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Adverse Childhood and Lifespan Stressors Take a Toll on MS Disease Severity

Dr. Wilner:

Welcome to *NeuroFrontiers* on ReachMD. I'm your host, Dr. Andrew Wilner. Joining me today to discuss her research focusing on stressors for patients with multiple sclerosis is Dr. Carri Polick. Dr. Polick is a postdoctoral fellow and VA scholar in the Duke National Clinician Scholars Program.

Dr. Polick, it's great to have you with us today.

Dr. Polick:

Thank you so much for having me.

Dr. Wilner:

So I'd like to start off with your study that was recently published in *PLoS One*, which examines the relationship between childhood stressors and chronic MS symptoms. Can you provide us a little background as to what led you to conduct this research?

Dr. Polick:

Well, MS is in my family. My brother was diagnosed after returning home from a combat tour in Iraq, and given the gene and environmental interactions with MS, I always kind of wondered how that stressful environment may have been an influence. Throughout nursing school, I did home care for people with MS, and they would definitely talk about their stressor history. And I would also care for MS patients as a nurse in the emergency department. And across all of my personal and professional experiences, one thing that always stuck out to me is that this population really endorses how stressors impact their disease.

While starting my PhD training, I learned about adverse childhood experiences, or ACEs, which were implicated in over 439,000 deaths annually, partially because of risky health behaviors as a means to cope, like smoking and drinking, but in large part due to the inflammatory and immune responses that create wear and tear on the body.

There's a good pyramid figure on the CDC website depicting categories of outcomes over time starting with ACEs at the bottom, then disrupted neurodevelopment, social, emotional, and cognitive impairment, the adoption of health risk behaviors, disease disability and social problems, and then early death as the top of the pyramid. And there's a lot of research connecting ACEs and a dose response relationship to the leading causes of mortality, such as heart disease, cancer, and diabetes. But until the last couple of years, there really hasn't been much focusing on how these experiences impact clinical factors for people living with multiple sclerosis, and I found this curious as MS is an immune-mediated inflammatory disease.

The research that we did have to work from is a bit limited because ACEs are typically measured as just a count of ten stressors, including abuse, neglect, and household instabilities, such as parental mental illness, substance misuse, incarceration, divorce, or a child witnessing domestic violence. However, there is a shift to expand criteria to include other stressors, such as poverty, community and school violence, discrimination, housing and food insecurity, as there's a growing awareness that these social drivers of health can elicit the same stress response. So we decided to kind of start back at the beginning to comprehensively measure an expanded set of stressors with more nuanced data on severity and duration to help determine whether there was a relationship between stressors and fatigue, pain interference in daily living, and psychiatric morbidity in people living with MS for this paper. And we also do have another paper coming, which focuses on disability and age at symptom onset as well.

Dr. Wilner:

Okay. So the research was not linking all of these childhood stressors to the risk of getting MS. It was linking the childhood stressors really to the severity of the MS that your subject population already had. Is that correct?

Dr. Polick:

Yes. That's what our studies are focusing on.

Dr. Wilner:

Okay. So what did you do to figure this out?

Dr. Polick:

We used hierarchical block modeling using clusters or blocks of similar predictors. Since this approach assumes collinearity to represent the latent constructs of stressor types, the focus is to evaluate if a block of similar predictors significantly contributes to the outcome and not necessarily focus on each individual variable because those estimates might be underestimated. To gain insight into which types of stressors relate to outcomes, assuming that stressors that happen to a child may differ from stressors that happen around a child, we clustered stressors into an emotional block, a physical block, and an environmental block. So we started with the base model of all the covariates that we wanted to account for, and then sequentially added blocks one at a time and evaluated whether the new block of predictors contributed significantly more variants over and above the previous block and whether it improved model fit. And we did this for each of the outcomes separately.

Dr. Wilner:

You had grouped these stressors now into three categories. Was one category sort of more potent than another, or did they all just work together? How did all that sort itself out?

Dr. Polick:

Yeah. I can kind of walk you through the results. So we did find that childhood emotional and physical stressors significantly associated with the overall presence of fatigue as well as the magnitude of fatigue, and it was the same case for pain interference, so childhood emotional and physical blocks of stressors related to experiencing any interference in their daily living because of pain and also the magnitude of the interference. For psychiatric morbidity, environmental stressors in addition to emotional and physical stressors were significantly associated with this outcome as well. And then our additional analyses also revealed that physical stressors associated with disability level and emotional and environmental stressors were associated with a younger age at symptom onset. So overall, we saw that stressors relate most to the so-called invisible symptoms of MS: psychiatric morbidity, fatigue, and pain interference.

One of the main takeaways is to really get clinicians to think about how they may want to engage with trauma-informed care, which is really shifting from thinking of and responding to a patient from a lens of "What's wrong with you?" to "What has happened to you?" And clinicians may find that this also helps them better understand their patients and maybe experience a little less frustration or burnout. For example, patients may seem like they're not adhering to the treatment plan, but they may have a high stressor history and then a new acute adult stressor, which poses barriers for mental health and managing care. There is research to show that people with a high ACE history have worse anxiety over the first year following an MS diagnosis, so they may need some extra support and care coordination.

So if we do incorporate screening, this could be something that's done on the clinic level. Some EHRs actually already do have a social determinants of health screener, and some screeners can fit into clinic flow, so if providers are a little bit more aware, they may be able to better connect patients with mental health referrals, smoking cessation referrals, and other community resources that may really help that patient navigate some of the stressors and barriers.

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. Carri Polick about her research on stressors in patients with multiple sclerosis.

You have related research about how the impacts of stress affect lifespan of MS patients. Would you like to tell us about that?

Dr. Polick:

So after establishing that comprehensively measured stressors aligning with the expanded ACE criteria do relate to invisible and physical symptoms of MS, we wanted to expand upon that to examine stressors across the lifespan. The stressors we included in adulthood again align with a lot of the social drivers of health, such as job insecurity and financial stress as well as experiencing divorce or losing a loved one. And we again used a hierarchical block modeling approach with covariates as the base model, then added the childhood stress experience, and then added the adulthood stress experience. And we found that both childhood and adult stressors were associated with MS disability and then only adult stressors were related to the relapse burden. For the invisible symptoms, it also reveals that both childhood and adulthood stressors significantly contributed to pain interference and psychiatric morbidity. And lastly, childhood stressors, especially the childhood stress severity, significantly contributed to fatigue in adults with MS.

So now we've shown that childhood stress matters and we have shown that lifetime stress matters for outcomes individually, but these

analyses don't account for positive factors that may attenuate the effects of stressors, and we need to work towards highlighting modifiable targets for intervention. So we also did a structural equation model, which showed that resilience, mental health, smoking, and sleep are all significant mediators between lifetime stressors and MS severity measured as a latent variable with multiple symptoms, because in reality, fatigue, pain, disability, and relapses are all occurring together.

Dr. Wilner:

Well, that's great. That really emphasizes the comprehensive interview that's necessary to take care of patients who have a wide background in terms of social determinants of health.

Now, you just mentioned sleep and smoking. I would think more sleep would be a good thing and more smoking would be a bad thing. How do those play in?

Dr. Polick:

Correct, yes. Those with a higher stressor load had a negative relationship to resilience, so then resilience also further mediated the relationship with smoking, sleep, and mental health. Those with higher resilience tended to have higher mental health, higher stressor experience, and lower resilience; they tended to be more prone to smoking. So we did really be able to get good insight into this pathway that we can hopefully then implement some earlier interventions to catch people before they have too much symptom burden or disability accumulation.

Dr. Wilner:

Now we've certainly covered a lot, Dr. Polick, but before we close, do you have any final takeaways you'd like to leave with our audience today?

Dr. Polick:

Trauma-informed care is important; screening is important; and there may be some clinician benefits to understanding your patient a little bit better and helping you maybe decrease some burnout. Broadly, this work is evidence to the body of literature supporting upstream preventative measures to reduce experiences of structural stressors across the lifespan, such as poverty, racism, imprisonment, and housing instability. The last thing I want you to think about is how we all have roles in these societal systems, so I urge you to think about ways that you could help address some of these structural stressors from the personal level to the policy level.

Dr. Wilner:

Thank you. This has been a great discussion on an impactful topic in multiple sclerosis research. Thank you very much, Dr. Carri Polick, for joining me on this program. It was a pleasure talking with you.

Dr. Polick:

Yeah, it was a pleasure. Thank you for having me.

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.