Research updates on management of neuropathic pain and spasticity

You can view this presentation at: youtu.be/ccAN8YvKHuU

[00:00:04] **Dr. Benjamin Greenberg:** This morning, you heard about the state of affairs of therapies from Anastasia. And then Mike talked about the research in the area. Now you've heard about the state of affairs for spasticity management from Dan. And we're gonna ask Mike to come back and talk about the research in terms of management of these symptoms. So, it's all yours. I'm sorry, Mikey.

[00:00:28] **Dr. Michael Levy:** All right. So, you know, we don't coordinate talks before we get on stage. So, you may have heard a lot of this from Dr. Narayan already and from Dr. Becker. And so, I'm not going to repeat all of these things. But you'll see that there are some common themes here. I'll just kind of stick to the newest greatest things that we're doing. So, everybody here who has neuropathic pain has... knows what this feels like. But for those who don't have it, the description is a burning electrical type of pain. It feels like a sunburn, as some people have described it, and it's incredibly common. In aquaporin-4 NMO. We had a patient day one time and we surveyed the group and 80% of people had neuropathic pain from their NMO. Most of the neuropathic pain comes from specific attacks in the spinal cord and sometimes in the case of MOG around the optic nerve, so oftentimes patients if they don't have neuropathic pain at first, they may have another attack and then get neuropathic pain after that. Some people with NMO or transverse myelitis may get it on their first event and you can usually trace it back to an MRI Lesion. As you can see here.

[00:01:53] Usually, the pain will be worse than that level or below and should be a lot less above it, if there is any at all. So, MRI can help us localize where the pain is. And this becomes important because I'm gonna show you the study from the scrambler device that tries to take advantage of spinal cord mechanisms to suppress pain. And if you know where the lesion is on the MRI or even just looking at the MRI report, you might be able to use this device and place it correctly. So, let me show you how that works. The device we used is called Scrambler. And it's not gonna be the one that you'll use. This machine costs $250,000 for an academic center. And I heard that if you're not an academic center, just a private practice, it costs $1 million. So, this is not gonna be the machine that you'll probably see unless you have millions of dollars, in which case please donate it to the SRNA and we'll do great research with it.

[00:02:57] So, this device, what it does is you can see where it where it plugs in; it emits an electrical signal, and the signal travels to those little electrodes that are placed on the body. And those electrical signals get taken up by nerves outside of the spinal cord and then get taken into the spinal cord. The idea is very similar

to bumping your toe or hitting your elbow and then you rub on it. You know, you bump yourself and then you start rubbing that area. You're not rubbing only the part that hurts your rubbing all around it. Because what you're doing is you're stimulating areas around what hurts. Because it turns out when you do that, the spinal cord suppresses other parts around it. It's the way that it was explained to me is imagine you have a spider crawling on your arm and you want to know exactly where that spider is so that you can whack it and kill it.

[00:03:54] So, part of that spinal cord processes is not just knowing exactly where you're feeling the spider, but then you suppress everything around it so that your localization gets really good. You could take advantage of that suppression mechanism just by rubbing different parts. You're suppressing other parts around it. And that is essentially how this machine works. You're just delivering a current and electrical current that's the same as rubbing around the part that hurts. And these devices can... this one's plugged in. It can stay on all day, but there are ones that you can buy on Amazon that are battery-powered and you can walk around your home with them and it's like getting somebody rubbing that area for you and making it feel better for as long as you want to keep it on. There's really no harm in in in trying it.

[00:04:47] So, we took this approach in a very scientifically rigorous way to use a sham control, meaning it feels like an electrical signal that's actually a vibration, and comparing it to the actual signal. So, we did a trial with 10 people on the device and 10 people with Sham. And here are the results. These box plots show your pain score before, immediately after, and then a bit after the treatments. What you could see on the left side in panel A is if you're getting the treatment, your score was about a five, average, before you started. And then it dropped to less than two. And then, after about 30 days or so, the scores come back up. It doesn't last forever. This device seems to last. This is a 10-day therapy and then it lasts about another 20 days after that.

[00:05:48] The sham, again, patients didn't know what they were on. We did it. We took surveys to see if, do you know if you were on the sham or if you want the real device. Everyone was wrong. People who were on the device thought they were getting sham people on... So, it was a really good study in that regard. And the sham group had a little bit of a response there. You could see that there was always a placebo effect. Everybody thought that they were getting the treatment, but then it wasn't sustained. It wasn't even very good. This was the first real proof in an NMO patient in a group of NMO patients that this type of approach worked. But the $250,000 price tag just made it impossible to offer it to people. So, we went for a smaller device. This is a picture from Amazon. You can buy one. This is still kind of on the expensive side. They have many many cheaper ones. They have some that are like 37 bucks and they all do the same thing. They all apply an electrical current.

[00:06:45] Some will say oh, we do this type of current, and some will say we do that type of current, and I don't really know which one's best. Yeah, if there is a best, because they all rely on that same spinal cord suppression mechanism. But this company was particularly interested in our disease. So, we partnered with them, it's a company called neural metrics, and they make the quell device and our trial design uses that little iPhone-looking thing, and then the H-shaped electrode, and I tried it on myself. It feels kind of funny. I put it on my neck and the way it works is you're supposed to turn it up until it hurts and then you turn it back down so you don't feel it, and that's how you know where your range is. And I put it on and after about 10 minutes I just didn't like it. I just ripped it off. So, I was not a big fan of this, but my patients are, and I appreciate that. And we sent it out to 46 participants, 23 who got treatment and 23 who got a program that does not work. It turns on for a minute and then it turns off and again, same type of thing where we're surveying to see if people know whether they're on sham or real device and we don't have the data for you. But I have the next best thing, which is Anastasia over here is on her computer, and I think she's running stats for it.

[00:08:08] So, I don't know that she'll have any data ready for us by the end of this conference, but we're working really hard on it. We really want to get to a point where we could tell people in clinic that this is a device that

could work for pain. And this is how well it works. And we really want to give people good scientific advice to manage pain with a treatment that does not involve any surgeries and no pills. And the worst side effect is that some people have an allergic reaction to that to the gel on the electrode. That's really the worst part about it. So, stay tuned for those results. You've heard about spasticity Dan Becker mentioned things like back life in pumps and that takes the thrust out of a lot of my slides coming up. But that's good because lunch is next and you don't want to hear me say the same things that Daniel just said. So, I'm gonna skip through those parts to get to this slide which has been brought up: marijuana and cannabis products.

[00:09:14] But I want to tell you about a study that we're doing with cannabis extract called the Nabiximols, which is a mixture of different extracts from the cannabis leaf. This is nasal spray product that is being developed in multiple sclerosis for spasticity. And we're interested really in NMO. First. But then I think there are questions about what can we use it in MOG. Can we use it in transverse myelitis? Maybe. But to get the science started, do you really want to pick a homogeneous patient population... So, you can understand the mechanism of action and then apply it more broadly. So, it's being developed in MS as we speak. We're put in a proposal for NMO and it's a nasal spray and you could use it up to 12 times a day and you just keep track of how many spasms you have. And just, empirically, when I talk to patients and they tell me -- maybe it's just that in Boston there are a lot of people on marijuana, it's legal there. But I would say that a lot of my patients have just told me that when they use these products for recreation or medicinal quality products that it helps their spasms.

[00:10:31] So, it'd be great if we could get it down to a science; figure out exactly which compounds are active, how much you need, how much you don't need, what the adverse effects are, and then be able to offer that to patients as well. So, that is another study being done by Anastasia; and the last part about this research enterprise in pain and quality of life is another great experiment, which is Anastasia. She is a fellow that is doing, that is devoted to quality of life and that is different from most of us. A lot of us started off in the science of transverse myelitis with Doug Kerr trying to figure out in mice and rats how the disease works and decoding the immunology. But, you know, I sometimes I talk to them blue in the face about all these immunological drugs, and patients just want to talk about how to feel better. And that's something that Anastasia is focusing on. So, if she's here next year, then the experiment is working. It means that her career is sustained by this approach. It's a little bit different and we're really trying to be supportive. So, with that, I think you know, I'll end there. I know it's not as much research as other areas, but this is an area of quality-of-life research that I think will expand over time. Lunchtime or questions.

[00:12:09] **Audience Member 1:** Yeah. I go to an acupuncturist who when he sticks the needles in, he sticks right because he's trying to recreate the path, he sticks them in up high and down low and runs a probe from one to the other to try and stimulate I guess some sort of feeling. Do you have any thoughts on that?

[00:12:35] **Dr. Michael Levy:** Acupuncture is essentially the same thing. It's stimulating the nerve, whether you do it through electrical signals or through a pain signal, it's still getting a signal into the spinal cord. And the hope is that in that distribution around it, it'll suppress the signal, the pain signals. And there are a lot of studies on acupuncture and multiple sclerosis, and they work. If you do the acupuncture wrong, then it doesn't work. So, acupuncture is a valid therapy, but it really does depend on the same mechanism and I think it's a lot more expensive than these trance cutaneous electric nerve stimulator devices. But you know what whatever works for you, you need to try it, and I always, when patients ask me about acupuncture, I say, well, don't mortgage your house over it. But if it works great, and if it works but you want to be able to do it at home without going out, then consider the Transcutaneous Electrical Nerve Stimulator.

[00:13:32] **Audience Member 2:** Is there any research or guidelines on electrode placement when using a TENS unit?

[00:13:40] **Dr. Michael Levy:** There is a lot of research into that. There are some who advocate for putting most of the signals on the lesion in the spinal cord versus above or below it. I would say that the data is mixed. A lot of people who have lesions at certain levels, have pain at other levels, and then you're not so sure where to put the electrode. In the scrambler study. We went by MRI and that seemed to really work. But it's not like we did the opposite study where if your MRI lesion is dissociated, we go with where the pain is. So, it really turned out to be a trial-and-error approach. We also have a lot of patients who have pain at different areas, right arm, and left leg. And then where do you put the electrode? Some of these transcranial electric nerve stimulators come with pairs of electrodes up to five pairs. So, you could put a pair on one leg, and a pair on one arm, and a pair on the legs, on the neck, or wherever. And then you just try different approaches until you find something that works. Yeah. Good question.

[00:14:48] **Audience Member 3:** Some questions that came in online, Dr. Levy. A physical therapist recommended infrared light therapy for my spastic leg. Is there any research on if this is beneficial?

[00:15:01] **Dr. Michael Levy:** Infrared therapy, I can stretch and think about how that might work. Maybe infrared light in general is a longer wavelength and can penetrate the skin. Maybe it's heating or stimulating the nerve in a way that's very similar to acupuncture, and maybe it would work. I think that that's something that is one of those things where if it doesn't hurt and you're not mortgaging your house, then it might be something to look into.

[00:15:33] Dr. Daniel Becker: Mike, there's something-- there's no data on spasticity, but the data is for neuropathic pain. So, experimental stuff. Nothing and nothing definitive. But I think as far as I understand, it's still a pretty expensive treatment. I mean, I know there was a local person in our area that had that device charging 150 bucks or so per session. So, it's yeah, there's not much data out there, actually none that I'm aware of for spasticity.

[00:16:03] **Audience Member 3:** Maybe one more. Is there a difference between a Scrambler and a Calmare machine? They look identical, but I've been told by the sales representatives that Calmare cost $80,000.

[00:16:13] **Dr. Michael Levy:** They are different devices and I don't know the whole history of it. I think they kind of-- one company spun off the other. I think Calmare owns the licensing rights to the scrambling machine. I don't remember exactly who owns what, though. And they are very, very similar. And then, some of these companies that make different TENS units, they insist that their electrical protocol is better. So, the idea behind Scrambler is that it's a scrambled mix of different electrical stimulations. Some of the devices on Amazon, they'll say, you know, if you want these four electrical signals, it's $37, and if you want 10 electrical signals, it's only $60 but there's no real data supporting any of these specific signals. It's really just what works for you. So, you just put it on different parameters until you find an electrical pattern that works for you.