Transcript Details

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MS and Structural Disconnectivity: Pathophysiology and Emerging Technologies

Announcer:
You're listening to *NeuroFrontiers* on ReachMD. On this episode, we'll hear about structural disconnectivity of the central nervous system in patients with multiple sclerosis, or MS, from Dr. Amy Kuceyeski. She's a Professor of Mathematics in Radiology and Neuroscience at Weill Cornell Medicine, and she spoke on this topic at the ACTRIMS Forum 2025. Let's hear from Dr. Kuceyeski now.

Dr. Kuceyeski:
Structural connectivity refers to the white matter connections or the wiring between various areas of the cortex, subcortex, and cerebellum. MS-related lesions that occur in the white matter can damage these axons, or myelin sheaths, which can reduce the efficiency or entirely break these connections. This is what we call structural disconnectivity. The result is oftentimes impairment in the individual, but it does depend on where these lesions are and what network they're affecting. For example, structural disconnectivity to and from the thalamus and primary motor cortices can be associated with more motor impairment, and structural disconnectivity in default mode networks, frontal parietal networks, and the cerebellum can be associated with more cognitive impairment. So the area in the location of the lesion greatly impacts the level of impairment and the type of impairment.

Largely speaking, more lesions mean more structural disconnectivity and more disease severity and disability; but again, it does matter where these lesions occur. So our studies and others have shown that the tissue around MS lesions, including the white matter tracts that the lesion is damaging and the endpoints of these damaged white matter tracts and the gray matter, can be negatively impacted over time from the initial area of lesion. For example, our studies show that looking at the gray matter regions whose white matter has a lesion on it may have more atrophy over time than regions whose white matter is not impacted. Our studies have also shown that paramagnetic rim lesions, or PRLs, often have more ongoing inflammatory activity within the lesion itself, and these can also—we found with our most recent work—cause increased inflammation on the same white matter tract as the PRL lesion. And the increase in inflammation wasn't the case when we looked at global levels of inflammation in patients with PRLs versus those that did not, but it was specific to these white matter tracts that were structurally disconnected or on the same white matter tract as PRL lesion.

Oftentimes we are working with population-level data, so most of the subjects that we have are relapsing-remitting MS patients, and this is the case across the board. So most of the results that we find are usually in our MS patients. And as far as I know, I haven't seen any robust evidence showing that there are very different patterns or sort of areas of location where the lesion can impact differently the subtypes of MS.

My lab has been working in creating tools where you can use clinical MRI to estimate the structural disconnectivity patterns. So the tool that we've developed in my lab called the Network Modification, or NeMo, tool, allows a person to take their lesion mask from a patient with MS just derived from, let's say, a T2 flair or another type of clinical imaging, and it can co-register that to a common space where we have all of these structural connectivities from a bunch of different healthy controls. And essentially, we take the lesion and we trace the white matter fibers, the structural connections that pass through that lesion, and then we can estimate in the gray matter how much disconnection there is due to that pattern of lesion. So it's a way of actually using our clinical MRI only. We don't have to acquire diffusion MRI, which is what we usually have to acquire when we want to estimate structural connectivity or dysconnectivity. And we take just those clinical MRIs, put them into this tool, and get an estimated structural disconnectivity from that lesion. And we've used this in the past in lots of different cohort population-level analyses looking at how the patterns of structural disconnectivity map to certain impairments, like EDSS scores or cognitive impairment, over time.

Announcer:

That was Dr. Amy Kuceyeski discussing structural disconnectivity in patients with multiple sclerosis. 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!