Excerpts from Real Talk on MS Fatigue: What Works, What's Next
Episode 406: From the 2025 Consortium of MS Centers Annual Meeting:
Part Two with Dr. John DeLuca, Dr. Brian Sandroff

TRANSCRIPT

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JOHN STRUM: 00:00

[music] I'm John Strum, and this is Real Talk MS.

It's June 10th, and we have a lot to talk about. This week, we're diving into part two of our coverage of the Consortium of MS Center's annual meeting. better known as CMSC.

The first person I spoke with at CMSC was Dr. John DeLuca.

Dr. John DeLuca is a senior vice president for research and training and co-director of the Center for Multiple Sclerosis Research at Kessler Foundation, as well as a professor in the physical medicine and rehabilitation and neurology departments at Rutgers New Jersey Medical School. And Dr. DeLuca's presentation at this year's CMSC annual meeting is entitled, What Does the Brain Tell Us About Fatigue? And I'll be asking you that in a moment. But first, I'm hoping you'll explain how MS related fatigue is measured.

JOHN DELUCA: 01:56

You know, it's really an important question because for over 100 years, we've been asking that question and we don't have a good answer. We do not have a good answer of how we measure fatigue. And so we don't have a good way of defining what it is. Therefore, we can't measure it. Therefore, how do we treat it? So it's a real problem. What we typically do is we use these. These instruments that presumably measure fatigue, but they're also contaminated by so many other factors, such as sleep and deconditioning and such, that we really don't know what we're measuring. So it's a real problem, unfortunately.

STRUM: 02:34

So hard to treat? And I think you may have provided some of the answers just now.

DELUCA: 02:41

Yeah, it's been really hard because, again, we have a hard time defining it, therefore we can't measure it. 1921, Musio asked, how do we define, measure an undefined entity? And we're still there today. And it's really a problem. So there may be things that we can do, but they're contaminated by other factors if you use these instruments. Therefore, we're not really measuring it. Even if people feel better. The instruments don't tell us that they are.

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STRUM: 03:08 So now I'll go ahead and ask the question. What does the brain tell us about fatigue?

DELUCA: 03:13 You know, it's really interesting. So we look at what's called state fatigue. That is fatigue in the moment. How do you feel right now on a scale of zero to 100 as opposed to trait fatigue are these instruments that are contaminated by these questions. We put people in the MRI scanner and we get... cognitively fatigue them. And we measure their state fatigue before and after each one. And what we find is that state fatigue correlates with changes in the brain, functional changes in the brain. And that state fatigue does not correlate with trait fatigue, which does not correlate with changes in the brain. So what we know is that we have this brain network and the hub of this brain network is the basal ganglia. And what's interesting is The basal ganglia is also the hub for the reward network in the brain. And so our approach is if you can reward people, does reward actually reduce fatigue? And the data on that is actually yes. So the brain is telling us that we understand how this network in the brain works. We understand this hub of the basal ganglia and its relationship between fatigue and on the other side, let's say reward. We can actually get to. understanding how to measure it and then how to treat it.

STRUM: 04:30 And it sounds like the nature of that treatment is non-pharmacological.

DELUCA: 04:35 Well, that's actually what I think what happens right now. The best treatment for fatigue at this point is cognitive behavioral therapy. I think that ultimately there will be pharmacological treatment, but it's got to be more specific than what it is today. We have to understand the relationship between pharmacological therapy and reward as well as just fatigue. And so I think we're going to really move forward to understanding that relationship in that the brain is telling us what we need to look at.

STRUM: 05:05 And from there, once the educational modules were developed and uploaded to kflearn, we needed to go through pilot testing, because you want to make sure if you're developing educational materials that, again, it makes sense to the target audience, right? So we pilot-tested with two different groups. The first one were 15 personal care assistants with little experience assisting clients with spinal cord injury. And that's important because you want to see, "There was the learning curve," right? So, "What did they learn over time in terms of going through all the modules that we developed? And did it make sense to PCAs who are new to SCI?" But then we also had a second group. We had a small group of PCAs who actually had experience working with

clients with SCI to also get their input about the content as well. And that was really important too because we wanted to make sure that, again, we weren't missing anything and that the content was consistent with some of their experiences as well.

DELUCA: 05:13 Yes, actually there is. There is data on fatigue. And interestingly, when you think about the data that I know from our center, the other hub in the fatigue network is the thalamus. And what's happening is the improvements from exercise are at the level of the thalamus. So that thalamus is also part of the fatigue network. So it all fits into a nice story. We just need to understand that relationship better. But if exercise is not rewarding, people won't do it.

STRUM: 05:45 Exactly right. Anyone who has taken out a gym membership understands that principle, don't they? Exactly.

DELUCA: 05:50 So what we try to do is we try to ask patients, what is rewarding for you that you haven't been able to do for a long time? So let's say you haven't, I love to read, but I don't read anymore because I can't remember it. Well, we get them to join a book club or we get them to do something that's rewarding to them. And some people it's exercise, some people it's something else. And that seems to be something that really helps.

STRUM: 06:15 There are more than a few people dealing with MS -related fatigue who are listening to this conversation. Speaking generally, what's the best plan for mitigating that fatigue for someone with MS to pursue right now?

DELUCA: 06:28 Yeah, I think it's to be honest with yourself and say, what is it that I can do that I haven't been able to do or I haven't wanted to do anymore? Be honest. Go out and try something that you'd love to do and stick with it. Start slow. Start slow. Be used to exercise. Start gardening. You know, start slow and try to build it up. Be honest with yourself and work with a professional, a neurologist, psychologist, occupational therapist to work on it. It's not going to happen overnight. But the brain is telling us that looking at what's happy, what makes us happy, what makes us really be motivated. can actually reduce fatigue.

STRUM: 07:11 And that is perhaps the single best prescription I have ever heard.

DELUCA: 07:17 Well, thank you. And I think it can help even those of us who don't have MS. For sure.

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STRUM: 07:21 Sure. Dr. John DeLuca, I want to thank you for all you have done and continue to do to really improve the lives of people who are living with MS. And thanks so much for talking with me today.

DELUCA: 07:31 Oh, thank you. It's been my pleasure, really.

STRUM: 07:34 Dr. Brian Sandroff is the Assistant Director of the Center for Neuropsychology and Neuroscience Research at Kessler Foundation and the Director of the Center's Exercise Neurorehabilitation Research Laboratory. I had an opportunity to talk with Dr. Sandroff and ask him some of the questions I've received from some of you about exercise and MS. In a moment, we'll hear my conversation with Dr. Brian Sandroff.

Now, the title of your presentation at this year's CMSC meeting is Exercise as an Approach for Mitigating Network Collapse in MS. And I want to ask you about that in a moment. First, I want to remind you of one of your past studies. A couple of years ago, you led a study that showed a robotic exoskeleton was effective in facilitating exercise rehabilitation among people living with MS. who had already experienced significant disability. I remember sharing the results of that study with my listeners and talking about how technology was really driving progress in rehabilitation. How are you seeing MS rehabilitation evolving? Can you compare MS rehabilitation today with what it was like 10 or 15 years ago? That actually was not a study that I led.

SANDROFF: 08:52 That actually was not a study that I led. That was from my colleague, Guy Androwis. I was helping out with that study. It's more of kind of a support system. And Guy's a great guy doing some really important work on robotics. But to answer your question directly, over the last 10 to 15 years, Things have gotten so much more closely aligned with the exercise as medicine movement in the general population where we don't just tell our patients to go out and exercise. That doesn't mean much anymore. Now everything is starting to move towards... precise prescriptions, exactly what to do, when to do it, how to do it. There are guidelines and things are becoming more and more home -based now since, especially since the COVID pandemic, where people have learned to value their time a lot differently now than they used to, where now people want things on their own, things that they can do themselves in a comfortable environment because driving 30 minutes to and from a place costs a lot in terms of time and effort and your ability to do things with your family and your job. So it's become a lot more tele -rehabilitation centric in recent years compared with previous years. So in terms of future directions,

we're really moving towards trying to deliver things to where people are as opposed to having them come to us.

STRUM: 10:16 Well, I think that's just a fantastic idea. And it's interesting how rehabilitation is moving. more toward precision rehab, just as the rest of medicine is moving toward precision medicine.

SANDROFF: 10:32 Yeah. All of a sudden, now you're starting to see studies in rehabilitation and MS on response heterogeneity. which looks at who might benefit the most from rehabilitation, from different programs, and what characteristics people have at baseline that may predict improving more, or maybe people who don't respond to interventions that maybe might need a different intervention. We're really trying to figure out how to help all people.

STRUM: 10:55 You know, I'm going to ask you a couple questions that my listeners have asked me to ask.

SANDROFF: 11:00 Wow, okay.

STRUM: 11:01 Does the effect of exercise training appear on an MRI scan?

SANDROFF: 11:08 And that is, it depends on what MRI scan. So if we're talking about a clinical MRI scan, not yet. And I'm going to say yet with kind of a wink in my eye because we believe that so far what's been done in the literature has been short -term exercise. And we don't necessarily think that short -term exercise is long enough to show major changes on brain volumes. As if you think about the disease -modifying therapy literature, the drugs that show effects on... brain volumes take one to two years to do so. So would 12 weeks of exercise necessarily be expected to change brain volumes? I don't think so. But I do think that exercise changes brain connectivity and brain activation in the short term, as there have been a number of studies published in the literature over the last couple of years that have shown improvements in functional brain outcomes. That is how the brain gets activated in response to seeing a stimulus or how it connects better at rest.

STRUM: 12:08 Depression is an MS symptom that affects about half the people who are living with MS. And when many people think about depression, they tend to think of antidepressants. Question one of my listeners has, can aerobic exercise have an impact on MS -related depression? So there are a couple of studies out there that do support an effect.

SANDROFF: 12:26 So there are a couple of studies out there that do support an effect. There are three meta -analyses, which are studies that look at the overall effects of exercise on an outcome in an entire field. And there

are three of them for exercise effects on depression and MS. And all three show that exercise overall is associated with moderate -sized reductions in depressive symptoms in people with MS. Now, that doesn't guarantee that aerobic exercise will reduce depressive symptoms in one individual person. But overall, there are significant effects in MS.

STRUM: 13:00 Cognitive dysfunction is another invisible symptom of MS. Can exercise improve cognitive issues for people who are living with MS?

SANDROFF: 13:09 So that one is probably the closest to my heart is that's where my research is most closely interested in. Overall, the evidence is a bit mixed, where some studies report cognitive improvements, others don't. But what we've been doing over the past decade plus is trying to figure out exactly what type of exercise, how intense it should be. what kind of cognitive domains should improve, what brain networks should improve in order to improve cognition. And we think we stumbled onto something important where we believe that aerobic walking exercise represents an intervention to improve cognition in people with MS. And this is based on a series of eight or nine studies that we've been conducting since 2011. And we just finished a study that recruited people with MS -related cognitive processing speed impairment. And we showed that aerobic exercise done, aerobic walking exercise done at home for four months resulted in clinically meaningful improvements in cognitive processing speed, which is the most common cognitive problem in MS. So we think we're on to something big and we're excited for what the future is going to bring here.

STRUM: 14:21 Well, I think that is really encouraging news. It's one of the symptoms that impacts people in a profound way, where in some ways they don't feel like they're themselves anymore even. And to find out that there could be a non -pharmacologic, you don't need another pill or injection or infusion, but can actually do something healthy for yourself that's going to have an impact on that invisible symptom that people can't seem to get treated. That's remarkable.

SANDROFF: 14:51 Yeah, that is one of the most rewarding and exciting parts of our research agenda is that cognitive problems in MS just lead to so many other problems like problems making relationships, social isolation, having trouble driving, unemployment, among other things. And to be able to self -manage that and potentially, you know, lessen the blow of cognitive impairment. With walking more, with exercising, something that we have guidelines for, that we have programs that we can provide support for people who are interested in walking. That would really be our dream is to put ourselves out of business.

STRUM: 15:30 That's great, really. So let's get to your presentation at this year's CMSC meeting. How is exercise a viable approach for mitigating network collapse in MS?

SANDROFF: 15:45 I'm pausing for a minute because I'm trying to distill a 40 -minute presentation down into a single question, and I love the question. There is a lot of momentum supporting exercises and approach to do this because the network collapse is essentially the hypothesis that functional problems and declines in MS are a product of the brain rewiring itself in the wrong way, causing brain atrophy or loss of volume in certain regions. And we think that exercise may provide the reverse of that where it may be able to strengthen connections within the brain. It may be able to help preserve brain volume if the correct exercise program is administered for a long period of time. And we have some preliminary data to support that such that we. think that there's a lot of smoke going on right now and we're looking for the fire. So we're in the process of applying for some large grants to test that very question of whether or not exercise can mitigate this network collapse as a major consequence of the disease.

STRUM: 16:48 Again, remarkable. You know, a year ago at this very meeting, you and I talked a little bit about a framework that you proposed for study design that would... make them a bit more uniform, a bit more usable, and increase the credibility of the outcome of those results. I'm just curious, are people getting that memo?

SANDROFF: 17:09 So, so far in the last year, I don't think there's been quite enough time for that to marinate, but I've definitely been reading studies that have given me kind of that wow moment. Like, this is a really well -designed paper. These results are great. Wow, this is so promising and exciting. As an example, the cognitive rehabilitation literature is getting stronger and stronger and stronger from a methodological point of view to where five years ago the field was mixed. Didn't really know if cognitive rehabilitation worked. But looking at the evidence this morning, I gave a presentation on kind of an update of that. There is a lot of converging evidence supporting the benefits of cognitive rehabilitation now to where studies are designed well. They're reporting improvements in the hypothesized direction. The papers themselves are

reporting everything. There's more transparency. There's imaging data to support the cognitive data. So really exciting stuff.

STRUM: 18:03 You know, every time I talk to you. I learn new things. Dr. Brian Sandroff, I want to thank you for everything you do to really improve the lives of people who are living with MS. Thanks so much for taking a few minutes to talk with me. I'm John Strum. Thanks for listening. Stay safe and make healthy choices.

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