Research Updates: Tele-neuropsychology and Neuropsychological Outcomes Associated with MOGAD

You can view this presentation at: youtu.be/R0axSDRnKkE

[00:00:04] **Dr. Michael Levy:** I think the applause was for Dr. Hutaff-Lee but also to welcome back Dr. Harder and give a research update on tele-neuropsychology and neuropsychological outcomes associated with MOGAD.

[00:00:21] **Dr. Lana Harder:** Yes, thank you. It's great to be back. I enjoyed the presentation by Dr. Hutaff-Lee very much. Some great practical suggestions and good discussion. I will try to move quickly so we will have time for questions related to this and possibly the previous presentation. So, there'll be two parts to this. I will be reporting out on two different studies. I'll start with part one which involves essentially a virtual healthcare model for neuropsychology and to do that I want to make you aware about the neuropsychological evaluation. This data that I have is related to pediatrics. I will tell you that our adult colleagues are further ahead of us when it comes to testing virtually. So, if you are in need of adult neuropsychological evaluation feel like that field has expanded a bit faster than ours. We wanted to make you aware of the kind of step-by-step process of the evaluation. I touched on this a little bit before, but we typically have a clinical interview followed by a testing session that can last for many hours and feedback.

[00:01:39] At the average time, at last check in the published data to do a pediatric neuropsychological evaluation is 12 hours. Not all of that is sitting with a patient or the patient family. So, some of that is outside of that time but it is lengthy and also want to mention that the traditional models require close proximity with a patient over several hours and you can see this depicted in the photos I've included. So, their test materials that were kind of passing back and forth between the patient in front of us and the examiner, and we're doing lots of things at once to complete the standardized testing. The reason this is important, maybe you're already thinking ahead is that in the context of a pandemic, this was very challenging to maintain as a service because we wanted to keep people safe.

[00:02:41] I'm gonna talk about how things evolved. So, we were actually studying tele-neuropsychology and pediatrics prior to the pandemic. And very fortunately, we were thinking about this already. The inspiration for that came from working with patients with rare disorders. So, this came from our clinic for demyelinating disorders, that's actually where we recruited for most of our participants. Our goal as a team was to promote access to specialty care. You can see my map of the United States, and too bad it isn't a globe because we've had folks coming from outside of the U. S. as well, but we realized that people were traveling great distances to see us and we wanted to make this service more accessible. So, we needed tools for that to

evaluate pediatric patients from a distance. I think probably by now any one of us could state all of the many benefits of telehealth.

[00:03:41] Access was a primary factor for us, when we designed our study. We also know it reduces barriers and burden on the patient and families. We've even now seen some data that telehealth models improve show rates many times, and that we reduce those trips required for immunocompromised patients. We also thought about how this could facilitate data gathering for research. I want to say it now because I don't think it's anywhere else. This model doesn't work for all situations and for all patients and providers. So, I want to acknowledge that although it's a great thing and we're very excited about this work. It is not necessarily for all. And so, I think that's important to say. The problem that we had, especially in the pediatric world is that we had no published studies in this area and across adults and pediatrics, there were no home-based studies.

[00:04:42] So, I mentioned our adult colleagues were ahead of us, but they were doing testing in other clinic or community environments, often with an assistant on the other end. So, no one had really ventured into the home for this type of research. We also had no idea how caregivers and patients would feel about this, so no satisfaction data out there to work from. The goal of our study, again, this was pre-pandemic, we did publish it in 2020 but we wanted to examine the feasibility of testing children from the comfort of their own homes and to determine if results that we obtained in our traditional model in person and then remotely if those would be significantly different. We also wanted to ask parents and patients, "What did you think about this? Were you satisfied with this experience?" And so, I mentioned before we recruited from our demyelinating disorders clinic. We also recruited through a family camp for individuals with MS. So, for those who participated we had 290-minute neuropsychological assessment sessions.

[00:05:58] The same kids were tested in person and then tested at home. We did counterbalance the order of sessions so we realized there could be a practice effect and we're testing them and over a period of days or weeks kind of back-to-back. So, about half had the traditional face to face assessment first and about half had the remote session first. So, our average days between sessions were about 16 but it ranged from 1-50. Here's a snapshot of our sample. We had 58 participate in this study. We had a very broad age range by design. We wanted to capture younger kids all the way up to our young adults and so that was 6 to 20 years of age, over half were female, and then you can see the distribution and race and ethnicity. We had 16% who caregiver, primary language was Spanish and we worked with our bilingual providers to carry out this study and provide resources in Spanish and forms in Spanish and then a mileage from children's and this is where you can see the distance people are traveling to come to our clinic, it ranged from 3 to 2033 with an average of 150 miles.

[00:07:23] Just very briefly on our hypotheses and results, we hypothesized that results obtained in each setting would not be significantly different and essentially that's what we found. When we asked how our participants felt about this, so we had a question overall, I was satisfied with the video-based testing session. We had favorable responses largely meaning they strongly agreed or agreed with this statement. You can see though there is some variability in going to the point from before, this may not be for everyone. And so, I will tell you too, we had a participant who came from a small town and really liked coming to the big city because it meant he got to go to his favorite restaurant, so he told me he strongly disagreed that he would much rather be with us in person, which I think is very valid, I understood that. So, here you can see that in response to video-based cognitive testing was as acceptable to me as in person.

[00:08:35] You can see again, largely favorable responses, but again, some scatter there. And then if given a choice and expressing preference, we saw some interesting things. So, I would say most, did not have a preference at all, but if you were to have a preference, our parents tended at 21% to prefer in person compared to our participants are youth who prefer remote assessment at 26%, so that was a really interesting thing to

note. So, overall, this gave us some initial support for the use of a pediatric home-based tele-neuropsychology assessment model. And we think that this may provide lots of opportunities for our patients, clinicians and researchers, we do need additional research of course, and we have to really carefully consider limitations of the approach. And I won't go into it today, I'm sure you all are thankful, but there is a-- I could spend a lot of time on the ethical and practical challenges that we have to consider as licensed professionals as well. This was interesting because when COVID emerged in early 2020, we like everyone and needed to change our plan for how we would deliver services.

[00:10:03] So, while we were closed to in person visits and we were cancelling those appointments, we were also saying we were open to remote visits and it did take us some time to get on our video-based service which is what we used in this study. So, this was all a lot of interesting messaging that we had to put out to our partners, patients and families. In the meantime, while we worked to get up on our secure platform, we did have a phone-based services in place. I've been asked before, "Well, you did this study and you had the platform, why didn't you go for it clinically?" And that's because that platform was approved for use in research but was not the platform used by the hospital.

[00:10:52] Fortunately, children's was set up with a virtual health department and had been set up for a long time. We as providers were not on it yet so there was a little bit of a delay but we were still reaching our patients and families by phone. Now added to our list of benefits, we could allow for physical distancing. And so, this work again coming out of a clinic for rare diseases demyelinating disorders is what really gave us a nice strong starting point to get up to speed and get where we needed to go to provide care to our patients. And this posed a big challenge for neuropsychologist as a whole around the globe. We were a part of many discussions worldwide about this and how could we innovate be creative as one person put it, we were sort of building the plane while it was flying and that I think it really captures the essence of that situation.

[00:11:53] So, we as providers who provide standardized testing, it is ingrained in us that we cannot change how we administer a test. We can adapt things in certain ways, but if we change the standard process that can really threaten the validity of our results. So this is something that is core to our training and that is why we need the research study, that's why we need studies like the one that we did and since this time there have been many more papers that have come out about this topic and specifically in pediatrics, which has been wonderful to see. And this is just a depiction of how quickly our colleagues started to really adapt to and embrace telehealth models and that exist today. So again, going back to my previous talk for anyone who might be thinking about pursuing services and neuropsychology, please be aware that I think a lot of us now, I don't speak for our entire community, but a lot of us now are using what we refer to as a hybrid model where some of our services are in person, some are virtual and we have a whole variety of ways we did not have established before to reach our patients and family.

[00:13:13] So, I think it's really an exciting time and is creating a better access for many of the patients and families we serve. Okay, so now I want to talk about the second study which relates to what we are learning about MOG and specifically about neuropsychological outcomes associated with MOG. As you noticed in my previous presentation, that's really what was missing from our conversation. So, I have a feeling that for those attending this event, you all have been talking about this a great deal over the weekend. So, I'll mention a few points but we'll jump quickly into what we are learning about the neuropsychological aspects, and again, you're surrounded by many experts in this area. So what we know is MOG is a glycoprotein important in the myelination of nerves in the CNS. And the clinical presentation depends on the target of the attack. Again, probably something that's been discussed a whole lot over the last couple of days. Relatively little is known about neuropsychological outcomes associated with MOG. If I look at the different clinical presentations in this orange rectangle, I could definitely start to speak to what neuro psych functioning might look like in each of those based on some of the information we do have but because we didn't have the ability to test

for MOG positivity until recent years, we haven't been able to systematically study this. And so, I mentioned that we screen the kids that come to our clinic regardless of their clinical presentation and diagnosis. And what we've been able to do is a retrospective look at our kids who have tested positive for MOG. And so we have 38 in the study that I'm about to share with you. The age ranges is quite broad, 5 to 19 with a mean age of 11. 66% female and then we have a 60% white, 26% black or African American, 11% Asian, 3% other, and then 16% Hispanic or Latino.

[00:15:41] You can see here and this is what we read over and over in the literature and the most common presentation of MOG would be ADEM and that was true for our sample at 60%. So, you can see the breakdown there of the other groups represented. So, I want to mention in our screening battery, these are some of the domains that we assess. When we designed this battery, we did it with demyelinating disorders in mind and thought about what areas might be the most vulnerable in the setting of a demyelinating disorder. So, we have a whole variety of things. We look at a lot of speeded measures, a lot of fine-motor, attention, learning and memory, and some of our executive skills. I'll talk a little bit more about that. And we also are looking at mood behavior, educational factors, and quality of life. So, I'm gonna give you again high level results as a group.

[00:16:41] When you looked at the scores, they were mostly in the average range, but when you zoom in a little closer and look at the individual level, there is great variability. And so the way that we decided to report out on this data was to look at how often. So in a percentage, a given score for a given participant fell below expectation. What do I mean by falling below expectation? I won't give you a lecture on how we measure things, um those who might be familiar, this is our normal curve. What we decided to do is to set a cut off at what we call one standard deviation below the mean. So, if a mean is 100, a standard deviation is 15, that is a score of 85, which corresponds to the 16th%ile. Anyone who was at that point or lower would be designated or counted in a score that went below average, essentially. To describe this a little bit better, what we saw, first of all, we have no established cognitive profile or expected trajectory.

[00:17:49] Sometimes we can gather that when we're studying a different medical population for this, there's nothing that stood out as most people with this condition have this problem. It just wasn't like that. So, for our frequencies of we'll call it impairment greater than 30%, showed problems in the areas listed on that row. So, fine-motor coordination, verbal learning and memory, simple and complex attention. And then so to a lesser extent we saw some of these others, this was greater than 20% problems with visual-motor integration which is essentially copying shapes that are increasingly complex. And we look at this to anticipate how an individual might perform in handwriting or note-taking things along those lines. Executive skills is a very broad term to describe higher-order skills that allow us to pursue and reach our goals. So, one that stood out to me was working memories have mental scratch pad, holding onto information to do something with it without writing anything down. So, that was a bit of a struggle.

[00:19:05] And then speed, so processing speed for especially motor-based tasks was a problem. I really want to highlight this finding. Almost half reported receiving educational support services. So, for me, as a neuropsychologist that could be a signal that there are some difficulties in that learning environment. I want to also touch on and give a shout-out to one of my actually former fellow Dr. Aaron Kennedy, who looked at psychosocial functioning in our patients with MOG. And so, it's a subset of the group that I just described in terms of their cognitive skills. The breakdown is going to be very similar to what you just saw. Dr. Kennedy looked at differences in internalizing mood symptoms compared to the norm or what we would expect and found no differences but did see some difficulties when it came to quality of life. And so, we had the parent rate the child and then the child really rate themselves. And so you can see the parents are letting us know that school quality of life, social quality of life are problematic. And the patient essentially agrees with that

and would add to that emotional difficulties as well. This really stood out to us and our findings for those with MOG. And so, when thinking about supporting, you take these two studies together and think about how do we support youth with this diagnosis? I'll say again, there's no one size fits all. We want to tailor our recommendations and treatment plans and we want to engage with patients, families, educators and other partners. Having said that some examples of recommendations that may be appropriate based on what we've learned in this research, and Dr. Utah Flee touched on some of this in terms of formal education support services, remembering about half of our kids with MOG are reported receiving these.

[00:21:19] So some of those things I might put in a report depending on the results of testing, but if I know for instance someone has difficulty with let's say paying attention, we would say seating in the front of the classroom might be helpful to help them focus, a reduced distraction environment when taking exams. So that would look like maybe small group or being more one on one with a proctor. Extended time for testing can also be very helpful, especially of processing speed is an issue and that was one of the areas we saw, where that kind of hands-on processing speed was difficult. And then note-taking assistance. So, I mentioned that mental scratch pad, working memory difficulty also attention processing speed. So having a copy of the notes, so you don't have to use that extra cognitive bandwidth to both listen to a lecture and then take down the information and then you can more easily focus on what the teacher is saying. And then repetition and rehearsal of information, what I saw when I dug down into the results are that individuals in this cohort had more trouble remembering information when they heard it the first time compared to when they heard it the fifth time.

[00:22:45] So, we give it test where we read a list over five trials. And so, the difficulty frequency was much lower after they had heard it, so that tells us repetition may be beneficial. Again, individual assessment is important for figuring that out for individual people, but we have a clue that this may be helpful for our kids with MOG. External aids, so we don't have to rely on that working memory holding things in our brains, we can put things down in list or use other strategies for that and certainly interventions targeting mood and social functioning. We've talked a bit about some of that today. I wanted to make some concluding statements here and again, leave some time for questions. So, it looks like our outcomes vary widely and again, much like I said earlier, having MOG positivity may present risk for neuropsychological problems. Not maybe for everyone. So it's again case by case and so individuals with MOG may benefit from some of the recommendations we've talked about, maybe others that were not included, but that would depend on individual needs. We know that we need more research in order to evaluate neuropsychological functioning in this area specifically because it's newer. It's just an area where we are lacking and need to focus. Finally, I want to acknowledge many of my partners in research for both of the studies presented. And because I love these pictures, I'm gonna show them to you again if you are here for the previous talk. So, thank you. Happy to take questions.

[00:24:47] **Dr. Michael Levy:** Okay. Thanks, Lana. We do have questions for you online. Maybe we can start with those and Roberta will give them to you.

[00:24:55] **Audience Member 1:** Yep. Thank you so much Dr. Harder for both of these talks. There are a couple of questions from your first talk. Was there any statistical significance in data based on length of time since diagnosis, was the data consistent for newly research diagnosed and those with established diseases?

[00:25:14] **Dr. Lana Harder:** So, that's a great question. We did look at time since onset that wasn't that model by Dr. Hade and we did not find a statistically significant difference there. I think this continues to be an area for research. So, we really are in a position to answer if there weren't differences. I would just say in the model, it didn't show up as a significant predictor of cognitive status, meaning impaired or not impaired.

[00:25:43] **Audience Member 1:** Perfect. Thank you. Another question that came in with depression being a leading factor for cognitive decline where studies conducted with those taking antidepressant medication versus those not doing so.

[00:25:58] **Dr. Lana Harder:** Also, a fantastic question. We did not systematically evaluate that piece of the puzzle. We have that information and could look at that and I think it's a great idea for a future study.

[00:26:14] **Audience Member 1:** Thank you so much. A question from a MOGAD patient, what cognitive testing would you recommend as a baseline and for ongoing monitoring? I definitely feel like there had been deuteration and memory and general cognition but it has been passed off as motherhood, aging, stress, lifestyle.

[00:26:35] **Dr. Lana Harder:** So, I like the point you're raising about baseline testing. So, for, I would say the majority of people we see in clinic there's no true baseline that exists because they're coming to see us because of a diagnosis. But we do think of that early testing and just the testing we can do as soon as we can do it as the person's baseline. So, we may not know who they were or how they performed prior to their diagnosis but getting an assessment I think as soon as possible and also, I'll mention making sure to be 30 days off of steroids is really key because we don't want to pick up on problems that are associated with steroids and then interpret that as being related to a medical condition. So, I would say a comprehensive neuropsychological evaluation looking at some areas mentioned, attention memory, all of those things.

[00:27:43] Also, a neuropsychologist is going to take down information that would help them anticipate maybe what things were like before the onset of the medical problems. So, in that sense, you can get a qualitative baseline. And then the great thing about having testing at any point is that over time you can compared to yourself so you can look at testing, let's say we do it today, 2022 then in two years we do it again, we'll be able to speak to areas of improvement. Maybe you've made some changes and had some intervention like we've talked about today, maybe there have been more medical events and we need to track changes associated with that. So, it really gives a nice way to again, do that tailored specific tracking and then the benefit of that is updating treatment recommendations and the treatment plan. Because we know from serial testing and I've worked with kids now, 10 plus years with these conditions and watch them go through lots of stages of life and development, we know that based on what the environmental demands are, the life demands, the treatment recommendations are going to change. I know it was kind of a long answer, but I hope that was helpful.

[00:29:09] **Audience Member 1:** Yes. Thank you so much, Dr. Harder. And one more question online and then we'll go to the audience here, is there any evidence on the role of functional neurological disorder on top of a diagnosis of TM as a predictor of cognitive status? And do these symptoms get better or worse with time?

[00:29:25] **Dr. Lana Harder:** That is a great question. I will take this opportunity to give a shout-out to my colleague Dr. Allison Wilkinson Smith who's actually co-directs and established a clinic in F&D in Dallas and has also been involved in the clinic we have for demyelinating disorders focusing on autoimmune encephalitis and other conditions. So, I don't have an answer to that question. I don't know about any information that is available. But I think that that is a great question and I'm gonna share that with her when I get to the office tomorrow to see what she says. If I'm not, mistaken, I believe Dr. Wilkinson Smith has been a guest on SRNA's podcast before. Maybe we need to bring her back to talk about this.

[00:30:14] **Audience Member 1:** Thank you so much, Dr. Harder. We have some questions in the audience. And then another question came in online but let's hand it over to the audience first.

[00:30:24] **Audience Member 2:** Hello Dr. Harder, is there any comparisons of AFM to TM and MOG?

[00:30:32] **Dr. Lana Harder:** You were mentioning the topic that is on my list of priorities for research. We have the data. We have not separated it out for comparison and I know our numbers have slowly been growing and I think we're getting to a place where we can make those comparisons, but we absolutely need to do it similar to the evolution where we've learned about MOG, I feel like AFM had an evolution where we could start to identify that apart from maybe broader term of TM. So, thank you for your question.

[00:31:08] **Audience Member 2:** I was gonna add one other thing. Is there any long-term research for these rare neurological diseases that for TM and MOG and that is there some ongoing research to track people over time?

[00:31:23] **Dr. Lana Harder:** So, that is an effort that we have underway in Dallas. And I'm sure my colleagues and other clinical settings have that as well. So, we do serial testing over years. We have looked at longitudinal data for MS specifically, not the conditions we're here talking about today. But that is again an area for future exploration and we are set up to do that and we have the information. And I think that's really in the case of MOG, we're just now getting to describe what we're seeing but doing that over time is really critically important. And I don't know if others at other centers are doing this as well but I would think they might be.

[00:32:14] **Audience Member 1:** Questions are coming in. So, I know we're a little bit over time but I'm gonna ask them until you stop me, Dr. Harder, and Dr. Michael Levy. How reliable would a neuro-psych evaluation from eight years prior be? My daughter was tested in second grade and was diagnosed with ADHD et cetera. But it wasn't until June that she was diagnosed with MOGAD, with the results from 2nd grade be relevant now.

[00:32:40] **Dr. Lana Harder:** That's a great question. So, there's an example of, you have a true baseline that is sounds like before the onset of the medical condition which is fantastic to have, it would be highly relevant. At the same time, it sounds like it might be time to update that evaluation. And I would say that kind of with or without the medical condition that just it's good to update that as demands change and development. So, the world is very different for you as a second grader compared to as you're getting into middle school and high school. I would absolutely recommend bringing that report if you should revisit and do a re-evaluation definitely relevant.

[00:33:28] **Audience Member 1:** Thank you, Dr. Harder. And we have a similar question here about a MOG-positive daughter that had her first neuropsychology testing at the age of 17 months while still recovering from an acute attack. And she's now three. And the person is asking whether it would be beneficial to have another test done or is it better to wait until she's about to attend grade school?

[00:33:51] **Dr. Lana Harder:** Okay, let me make sure I have this correct. So, first testing at age 17?

[00:34:01] **Audience Member 1:** 17 months while still recovering from an acute attack and she's now three years old. Would it be beneficial to have another test done now or is it better to wait until she's about to attend grade school?

[00:34:14] **Dr. Lana Harder:** So, I think it would depend on how she's spending her days now. And if there could be implications for providing support services if we're in pre-school or depending on or therapies, if things are getting in the way of therapy, if that's something that's happening. Otherwise, I think you could wait until closer to school, beginning the testing at 17 months compared to the toddler age or kind of pre-kindergarten is gonna look very different but still that early assessment information is meaningful. It will just be harder

to do a direct comparison because those tests are so different. More of the developmental assessments when we're very young compared to all of the things we can test as a child ages.

[00:35:04] **Audience Member 1:** Thank you. Final question. I think for MOG patients, can mood be affected by the disorder itself, like its effects on the brain or the mood effects usually caused by the patient's reaction to their physical symptoms and social limitations?

[00:35:19] **Dr. Lana Harder:** Fabulous question and we talked about this a lot and I think it came up first for me working with MS. So, I'll kind of extrapolate knowing that these are very different conditions. But there is discussion about the disease itself, MS having a biological impact on mood. So, we know that that can happen. That's the thing that can happen in the setting of inflammation impacting the brain. I don't think we have the definitive information about whether or not that's happening in MOG. It's still on our radar, we're still looking for that.

[00:35:58] I think in this study by Dr. Kennedy, she did not find significant differences from the norm, from what we would expect when it came to mood. So, I think that question is still really not fully answered. I don't think we have a lot of evidence. I think it's possible and for anything that we talk about like this it's really impossible to tease that apart. So, we have to consider that yes, there is a medical condition that is at play and we also know that there is the kind of psychological response to that to the social environment. So, we know it's probably a combination of things but I don't know that we have successfully answered that question yet again with MOG being so much newer relative to MS.

[00:36:56] **Dr. Michael Levy:** Wonderful. Thank you, Dr. Harder. Much appreciated. Thanks for taking all those questions. This applause is for you. All right, we're gonna take a break now. If you haven't visited the rooms next door and Catalina and Caramel, please take the opportunity to do so. We'll reconvene here at 11 AM and you'll hear Dr. Cabahug and Dr. Hanebrink on, well, Dr. Cabahug is talking about bowel bladder and sex dysfunction, and Dr. Hanebrink on adaptive tools and technology for quality-of-life improvement. Thank you, everyone.