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Disparities in DMT Access: Women with MS Are Less Likely to Receive Treatment

Dr. Wilner:
Welcome to *NeuroFrontiers* on ReachMD. I'm your host, Dr. Andrew Wilner. Here with me today is Dr. Victoria Leavitt to discuss her research on the effect of disease-modifying therapies for MS on neurocognitive function. Dr. Leavitt is the Director of the Translational Cognitive Neuroscience Laboratory as well as an Assistant Professor of Neuropsychology at Columbia University. She recently presented this research at the joint ECTRIMS-ACTRIMS meeting in Milan, Italy, and the results will soon be published in the journal *Multiple Sclerosis and Related Disorders*. Dr. Leavitt, it's great to have you with us today.

Dr. Leavitt:
Thank you so much. It's great to be here.

Dr. Wilner:
So let's start with some background, Dr. Leavitt. Tell us about your study and its main objectives.

Dr. Leavitt:
So I'll just start by telling you my main objective and the work of my lab. What we study is cognition, and we're looking for optimizing cognition in everyone, but particularly in neurologic populations. And as a theoretical framework, we look to theories of cognitive reserve, brain reserve and brain resilience, and companion theories, all of which basically say there are individual differences. Some of us are better able to withstand age and disease-related insults and injuries to the brain better than others to maintain our cognition, and this is very interesting to me because we don't know what those things are. We don't know what allows some people to be more successful cognitive agers than others.

So we look at this in MS because this is kind of a population that avails us of a special opportunity in that they are much younger than the aging and elderly populations that we tend to think of when we hear the words cognitive aging and younger than people with Alzheimer's disease where we arguably do the most investigation of age-related changes on cognition. So in MS, the average age of onset is 32. And looking at these people to see who does better in terms of the cognitive symptoms that come about is a very interesting window into understanding brain resilience and cognitive reserve. Right now, this particular line of research starts from looking at DMTs, disease-modifying therapies, which are our best first-line treatments and are now—because of the level of evidence we have to support their efficacy—being recommended for everyone with MS. Consideration of DMT therapy is encouraged. It's part of the clinical guidelines. And so my question was what's the effect of being on a DMT on cognition? That was the starting point for this research.

Dr. Wilner:
Okay. So you have a relatively young population with what is often a neuro-progressive disease, multiple sclerosis, and the question is: how does treatment affect cognition? So how does one measure cognition?

Dr. Leavitt:
Oh boy, you jumped right to the most important question in my mind. I would say first and foremost, our methods are insufficient right now. We have a bunch of tools, and I don't want to not honor the neuropsychologists who have been developing tools for over a century, but the tools I feel are not sensitive enough to pick up on the type of subtle changes that occur in people who are in their early 30s or 40s, people who are young, high-functioning, in the prime of their life, and people who have access to these DMTs, which are a game changer in MS. They're a game changer because they're helping people live with less relapses, they're more disease-free, and

they stave off progression. So we need more sensitive measures of cognition.

Let me just make it very clear that we only used one measure of cognition. The cohort that we had access to is a cohort called MS-PATHS, and Biogen has been collecting data for almost 10 years now across 10 centers in three countries, and the cohort is now 20,000 patients strong. So what it lacks in depth, it makes up for in breadth, not that those two things are two sides of the same coin. But that's just to say why we only had one cognitive measure for the investigation that I did.

Dr. Wilner:
What did you find?

Dr. Leavitt:
We looked at a single time point of data because as well, MS-PATHS follows people over time, and we at this point have up to as many as fifteen time points of data. So we can do incredible, exciting things with trajectory of change, but in this study we did not. At this study, we took a very simple coarse approach. We said, "Can we see differences in people who are either being treated with DMT or not being treated with DMT at a single time point in terms of their cognitive function on this one test that we tend to give to everybody with MS as kind of a cognitive screening instrument?" The paper and pencil version of this test is the SDMT, and all MS neurologists know about the SDMT because it's also the number one main cognitive outcome. If there's a cognitive outcome included in a drug trial, it's the SDMT. This was an iPad tablet version of that test called the PST. So we had that measure, which is kind of an important one for the field of MS, and then we just looked at differences in performance on that measure—again, between people who were either being treated currently or not being treated currently. And we found a difference. We found that the people being treated did better, which was not surprising to me.

The more exciting part of my study was actually having to do with demographic differences. And this is something that I really want to talk about because I went in with a pretty strong a priori hypothesis that there were going to be sex differences in DMT treatment, and that's because I had begun to see sex differences in everything that I look at with regards to my data, the data that I have, which is from hundreds of patients, not thousands. And MS is also affecting women more than men three times to one. So I think in this population especially, it's important to look at sex differences and to think about whether the disease is affecting women differently than men.

So when we looked at whether women and men differ in terms of being treated with DMTs—and remember, the current treatment guidelines recommend consideration of DMTs for all patients with MS—what we found was that less women are on DMTs at a single time point than men. And I think that this is really striking and really important for us as a field to figure out what's going on.

Dr. Wilner:
Even correcting for the increased 3:1 ratio? So it was less than 1:1?

Dr. Leavitt:
Right. We looked at it proportionally. So regardless of the fact that three times as many women have MS, if you're a woman, your chance of being on a DMT right now is lower than if you're a man. The other important thing is we corrected for differences in age, disease duration, and disease burden measured by atrophy in the brain and T2 lesion volume. So generally, men seem to have a more precipitous disease course than women for reasons we don't know, but we corrected for all of the variables that might explain that, and we still found that women were less likely to be on a DMT than men. Now you might think—and I think for me the first thought was—well, women get pregnant and they nurse, and they do all these things related to babies. Maybe they didn't want to be on DMTs when they were going through their fertile years. And we looked at the effect across the life course, and what we found were that the differences between women and men emerged at two time windows. They emerged in the mid-30s to mid-40s, which kind of is the childbearing years, and then they emerged again in sort of the late 50s, early 60s. I'm not quite sure what's explaining it, but I think it's important to have this initial report out there so that we can focus on it as a field and set our attention to this.

Dr. Wilner:
For those just tuning in, you're listening to *NeuroFrontiers* on ReachMD. I'm Dr. Andrew Wilner, and I'm speaking with Dr. Victoria Leavitt about her research on neurocognitive function among patients treated versus not treated with MS disease-modifying therapies.

Okay, Dr. Leavitt, so let's continue with this somewhat unexpected finding that women with MS were less likely to be treated with disease-modifying medications than men. So this was kind of just an empirical observation. What are your theories?

Dr. Leavitt:
Now that I've presented this work at a couple of different conferences—not only Milan that you mentioned before, but last year or two years back I was presenting it in Seattle—one thing I'll say is that this result inspires a lot of emotions in people, and I've been surprised by that. I have had people really, really upset by these results, and I think it's an interesting thing. I've had MS neurologists say, "Well,

listen, I think I give all of my patients the care that they require regardless of what type of person they are, and I think that the suggestion that you're making here, you can't say this." I actually had an MS neurologist stand in front of my poster and say, "You can't say this." And I said, "I'm not sure what's going on. I don't understand. Please help me understand." And then this person explained that they think that they're giving each of their patients personalized care. And I think that although I'm sure that that's true, we still have this finding in a large cohort that on the whole, women are less likely to get DMTs than men.

Now I'm starting to do some research in my lab looking at clinical subtypes, and it seems that women and men present a little bit differently. Men seem to have a greater preponderance of motor symptoms—so walking speed decreases and falling—whereas women may have a cluster of symptoms that's more closely aligned with cognitive impairment, fatigue, anxiety, and depression—those unseen invisible symptoms—and I think that that may be guiding the way that they're being treated. I don't want to say anything that's going to upset people, but I'm not sure. It could be that the symptoms you report have an influence on the treatment that is recommended to you by your neurologist.

Dr. Wilner:
And as you suggested earlier, the disease might be different in ways that we don't appreciate, just as you're describing now, with the symptom complex that men may simply have a different variation of the disease that's more likely to be treated or it could be men's personalities. It could be women's personalities. It could be access to care. You haven't mentioned that, but that's clearly a possibility. Let's go back for a second to your neurocognitive findings. Was there any difference in men versus women in those who were treated or not treated? Can we talk about that?

Dr. Leavitt:
I thought you might ask me that, and as it happens, no, there wasn't. And I thought that there would be, but there wasn't a difference. One thing I do want to mention though with regards to resources that you touched on a second ago is that the other demographic difference we saw in people treated versus not treated was education. So having more education made you more likely to be treated with a DMT. This might sound like it's not surprising, but let's stop for a second and say maybe it should be. Maybe it should be surprising. Maybe we should stop accepting the fact that people who have access to more resources are likely to have better treatment for their diseases. And we should say, "Why is that happening, and how can we stop that from happening?"

Dr. Wilner:
Before we close, do you have any takeaway messages for our audience?

Dr. Leavitt:
I'd love to give a takeaway message. I think a lot about the precision medicine movement, something that became really popular in the early part of this century. It was really promoted by President Barack Obama. It really came around as a buzzword in relation to the human genome project where we thought that once we had cracked the human genome, we'd be able to tailor treatments to everybody based on your genetic profile. And as it turns out, that has eluded us to a degree that we didn't anticipate because of epigenetic interactions and so forth and so on. My point is, if we want to start really practicing precision medicine, we could start with whether you're an XX or an XY carrier. We could start right there. We could have treatments for women and treatments for men, and that to me seems like something that drug companies would be excited about, that we could really move forward, and that would result in better treatment for everyone. So that would be what I would hope this work would serve as a catalyst for.

Dr. Wilner:
Well, with those final comments in mind, I want to thank my guest, Dr. Victoria Leavitt, for joining me to discuss her study on the use of disease-modifying therapy and its effect on neurocognition as well as a difference between the sexes. Dr. Leavitt, it was a pleasure having you on the program.

Dr. Leavitt:
Thank you, Dr. Wilner.

Dr. Wilner:
For ReachMD, I'm Dr. Andrew Wilner. To access this and other episodes in our series, visit *NeuroFrontiers* on ReachMD.com, where you can Be Part of the Knowledge. Thanks for listening.