

# 67| Neuropsych Bite: Pediatric Multiple Sclerosis – 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 second Neuropsych Bite with Dr. Lana Harder. Today's episode is on pediatric multiple sclerosis, or MS. Lana is board certified in clinical neuropsychology and pediatric neuropsychology, and she is an associate professor at UT Southwestern.

**Ryan Van Patten** 00:45



If you're interested in MS more broadly, we recommend before listening to this episode you check out number 62, which is MS with Dr. Peter Arnett. And, with that, we give you our conversation with Lana.



**Transition Music** 00:59

**John Bellone** 01:09



All right, so multiple sclerosis, or MS, is a chronic central nervous system demyelinating disease that's known to occur in young and middle-aged adults. Many people might not know that it can also occur in children. Can you tell us about the growing recognition of pediatric MS?

**Lana Harder** 01:29



Sure. I would say over the last 10 to 15 years there's been this increasing acknowledgment and literature focusing on MS in childhood. It's thought of as this early onset MS, which is considered rare - even though MS is not rare, when the onset is prior to age 18 it's considered a rare disorder. So we've learned a lot in this time, but still have a lot of work to do. I would say particularly as it relates to the complex array of symptoms that our patients have - cognitively, in terms of their mood, fatigue, sleep, and so forth. I think we need to better understand how all of these symptoms interact to help us guide treatments and interventions for these patients.

**John Bellone** 02:15



Before we dive a little more into the symptoms, can you talk through the pathophysiology of pediatric MS and how it might differ from the adult variant?

**Lana Harder** 02:26



Sure. So a lot of the things we know about adult MS are consistent with pediatric MS. This is an autoimmune disorder impacting the myelin, which we know coats the

axons and allows for that smooth, rapid transmission of signals between neurons. So in these autoimmune demyelinating disorders, we have an attack on the myelin, which compromises those signals and creates a lot of symptoms and a lot of problems. We can talk about that more as we go. So, for kids, they tend to have more relapses than adults, but they recover better from those relapses. Another thing is that they tend to have a longer, kind of, “runway” before reaching disability compared to adult-onset MS. We think there are probably some differences in pathophysiology based on these observations, but I don't think we quite know what those are.



**John Bellone** 03:25

The types of MS, do those hold in the pediatric group?



**Lana Harder** 03:30

That's a great question. The vast majority, 95+% of kids with MS have that relapsing-remitting type of MS. It's very rare to see the other subtypes.



**Ryan Van Patten** 03:43

Yeah, primary progressive type - that would be especially sad in children, but it's extremely rare.



**Lana Harder** 03:49

Yes, I think I've seen only one of those in a child.



**Ryan Van Patten** 03:52

You mentioned that pediatric MS is rare compared to adult MS. The prevalence rates I've seen are about 2 to 5%. Is that about accurate?

**Lana Harder** 04:04

We think that's about accurate. It is consistent in the literature, the 2 to 5% rate. A couple of things, though, come to mind as I wonder if that's an underestimate. One is that, because it is so rare, it is not at the top of the differentials when a child presents with symptoms that are reflecting pediatric MS. So I have wondered if it's underdiagnosed. The other thing is that our adults who have MS and were diagnosed in adulthood will reflect on childhood and adolescence and remember things and wonder, “Was that an early manifestation of the disease?” It's just so hard to know that in retrospect.





**Ryan Van Patten** 04:45

Interesting. Yeah, I hadn't thought about that. And I should have been clear, 2 to 5% of all MS cases are thought to be child MS, but you're suggesting that that rate could be a little bit higher for those reasons you mentioned.



**Lana Harder** 05:00

Exactly. That's right.



**John Bellone** 05:01

Yeah. And as recognition grows among clinicians and parents, maybe they'd be more likely to consider that, like you mentioned.



**Ryan Van Patten** 05:10

Yeah, we've seen that in some neurodevelopmental disorders. So I believe increases in rates of autism spectrum disorder, for example, one possible reason for that could be because clinicians are more aware of it, people in general are more aware of it. So it could be that it was there all along, and we're just starting to diagnose it more.



**Lana Harder** 05:27

Yes.



**John Bellone** 05:28

I guess one other possibility is that as our neuroimaging power improves, we're seeing more lesions that we didn't see before.



**Lana Harder** 05:37

Sure.



**Ryan Van Patten** 05:38

You mentioned that one potential reason for the low prevalence could be because pediatric MS hasn't been as recognized. So, it's not at the top of a differential for a lot of neurologists. With that in mind, I'm wondering if you could distinguish for us, briefly, pediatric MS from other demyelinating diseases that can occur in children, such as transverse myelitis, acute disseminated encephalomyelitis, and neuromyelitis optica.

**Lana Harder** 06:08



Sure, yes. I think things to think about in making these differentials is the location of the lesions and then the course over time. So we know that MS is associated with lesions in the brain, the spinal cord, optic nerve, and it's chronic or recurring - we see these relapses over time. Transverse myelitis is restricted to the spinal cord and is associated with a one-time event, generally speaking, so that's a difference there. Acute disseminated encephalomyelitis, or ADEM for short, is probably one of the more tricky differentials because you have the same location of lesions - brain, optic nerve, spinal cord - or at least it's possible to have lesions in all of those areas. It's also thought to be a one-time event. Some differences I will mention between MS and ADEM that are really important - and, by the way, I do not envy my medical colleagues who have to figure these things out on the front lines. And so with ADEM, a hallmark of that is that there is encephalopathy, mental status changes at onset. We do not see this in MS. So that's one important point to make. And again, ADEM is thought to be a one-time event. Also, it occurs in younger children. So the average age for onset in ADEM would be about 5 to 8 years, whereas in MS it's more in the teen years. So those would be other things. When we do the medical workup, there are some things that are seen in MS that we don't tend to see in other myelinating disorders or that might favor an MS picture, and that would be the oligoclonal bands in the CSF. Something that we can see associated with neuromyelitis optica - which is a spinal cord and optic nerve disorder that is chronic, so we see those relapses - and it can be associated with anti-aquaporin-4 antibodies. So that would help with a differential in a medical workup. So those are some ways to think about the different ones. It's pretty complicated.

**John Bellone** 08:21



Yeah, yeah. Like you said, it's good that our physician colleagues are the ones who are dealing with this and parsing it out. [laughs] Yeah. You alluded to, earlier, some of the common cognitive and emotional sequela, can you maybe do a deeper dive into those and if they differ from adult MS?

**Lana Harder** 08:44



Sure. So I know that in the adult literature, they talk about 40 to 60% have cognitive problems, that's typically what you read over and over, whereas about a third in pediatric MS will have those cognitive problems. I just have to point out that there are methodological differences across studies. So when we say "cognitive impairment", and when anyone says that, I think it's important to find out what their definition is. We can all appreciate, we don't have an agreed upon definition of that,

particularly for research purposes. I wish that we did. So sometimes we see a composite score that's past a certain cutoff, we may see that someone has "failed" a certain number of tests in a given battery. And so it really just depends on how that's been measured.

**Ryan Van Patten** 09:36



So the differences in cognitive prevalence rates that we've seen may not be due to any true differences in MS as far as we know. We've seen that more adults with MS seem to have cognitive impairment compared to children with MS, but that might just be due to differences in methodology.

**Lana Harder** 09:57



Exactly, exactly. Some of our data has suggested these rates could be a bit higher in children. But if I were thinking of reasons why we might be seeing higher rates of cognitive problems in adults versus pediatrics - you know, we know we said earlier that our children recover better from relapses compared to adults. They also haven't had as long to accumulate disease and disability as adults. Or, at least, it's a pediatric onset, so the plasticity of the pediatric brain could be protective in that regard. Also, we know that cognitive problems may emerge over time. So it may be that children as they grow into adults with MS, will show higher rates of cognitive difficulty. We are lacking our longitudinal data in this area so it's kind of hard to say.

**John Bellone** 10:54



Yeah, what I've seen, though, is it seems like it's across a number of different cognitive domains that could potentially be affected. I guess it depends on where the lesions are. Do you want to say anything about that?

**Lana Harder** 11:06



Absolutely, I think when we look across a neuropsych battery, there are lots of things we measure. And it kind of seems like when you read about pediatric MS that almost every area has shown up as a problem in this population. And, like you said, maybe it's because of where the lesions are exactly or how the impact of a demyelinating disorder on the developing brain has impacted it. I will make a couple of notes. I do think, of the demyelinating disorders we've talked about in pediatrics, MS is one that's associated with more difficulty or deficits compared to the others, and sometimes more global cognitive problems. So we have seen differences in IQ. But, more often, what we see are language difficulties, which is a difference than what we see in adults. Adults with MS do not tend to have language problems, that tends to be spared. What we see early on in the disease process is problems with

attention and processing speed. And then a very high frequency area for problems would be visual-motor. And we do think that motor-based problems could undermine performance across other neuropsych measures. So we have to think about that. Executive skills is something that's been variable in terms of our findings in the literature. But we do see a lot of difficulty with memory, in verbal and visual areas, as well.

**John Bellone** 12:38



One other difference that I saw in my reading between pediatric and adult MS is that kids often have more infratentorial lesions, so cerebellar lesions, than adults. I'm not sure of the prevalence rates, but it was something else I saw.

**Lana Harder** 12:54



Yes. Yes, that's correct.

**Ryan Van Patten** 12:57



Lana, could you say a few words about fatigue in children? It's common in MS in both adults and children, to my understanding, and I can imagine that it could have a big impact on their quality of life.

**Lana Harder** 13:09



Yeah, that's right. I think fatigue is one of the highest frequency symptoms that has the biggest detrimental impact on individuals with MS. I know that's been established very well in the adult literature. For kids, the rate is up to 75% of those with MS suffer from fatigue. A lot of the work we've done in recent years, and that I've done along with my research students, has been trying to understand the relationship of fatigue, cognitive functioning, and mood - there is literature to say that all of these things can correlate, or go together. So I think, going forward, we're working to better understand that relationship so we can figure out where to target our interventions for these kids.

**John Bellone** 13:18



And then I'm also curious about the impact of pediatric MS on psychosocial and academic functioning. I've also read that about half of children have some kind of psychiatric diagnosis. Can you talk through these types of symptoms?

**Lana Harder** 14:13



Yeah, I mean, you're exactly right. The rate has been anywhere from 30 to 50%. These tend to be more internalizing symptoms like anxiety, depression, we definitely see adjustment disorder, and then symptoms of ADHD as well. And there is a good bit of literature documenting school, social, daily living skills difficulties for these individuals. In our research, in our data, we see that about a third of our kids have school problems. And so they're struggling in one or more areas of school and often have special education services or accommodations that are in place to support them.

**Ryan Van Patten** 14:59



What do we know about long-term outcomes and children with MS? Do they typically grow up to be adults with MS? Does it often develop into a secondary-progressive? Or maybe there hasn't been enough research yet to know.

**Lana Harder** 15:13



So, a few things. I think we've mentioned that our kids tend to have more relapses, but recover better. Their progression to disability is slower than adults, but they reach that disability status earlier, so at a younger age. So those are some things we know about the progression on the medical side. When it comes to neuropsych functioning, very few longitudinal studies exist and they are really variable. You can see kids actually improve over time, decline, or remain very stable. So that is something we just don't know a lot about. We do think that there is a protective factor to higher cognitive reserve, and this has been measured in terms of their overall IQ. We think that that can be protective from showing decline over time.

**John Bellone** 16:05



This might be a difficult question, but what might be the potential etiology of MS at these younger ages? I don't know if you want to say anything about the environment or genetic predispositions that might play a role here.

**Lana Harder** 16:21



There is quite a bit of research looking into some of the things you've just mentioned. So genetics being a factor, sun exposure, or vitamin D levels. So they've looked at people's distance from the equator, thinking of sun exposure and vitamin D, such that your risk is higher the further away you are from the equator up to age 15. They've studied viruses - all kinds of different things. But the thing that you hear the most is that it's a combination of factors that make a person susceptible to the onset of MS. So a little bit vague, but we do think that the

components I mentioned are all pieces of that. There's also been some emerging research around exposure to secondhand smoke and other environmental factors that may put a person more at risk. So that's evolving.



**Ryan Van Patten** 17:13

Are girls at higher risk than boys, mirroring the adult literature?



**Lana Harder** 17:17

So that is one of the more fascinating points, I think, about pediatric MS. If you look post-puberty, you do see that girls outnumber boys. If you look at a pre-puberty sample, it's actually the other way around - so boys are outnumbering girls a little bit more. So there are some thoughts that hormones play a role here. We also know that during pregnancy, your risk for a relapse actually goes down. So I think there's, again, something to that. But I think that's something we're still looking at.



**Ryan Van Patten** 17:52

Yeah, interesting. Lana, I'm wondering how often you see children with pediatric MS clinically, and just broad strokes, what the neuropsych evaluation looks like?



**Lana Harder** 18:03

Sure. So I probably see patients with MS weekly, because I'm in a multidisciplinary clinic. Actually, this group is one of our largest in our specialty clinic. These are typically teenagers. I want to mention that because developmentally they're at a stage where they're expected to become more independent. But, by contrast, when you're diagnosed with and are facing a chronic medical condition, you actually need a lot more support. So there's a conflict going on there. And as we mentioned before, they're facing a host of symptoms - cognitively, in terms of emotional functioning, fatigue, trying to succeed in school - and then this is hitting the entire family as well. So there's a lot to navigate and manage. In our clinic, our goal is to screen every patient that comes through with a brief cognitive battery, it's about 60 minutes long, to determine if we need the full neuropsychological assessment. So, at a minimum, typically we're consulting with them and providing that screener which allows us to give some feedback and potentially some recommendations. But very often we're moving toward the full evaluation. And then working through I would say some common challenges - cognitively, that would be relative to processing speed, memory, those mood related symptoms, and fatigue. Also, we work very closely with our patients to navigate the school setting. So, you know, MS is largely an invisible disability, not in every case, but our patients talk to us about this. And I think it's hard to communicate that this is a disorder that can have a

profound effect on someone's performance in a classroom, and that can vary day to day. So I think that also makes it difficult - you know, why were you able to do so well this day but now you're struggling today? So we have to really work with schools to implement supports that stay in place all the time so that our teens have what they need when they need it. And then the last thing I would say is we spend a lot of time talking about transition to adulthood. So really starting at age 13 in our clinic we're going to talk to patients about that. But I think for our MS patients, that's something we work with them very closely - on understanding MS, what it means for them, and how to advocate for themselves in the future.

**John Bellone** 20:31



And then just to wrap things up, in terms of intervention, are you aware of any literature on the effectiveness of cog rehab or training for pediatric MS? Or even adult MS, for that matter?

**Lana Harder** 20:45



So I'm aware that the adult MS literature is ahead of us when it comes to rehabilitation, as well as other pediatric groups. There's research on cognitive rehab, certainly in other pediatric populations. Thus far, I am unaware of anything in the literature other than to say we really need this work to be done for our patients. But that doesn't stop us from providing our patients with, I think, a lot of meaningful recommendations for how they can manage MS on a day to day basis. We've touched on a couple of those relative to school programming. But I would also say, individual therapy is something that we refer our patients for frequently. Sometimes a family-based therapy that has a medical focus can be really helpful for the family, kind of wrapping their minds around MS and what this means for the entire family. A big area of emphasis, and there is some literature on this, is camps for teens with MS and support groups, peer support groups. We know how important peers are in the teenage years, so there's been some positive evidence for that. My team members and I volunteer for two different camps each year to stay engaged that way with our patient populations. And then I would say, oftentimes, our teens need support for medication adherence. We haven't talked about this so much, but our disease-modifying therapies really help hold off those attacks, those relapses in MS. And it's so critical that our teens are able to stay on those medications, so we often come in to provide some support on adherence as well. And there's a whole, you know, a longer list of these things, but those are just some highlights for you.

**John Bellone** 22:34



Perfect.



**Transition Music** 22:34

**John Bellone** 22:38



Well, that does it for our conversation with Lana. If you haven't yet rated us in Apple podcasts, please just take the less than one minute to do that. A 5-star rating really helps us a lot. We really appreciate everyone who's already done that, and for all of you who will go leave us a rating. And, as always, thanks for listening and join us next time as we continue to navigate the brain and behavior.



**Exit Music** 23:02

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**John Bellone** 23:26



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**Ryan Van Patten** 23:37



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