www.pnas.org/content/109/6/E368.full>

Predicting Dravet Syndrome Outcome (you can't)

The short answer is that you can't. There are different studies that correlate different things with Dravet outcome, but they sometimes contradict each other and they always have exceptions.

For example my daughter's mutation is in the pore forming region of the SCN1a gene.

According to one study mutations in this region should have the most severe outcome, yet (as of age 6) LJ still has a mild case of Dravet syndrome. Likewise if you find a study that says your child should have a mild outcome it's not like you're home free. The future for all of our kids is unknown (despite some early studies that said all of our kids would have poor outcome).

Personally I hope for the best, but am ever mindful that at anytime things could take a turn for the worse.

If you're like me, despite hearing that you can't predict Dravet outcome you still want to see the stats. If so, below are a few relevant (and sometimes contradictory) studies I've come across:

Research

[Cognitive and behavioral outcomes of epileptic seizures] 2006

- <http://www.ncbi.nlm.nih.gov/pubmed/17105481>
- <http://onlinelibrary.wiley.com/doi/10.1111/j.1528-1167.2006.00709.x/abstract>
- **Interpersonal relationships rarely exceeded the developmental level of 2 years of age.**
- Hyperactivity and "psychotic-type relationships" were observed and some of the children had autistic traits.
- The presence and degree of psychotic features could vary in a given child.
- All the children experienced periods of "lesser excitation" during which they could relate better with others.
- An interesting exception is the small study by Wolff et al. in this symposium, which has confirmed the **pattern of normal early development followed by severe cognitive impairment and marked slowing or stagnation between 1 and 4 years.**

[Dravet syndrome: early clinical manifestations and... [Brain Dev. 2010] - PubMed - NCBI]

<http://www.ncbi.nlm.nih.gov/pubmed/19854600>

- The clinical history of 37 patients with clinical diagnosis of SMEI, associated with a point mutation of SCN1A gene in 84% of cases, were reviewed with particular attention to the symptoms of onset.
- At the last evaluation, performed at a mean age of 16+/-6.9 years, mental retardation was present in 33 patients, associated with behavior disorders in 21.

[Cognitive development in children with Dravet synd... [Epilepsia. 2011] - PubMed result]

<http://www.ncbi.nlm.nih.gov/pubmed/21463278>

Slowing of cognitive skills represents one of the diagnostic criteria of Dravet syndrome. This Italian multicentric study aims at clarifying the roles of epilepsy and/or underlying genetic alteration in determining the cognitive outcome. The study includes infants that were either in follow-up (retrospective study: 26 cases) and newly diagnosed (prospective study: in progress). Our multicentric study shows that slowing of cognitive achievements becomes evident during the second year of life in all cases, and that **the epilepsy phenotype indeed has a prognostic value**. In this study **the early appearance of absences and myoclonic seizures is associated with the worst cognitive outcome; whereas convulsive prolonged seizures do not seem to represent, per se, a bad prognostic factor for mental outcome**. In this study, **statistical analysis failed to reveal differences in the cognitive outcome with regard to the presence and type of SCN1A mutation**.

[Cognitive and behavioral characteristics of children with Dravet syndrome: an overview (APR2011)]

<http://onlinelibrary.wiley.com/doi/10.1111/j.1528-1167.2011.02999.x/full>

- There are several studies on the clinical findings, including developmental features, in large series of children with severe myoclonic epilepsy in infancy (SMEI) or Dravet syndrome (DS) (Dravet et al., 2002; Fukuma et al., 2004; Caraballo & Fejerman, 2006). **After an apparent normal development the onset of a cognitive decline seems to occur after the second year of life. Mental retardation (MR) observed in all patients, with a wide variability (from mild to severe) mostly between the moderate and severe range, is often associated with a progressive neurologic deterioration (pyramidal signs, ataxia, clumsy movements). Behavioral disorders, which can also include autistic features, are common. Typically their evolution changes with age from hyperactivity toward slowness and perseverance.** The syndrome has been thus included into the epileptic encephalopathies. **Dravet et al. (2002) stressed that cognitive stagnation fades at 6 years of age and a relatively positive evolution may occur afterward in the sense of a stable cognitive development and a more adaptive behavior.** There was controversial evidence about the causative relationship between the epileptic disorder and cognitive/behavioral impairment.
- It is noteworthy that **the behavioral disorder was more pronounced in patients with more severely impaired cognition**, suggesting a secondary genesis or a concurrent severity.
- **Anecdotic cases, even with genetic mutation (SCN1A), may show a cognitive development in the normal range (one case assessed when already an adolescent: Buoni et al., 2006; two patients assessed, respectively, at 5 and 6.3 years: Ragona et al., 2010).**
- **In a retrospective study (unpublished data) generalized impairment in several domains were observed (visual attention, verbal, visual and working memory, executive functions) while language (naming and comprehension) was surprisingly, often relatively spared.** Wolff et al. (2006) had found language results to

be heterogeneous. **It is noteworthy that the impairment of specific cognitive skills would be frequently found in DS, even in patients with an IQ in the normal range.**

- In a recent study (Ragona et al., 2011), a statistical analysis on 26 patients **failed to detect any significant correlation between severity of cognitive decline and various clinical variables** including age at seizure onset, months with absences, and myoclonus before age 36 months, and mean number of prolonged convulsive seizures. However, **the authors underscore that in a group with good cognitive outcome, early absences or myoclonus were generally not observed.**
- **Surprisingly, the same study (Ragona et al., 2010) indicates that the number of episodes of convulsive status in the first 18 months of life correlates positively ($p < 0.05$) with higher global quotient at outcome (60 months).**
- However, **the paradoxical absence of a positive relation between early convulsive status and developmental skills may raise the question about possible causes other than epilepsy accounting for the cognitive impairment.**

[Mouse with Nav1.1 haploinsufficiency, a model for Dravet syndrome, exhibits lowered sociability and learning impairment] 16AUG2012

<http://www.sciencedirect.com/science/article/pii/S0969996112002902>

- early appearance of myoclonic and absence seizures are not always associated with severe cognitive decline (Ragona et al., 2010; Wolff et al., 2006).
- Dravet syndrome children show poor social interaction skills, which become apparent during early childhood and rarely rise above the level of those of a 2-year-old (Cassé-Perrot et al., 2001; Riva et al., 2009; Wolff et al., 2006).
- Ataxia usually appears in Dravet syndrome children from the second year of life (Dravet et al., 2005). Their imbalance gait tends to disappear after the fourth year of life, whereas some patients continue to have severe ataxia.

[2012 International Meeting for Autism Research: Dravet Syndrome- Genetic Analysis of SCN1A and PCDH19 Mutations for 17 Chinese Children]

<http://imfar.confex.com/imfar/2012/webprogram/Paper10671.html>

- We found a relationship between the type of mutation and the degree of intellectual disability ($p < 0.05$), with **truncating/splice site mutations associated with moderate/severe mental retardation**. At the evolution of the disease, **79% (11/14) of DS patients with SCN1A mutations had features which fit into the diagnostic criteria of autism spectrum disorder (ASD)**.
 - These links appear to be referring to the same study
 - <http://dravet.org/newsevents/detail/SCN1A-PCDH19-Mutations-Intellectual-Disabilities-Kwong>
 - http://www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0041802?utm_source=feedburner&utm_medium=feed&utm_campaign=Feed%3A+plosone%2FNeuroscience+%28PLOS+ONE+Alerts%3A+Neuroscience%29
 - The truncating/splice site mutations were associated with moderate to severe degree of intellectual disability ($p < 0.05$). During the progression of disease, 73%

(11/15) had features fitting into the diagnostic criteria of autism spectrum disorder and 53% (8/15) had history of vaccination-induced seizures.

[Prognostic, clinical and demographic features in SCN1A mutation-positive Dravet syndrome]

<http://brain.oxfordjournals.org/content/early/2012/06/17/brain.aws151.abstract>

<http://dravet.org/newsevents/detail/survey-dravet-medications-sodium-valproate-benzodiazepines-topiramate>

- They also found that the **clinical features that predict a worse developmental outcome included status epilepticus, interictal electroencephalography abnormalities in the first year of life, and motor disorder.**
- **No significant effect was seen for seizure precipitants, magnetic resonance imaging abnormalities or mutation class (truncating versus missense).**

[Epilepsy is a Disease (Not a Disorder) - One Individual's Perspective | epilepsy.com]

<http://www.epilepsy.com/node/996943>

- “Thinking, Memory, & Epilepsy” is the title of a section from the website, epilepsy.com. “If you have mostly primary generalized seizures, like absence, myoclonic, or tonic-clonic (grand mal) seizures, you are much less likely to have problems with your thinking than someone who has partial-onset seizures (seizures that begin in one area of the brain, often the temporal lobe). Some people with epilepsy of this kind do experience problems with their memory, language, or other kinds of thinking”.
 - “Seizures, especially ones that start in the temporal lobe, can cause a major blow to the hippocampus. The hippocampus is very sensitive to changes in brain activity. **If seizures starting here go untreated, the hippocampus starts to harden and shrink. Then it is as if the librarian has gone on strike. Information may be stored, but in a disorganized way**”.
 - “In general, it is thought that the earlier the age of onset seizures, longer duration of seizures over time, prolonged unremitting seizures (status epilepticus), and increased exposure to A.E.D.s are more likely to be **associated with cognitive problems**”.
 - Other articles do discuss the age at which the first seizure occurs. “Age of Epilepsy Onset Linked to Cognitive Impairment”, from a journal called Epilepsia, was written by Kati Rantonen and Kai Eriksson. It states, “**Age of seizure onset may be a significant predictor of cognitive impairment in preschool children with epilepsy**”.

[Focal Scn1a knockdown induces cognitive impairment without seizures (21DEC2012)]

<http://www.ncbi.nlm.nih.gov/pubmed/23318929>

Intellectual disability in DS begins early in development and is permanent; scores on the developmental quotient typically drop to 20–40% of normal within the first 6 years of age and, as adults, IQ scores are below 50 in the majority of cases.

[Prognostic, clinical and demographic features in SCN1A mutation-positive Dravet syndrome]

28APR2012

<http://www.ncbi.nlm.nih.gov/pubmed/22719002>

- When we compared patient ages at seizure onset in relation to the precipitant type (fever/illness, no precipitant or vaccination), we found that
 - **the vaccination group had a significantly earlier onset of seizures with 4.0 +- 1.0 months** (median +- semi-interquartile ranges)
 - compared to the fever/illness group with 6.0 +- 1.0 months
 - and those without a precipitant 5.0 +- 1.5 months [$\chi^2 = 7.83$, degrees of freedom (df) = 2, $P = 0.020$).
- **we found that vaccination-triggered seizures presented significantly earlier** than those without precipitant or with fever/illness, **nevertheless vaccination itself had no impact on the developmental outcome** (McIntosh et al., 2010).
- **two-thirds of children with Dravet syndrome scored in the abnormal range (>90th percentile) of 'hyperactivity/inattention' and one-third in the abnormal range for 'conduct problems' (Brunklaus et al., 2011).**