75| Neuropsych Bite: Anti-MOG Associated Disease – With Dr. Lana Harder

July 15, 2021

NAVIGATING NEUROPSYCHOLOGY

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Speakers: Lana Harder, John Bellone, Ryan Van Patten

Intro Music 00:00

John Bellone 00:17
Welcome, everyone, to Navigating Neuropsychology: A voyage into the depths of the brain and behavior, brought to you by INS. I'm John Bellone...

Ryan Van Patten 00:26
...and I'm Ryan Van Patten. Today we have our final Neuropsych Bite on demyelinating conditions in children with Dr. Lana Harder. Today's topic is

anti-MOG associated disease. If you don't know what that is, no worries, we'll explain it in the episode. Lana is board certified in clinical neuropsychology and pediatric neuropsychology, and she's an associate professor at UT Southwestern.

John Bellone 00:52

We recommend listening to the previous Neuropsych Bites with Lana on pediatric MS, transverse myelitis, and acute disseminated encephalomyelitis before hearing this one, because the earlier conversations provide important context that's going to be helpful when learning about anti-MOG disease. And, with that, we give you our conversation with Lana.

Transition Music 01:13

Ryan Van Patten 01:22

So in 2011, myelin oligodendrocyte glycoprotein, or MOG, antibodies were found in neuromyelitis optica spectrum disorder, and I believe you recently started seeing children with anti-MOG disease in your clinic. It's been obvious to me that this is a relatively recent discovery because I had a really hard time finding papers on it [laughs], compared to the other demyelinating conditions we've talked about. So give us a broad overview of anti-MOG.

Lana Harder 01:52

Sure. I want to first thank you for saying what MOG stands for so I don't have to.

Ryan Van Patten 01:56

[laughs] I struggled through it, but I made it.

Lana Harder 02:02

I've had to practice. [laughs] So patients with anti-MOG associated disease test positive for the anti-MOG antibody. And the reason that that's important - So, MOG is a glycoprotein important for myelination of nerves in the central nervous system. And so you have this antibody acting against the myelin and undermining its integrity. And, as we've discussed with other myelinating disorders, this is an attack on that insulation, the myelin, around the axon that allows for that rapid transmission in signals between neurons. And that's a problem because it breaks down those signals and may make us less efficient, or break down our capabilities in performing motor tasks, or whatever the case may be. That is highly dependent

on where in the central nervous system this has taken place. So when we think about anti-MOG, this can show up in a whole variety of ways. I guess we could say, "Think of it as a syndrome". So it could be associated with acute disseminated encephalomyelitis, ADEM, or it could be associated with transverse myelitis, neuromyelitis optica, or optic neuritis. So that's the clinical manifestation, but then we would test for the antibody to see, “Is this the anti-MOG associated disease?” If it is, there is a higher rate for recurrence and these relapses that we've been talking about.

John Bellone 03:36
Right? So that's good to clarify. You can have both. You can have ADEM and anti-MOG antibodies, right?

Lana Harder 03:43
That's right. That's exactly right. So just to complicate things even more.

John Bellone 03:48
[laughs] A whole extra layer to the onion of demyelinating disorders.

Lana Harder 03:51
That's right.

John Bellone 03:53

Right, so you can have ADEM with or without anti-MOG antibodies. How common is anti-MOG disease? And what are the typical symptoms, if there are any typical symptoms?

Lana Harder 04:04

Yeah, so it's quite rare. The latest thing I've been able to find was 0.16 per 100,000. But as I understand it, we don't really have the best data on this. This is still a relatively newer area that we're all learning about together. So if we think about common clinical symptoms, we would just go back to what we know about symptoms of optic neuritis, symptoms of transverse myelitis, symptoms of ADEM, or neuromyelitis optica. It really maps on to those conditions. And as we've said before, it really depends on the extent of damage and inflammation in the regions affected by each of those disorders.

John Bellone 04:46

So we might see an acute encephalopathy, like we would see in ADEM, or we might see blurred vision or double vision, like we might see in some kind of optic neuromyelitis or neuritis.

Lana Harder 04:57

Exactly.

John Bellone 04:58

Those kinds of symptoms right?

Lana Harder 04:59

Yeah.

John Bellone 05:00

So when physicians are trying to parse out whether ADEM is associated with these anti-MOGs, do you know if they just routinely screen for these antibodies when there's ADEM present or neuromyelitis optica present?

Lana Harder 05:13

So my understanding is that we have started to screen for this much more routinely than we did before. And I think particularly in a case where we've seen a recurrence in a condition we thought was otherwise a monophasic problem, or a one-time event, that would then trigger a check for that. But I do think that it is being checked more routinely. I also want to mention, in pediatrics, and I've seen several papers that document this, and our clinic looking at some of our numbers, I would say about half are manifested as ADEM, but we definitely see all the conditions that I've already mentioned. So it's possible in childhood to have any one of those, but I think the higher frequency condition would be ADEM.

John Bellone 05:59

Okay. And I'm assuming the neurologists that you work with, or the other professionals who are trying to parse this out, they're probably more aware of this maybe at your academic medical center than at other places. Do you know if this is something that's routinely looked at elsewhere?

Lana Harder 06:14

So I think certainly the specialty clinics around the country are very well aware of this and are testing for this. I don't have a great sense of, you know, just sort of in the general clinical settings what people are doing. That's a really great question.

John Bellone 06:29

I guess this could be something that the neuropsychologist, if they saw an ADEM case, they could potentially make a recommendation to look for these antibodies if maybe that wasn't already done, I'm thinking.

Lana Harder 06:40

Sure. And there are papers they could pull to share with their colleagues. One thing I was glad to see is a lot of the papers coming out on this topic are in the journals that focus on MS and related disorders. So, that's good that they're putting this information in front of those specialists.

Ryan Van Patten 07:02

I'm interested in treatments for anti-MOG. We've already talked about treatments for other demyelinating conditions, and you've repeated them a few times, which I appreciate. [laughs] Things like steroids, IVIG, immunosuppressants. Is there anything unique about anti-MOG? What do you know about medical treatment for it?

Lana Harder 07:20

Yeah. So the sense I have from the literature and working in this clinic is that our very first line is steroids. And then the second line is IVIG and the plasma exchange. For long-term management, to hold off attacks, we think about disease-modifying therapies in MS. It doesn't seem that those have been as effective in this anti-MOG associated disease. But instead, they have recommended some of the first line treatments - a couple of examples of that would be rituximab, which is targeting the cells that produce the antibodies. Another example would be IVIG done on a monthly basis. So, you know, regularly.

John Bellone 08:04

Okay, and since this is not monophasic, like some of the others that we've talked about, this is a recurring disorder, these antibodies on a recurring basis attack the myelin. How do the long-term outcomes compare with multiple sclerosis, for example?

Lana Harder 08:22

Yeah, so unfortunately, we don't know a whole lot on this topic just yet. I will tell you, folks are working on this. Since it's relatively new, we are looking to describe the cognitive profiles associated with this. I think this is the fun of being a neuropsychologist in an evolving field. Because, you know, when I started in this clinic, gosh, 12+ years ago, we knew nothing about MOG. But at the same time, I think we can look at the ADEM literature in children and we might get some clues because I could imagine that we had kids that were positive for anti-MOG in those cohorts, but just had no idea. So I think that's one place we could go. But of course, it's not like those children have been pulled out and have been identified. We need to do that prospectively.

Ryan Van Patten 09:15

Something I've gotten from our conversation with you is that, if a neuropsychologist is working with children - or I'm sure this applies to adults as well - with these autoimmune demyelinating conditions, they don't separate cleanly into different buckets. And so we should know about autoimmunity more broadly, and each of the disorders, and how they interact. Would you say that's accurate?

Lana Harder 09:40

Yes, yes. I think that is as well put. The heterogeneity of these conditions, you know, even within one condition, like MS, makes it really difficult to pinpoint a cognitive profile associated with it. It's nearly impossible.

Ryan Van Patten 09:57

Yeah. John, do you have anything else about anti-MOG? I wanted to ask her a professional development question.

John Bellone 10:02

No,I don't have anything else. Lana, was there anything else for anti-MOG that you wanted to say?

Lana Harder 10:09

Just that I suspect we've been seeing these patients for a really long time, probably since we opened our clinic, even though, as we said, we didn't know it. So I think that going forward, we'll have a lot to learn about this. And in the meantime, as clinicians, we'll continue to work on individualizing every assessment, just like we always do, to try to see what those unique difficulties are so that we can plan with the patient to make things easier and make things better for them.

Ryan Van Patten 10:41

Yeah, that's great. So I'm interested - this is a very niche area for neuropsychology, at least in my experience, demyelinating conditions in children. So it's very cool that you have all this knowledge. I'm wondering how you got into this sort of niche specialty area. And if you have general advice for people who might want to start seeing these cases, or who might be seeing them in their medical setting?

Lana Harder 11:04

Sure. Yeah. So my very first exposure to these patients was at the Kennedy Krieger Institute, actually, during my pre-doctoral internship. So flash forward, when I became a faculty member at Children's in UT Southwestern, the timing was such that we were opening a specialty clinic - we had recruited a neurologist from Baltimore, Dr. Benjamin Greenberg, to open this center. And in a lot of ways this was the right place at the right time. But based on my prior experience and even having a friend in college who had transverse myelitis, I was very excited to jump on board and join this team. And then everything from there has developed into a specialty. And I have had several people from pediatric hospitals, neuropsychologists, contact me about building these programs. I've seen them pop up all around the country, which is so fantastic and exciting. These patients need a home. They are, I think, often isolated in their experience because you just don't hear about that many people who have these conditions. So to have a place you can go, with experts who know what you're facing, and really understand it, I think, is incredible. Then as it relates to a desire to see the patients, I think neurology is the best place to go in a hospital. Reaching out to neurologist colleagues, or those who manage triage for neurology, to better understand what those patient referrals are like and identifying those. And hopefully partnering with the care provider in neurology to potentially create a referral stream to neuropsychology. And/or better yet, have that be the neuropsychologist who comes to the clinic and sees these patients and maybe starts to form a multidisciplinary clinic, which is what we have in Dallas. So I do think because of the complexity of the symptoms that are associated with these disorders, they really need a team approach. And I think that partnering with our colleagues in all different specialties allows us to do the most for our patients.

Ryan Van Patten 13:20

Yeah, that's great. We will link to several papers on these disorders. For people who are interested in reading more, do you have any particular recommendations for where a neuropsych trainee or professional might go to find more information? Books in neurology? Or specific papers to learn more about these conditions?

Lana Harder 13:39

Sure, I think a lot of our neuropsychology textbooks, even the board prep books, but many books that have been put out by our colleagues, including those on lifespan neuropsychology, have chapters frequently on multiple sclerosis. And often they'll have sections on some of these other conditions we've talked about. During our talk today, you all have mentioned a review paper that was led by one of my former research students, Dr. Alexander Tan, which I think just gives a great overview of pediatric myelinating disorders through a neuropsychology lens. I think that's just a great place to start if you're starting to see these patients. And there are lots of other papers referenced in that paper, which would be good places to go. But I'm excited and encouraged to see emerging literature in this area, and that we continue to learn more about what's going on and to identify these biomarkers associated with the conditions. To give us more understanding, but also precision in and how we work with these patients and get them what they need. So, those are some places I would start for learning more. And then of course, I'm happy to hear from anyone who has questions or wants to consult about a case or starting a program or anything along those lines.

Ryan Van Patten 14:58

Yeah, that's great. I can attest to how good that Tan paper is because I'm not a pediatric neuropsychologist, nor am I an expert in demyelinating conditions, but I found it really helpful.

Lana Harder 15:08

Oh, excellent, thank you.

John Bellone 15:10

We'll definitely link to that in our show notes for anyone who's interested. For all of these Neuropsych Bites, we'll have that paper linked up. I'm glad you mentioned the lifespan piece of it too in your comment just now. You're right, we might not realize that but, whenever we have a recurring childhood disorder, that child's going to become an adult and we're going to "pass the baton" from the child neuropsychologist to the adult neuropsychologist. And so we really all need to be aware of these different demyelinating conditions, especially the recurring ones that are likely to continue into adulthood.

Lana Harder 15:46

Yes, yes, I think it's important on both sides. For us in pediatrics to understand what this could look like in adulthood so that we can prepare our patients. And that our

adult colleagues can understand the implications of having a disorder like these in childhood or adolescence. So I agree.

Ryan Van Patten 16:06
Yeah. Well, this has been great. Lana, thank you. You've been such a good sport. We've hit you with so many different questions on different disorders in one conversation.

Lana Harder 16:17
I've enjoyed visiting with you all. Thanks so much for having me.

John Bellone 16:21
Thanks again.

Ryan Van Patten 16:22
Take care.

Transition Music 16:22

John Bellone 16:27
Well, that does it for our conversation with Lana. Be on the lookout for more Neuropsych Bites in the next few months. And, as always, thanks for listening and join us next time as we continue to navigate the brain and behavior.

Exit Music 16:41

John Bellone 17:05
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Ryan Van Patten 17:16

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