

# 73| Neuropsych Bite: Acute Disseminated Encephalomyelitis – With Dr. Lana Harder

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**Speakers:** Lana Harder, Ryan Van Patten, John Bellone



**Intro Music** 00:00



**Ryan Van Patten** 00:17

Welcome, everyone, to Navigating Neuropsychology: A voyage into the depths of the brain and behavior. I'm Ryan Van Patten...



**John Bellone** 00:25

..and I'm John Bellone. Today we have our third Neuropsych Bite on demyelinating conditions in children with Dr. Lana Harder. Today's topic is pediatric acute

disseminated encephalomyelitis, or ADEM. Lana is board certified in clinical neuropsychology and pediatric neuropsychology, and she is an associate professor at UT Southwestern.

**Ryan Van Patten** 00:46



As you'll find out from this episode, ADEM is a rare condition. Some of you may be wondering why we're talking about rare diseases on NavNeuro at all, given that there are other pediatric neuropsychiatric disorders with much higher prevalence rates. John and I believe that, although ADEM and some of the other demyelinating diseases are rare, it's important for us to be familiar with the broad strokes here. We don't want to spend 100% of our time on ADHD, autism, TBI, and epilepsy, for example, and neglect these lower base rate conditions. In order to be well-rounded neuropsychologists, we need to be familiar with everything in our purview. This is why we're releasing brief NavNeuro episodes to cover everything from limbic encephalitis and Balint syndrome to ADEM and pediatric transverse myelitis. So, with that in mind, we once again give you Dr. Lana Harder.



**Transition Music** 01:42

**John** 01:51



So, similar to transverse myelitis, acute disseminated encephalomyelitis, or ADEM, is a monophasic disease of spinal cord inflammation. In our previous Neuropsych Bite, we talked about the term "monophasic" - that it means one occurrence of demyelination as opposed to recurrent events of demyelination. But, unlike transverse myelitis, ADEM is more common in children than in adults. Typically, the children are pretty young from what I've seen - around 5 to 8 years old. Can you tell us a little bit about ADEM, especially the pathophysiology and how it might compare to TM or multiple sclerosis?

**Lana Harder** 02:34



Sure. So acute disseminated encephalomyelitis, or I prefer to say ADEM for sure [laughs] - is an autoimmune disorder of the central nervous system. So, by definition, there must be brain involvement. There may or may not be spinal cord or optic nerve involvement in those cases. So, what we know about these autoimmune demyelinating disorders is that the immune system, by mistake, is attacking the myelin - that protective coating around the axons that allow for that smooth, rapid transmission between neurons. And that attack can really disrupt our functioning in a whole variety of areas. When you think about a condition like

ADEM, because it can be almost anywhere in the central nervous system, that means you can get almost any neurologic symptom. And, so, there are lots of symptoms that can arise from that.



**John** 03:32

Must be hard to diagnose because of that, I'd imagine.



**Lana Harder** 03:36

That's right. Because there's not one or two specific symptoms that we can see and say, "Oh, that's ADEM." So then, you know, it's really important to tease apart and differentiate from these other demyelinating disorders.



**John** 03:52

Yeah. I know, in a previous episode, you mentioned one differentiation between MS and some of these other disorders is that in MS there are oligoclonal bands in the CSF. Any other pearls in terms of differentiating?



**Lana Harder** 04:07

Yes. I think one of the most important things is, in the onset for kids with ADEM, they're going to show an encephalopathy that we don't see in the other demyelinating disorders. So, that might look like changes in mental status, confusion, personality changes. That is something that I know they're looking for in the very early stages of this disorder. Also, as you've mentioned, we do tend to see ADEM in younger kids as compared to something like MS - which does also involve the brain, spinal cord, or optic nerve - that tends to be seen in older kids. Although there's a range of ages, MS tends to be seen at an average age of 15 or so.



**John** 04:49

As we talked before, you can also have pediatric MS, which just muddies the water even more in terms of differentiating these, right? It might be good for our listeners to know about the word "encephalomyelitis". The "encephalo" is the brain part, and "myelitis" refers to the spinal cord part. So, in the name, it refers to both the brain and spinal cord.



**Ryan Van Patten** 05:13

I've read ADEM described as a post-infectious monophasic event. Can you talk about the infectious process? And then, of course, the subsequent immune reaction, but in particular, the infection in ADEM?

**Lana Harder** 05:25



Yeah, so many of our patients who experience ADEM do so following an infection. This could be anything - respiratory, GI. So, the theory is that the immune system has been triggered by that infection to clear the body of it. But then the immune system, by mistake, causes damage to the brain. There's this theory I find really fascinating, and by no means am I an expert in this, but it's molecular mimicry. So, there's something about the protein associated with that infection that resembles a protein in the brain. And it triggers a response against the self. It's making an error and going after the wrong thing. I think that's a really interesting theory behind what might be going on in ADEM and in these other disorders.

**Ryan Van Patten** 06:15



So there's not a particular type of infection, necessarily, that precedes ADEM? It could be a cold or something more severe. You said it could be respiratory or cardiac - there's no way to pin it down? To know if my child is sick with X infection, ADEM is very likely?

**Lana Harder** 06:33



Exactly right. It isn't something that we've honed in on specifically.

**Ryan Van Patten** 06:39



I see.

**John Bellone** 06:40



Do we have a sense about the overall prevalence of ADEM?

**Lana Harder** 06:45



I'm not sure how clear this data is. The most recent that I've heard is 1 per 125,000.

**John** 06:52



Okay, so pretty rare?



**Lana Harder** 06:54

Very. Yes.



**John Bellone** 06:56

And, given the spinal cord inflammation, what are some of the common physical symptoms of ADEM?



**Lana Harder** 07:03

So, common physical symptoms, as we mentioned, could be any neurologic symptom just because the central nervous system is sort of fair game with ADEM. I've mentioned mental changes, which we would expect to see in ADEM. There could also be numbness, weakness, problems with balance and walking, visual changes - so, that could be vision loss or double vision. We see headaches, bowel or bladder changes. In severe cases, our patients can become unresponsive and even go into a coma.



**John** 07:36

Yeah, right. There's just so many different potential symptoms, which is similar to MS and some of these other disorders. What are some of the common medical treatments given to these children?



**Lana Harder** 07:48

So, early on, in that acute phase, the goal is to reduce inflammation as quickly as possible. Timely treatment is so essential across all of these conditions. So steroids are typically a first-line treatment for that. There's something called "plex", or plasma exchange, which is sort of like a cleansing of the blood. IVIG is another common treatment for this. In extreme situations, they may go to something that involves more immunosuppression, like methotrexate. But I think that's in a minority of the patients, from what I understand.



**Ryan Van Patten** 08:25

Got it. So, let's move on to cognitive effects. You co-authored a 2017 review paper with Alexander Tan and others, and covered cognitive effects of different demyelinating autoimmune conditions. For ADEM, as I recall, you estimated roughly a 15 to 20% rate of cognitive impairment. Of course, you know, we all define cognitive impairment differently, as you have said to us before. So, if you don't mind, can you summarize the literature on cognition in ADEM, including any papers that came out after your review paper?

**Lana Harder** 09:00



Sure. Yeah. I would say we still have very few studies that relate to cognition in ADEM. I see this as an area of opportunity for researchers in this area. We really only started seeing this work systematically conducted in about the early 2000s. So, documented areas of difficulty have included really wide-ranging problems. But, I would say, kind of boiling it down to the most common I have seen are attention and processing speed problems. And ADEM appears to be associated with more favorable outcomes compared to MS overall, which I think makes sense when you consider MS is a chronic brain-based problem. In MS, we see that they may have more severe impairments that might be more global, or at least show up across more areas. A couple of things that stand out to me from the ADEM literature are that young age at onset could be considered a risk factor for poorer outcomes. But, I have to say, the literature is not completely consistent on this point. So, again, I think we need more studies. We also see an association of ADEM with poorer cognitive function and more problems with behavior, emotional functioning, quality of life, and school. So those are some points, highlights I would say, from the literature.

**John Bellone** 10:25



Maybe this was clear earlier and I missed it, but since ADEM is a monophasic disease relative to multiple sclerosis, this means that there is an acute, single event that causes symptoms. Once it's treated, is it typically in intermission forever? Or do you know if this can recur later on, just less frequently? Can you walk us through that?

**Lana Harder** 10:52



Yeah, sure. So, classically, ADEM is thought of as this one-time monophasic event and we do not expect it to return. Because if it returns, it's more likely to be one of the recurrent diagnoses - maybe MS or something like that. As we'll have the chance to talk about later, there's a recent discovery of an antibody against MOG - which, again, we'll describe more in another episode - that is associated with recurrence and can be seen in the context of ADEM. So I definitely want to mention that here in this conversation.

**John Bellone** 11:30



Yeah, that's good to know. So, if it started to recur, then we would be thinking that this is not ADEM. That this is something else like multiple sclerosis, let's say, or look for other possibilities. Is that right?



**Lana Harder** 11:43

Yes. It gives us the clue that something else is going on that's much more persistent than what we would have historically seen with ADEM.



**Ryan Van Patten** 11:51

But the prognosis for something like ADEM, probably, on average, is much better, right? Because it's monophasic, compared to MS, for example.



**Lana Harder** 12:00

I think the takeaway from at least the existing literature is that - you know, thinking of neuropsychology, the outcome is more favorable as compared to a chronic condition like MS. I would agree with that.



**John Bellone** 12:13

Right. I was wondering about the long-term outcome for ADEM relative to MS since it is not a recurring disorder. Can you walk us through a little bit about the cognitive profile relative to recurring disorder?



**Lana Harder** 12:28

Yes. I think we tend to see more isolated cognitive difficulties, like in attention and processing speed in the context of ADEM as compared to something more chronic, where there's this disease acting on the brain over and over. Especially during a period of development - during childhood and adolescence - where we would tend to see more severe deficits, perhaps more global cognitive problems, or at least cognitive difficulties across several different areas. I will point out - and this is more of a clinical observation and it's something that stands out to me when it comes to ADEM and we do see this in the literature - is that cognitive functioning can vary widely. You might see mean scores as a group in the average range, but there is a wide range. And one thing I've noticed, clinically, is that for our patients that had a more complicated course of ADEM - and you remember that I mentioned that in severe cases of ADEM they may become unresponsive or go into a coma - there can be increased intracranial pressure, and all kinds of things can happen because of that. So I have noticed that, for those patients, they do tend to struggle a bit more, as you might imagine, over time. There's more damage to the brain in those acute phases that really leaves them with a burden of cognitive dysfunction over time. I think that's worth mentioning.



**John Bellone** 13:59

Yeah, it makes sense. If there is co-occurring increased intracranial pressure, we will potentially see stretching of axons and all sort of hydrocephalus-related symptoms, which could be more long-term than just the acute demyelinating lesion.



**Lana Harder** 14:18

Yes.



**John Bellone** 14:18

I'm glad you mentioned that. And then maybe to round things out, is there anything unique about the neuropsych eval with kids with ADEM compared to other disorders?



**Lana Harder** 14:29

Yeah, I think we've covered that pretty well. You know, in general, I would say these patients can do quite well in their recovery. I think there was one study that showed that, with more time, they are improved cognitively. On the flip side, I have to say that I have seen kids who go through their acute phase, get back to school, seem to be doing okay, and then we go a couple years out and, as demands increase in their environment, they actually struggle to keep up. So it's kind of this delayed, you know, ability to see the problem. As those demands increase, we start to see them struggle to keep up with their peers. So, for that reason, we follow our kids with ADEM for several years after their event. Even if we think they're in the clear, and they're probably not going to experience a medical event again, we do keep a close eye on them for those reasons that I mentioned.



**Transition Music** 15:27



**John Bellone** 15:31

Well, that does it for our conversation with Lana. If you haven't visited the NavNeuro INS CE webpage recently, we encourage you to check it out. We recently released a batch of new NavNeuro episodes for CEs. So we think that there is now enough content to be relevant to anyone. Again, that website is [navneuro.com/ins](http://navneuro.com/ins). And, as always, thanks for listening and join us next time as we continue to navigate the brain and behavior.



**Exit Music** 16:00

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**John Bellone** 16:24

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**Ryan Van Patten** 16:35

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