Transcript Details

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Emerging Technologies in MS: Neuromodulation and Myelin Regeneration

Announcer:
You're listening to *NeuroFrontiers* on ReachMD. On this episode, Dr. Cristin Welle will discuss how neuromodulation can promote myelin repair. She's a Professor of Neurosurgery and Physiology at the University of Colorado Anschutz Medical Campus, who has experience in neurotechnology translation with previous work with the FDA, and spoke on this topic at the ACTRIMS Forum 2025. Let's hear from Dr. Welle now.

Dr. Welle:
Neuromodulation, most broadly, is directly activating parts of the nervous system for a therapeutic effect. In most neuromodulation technologies that exist today, this is done via electrical stimulation of the nervous system. This can be done through implanted electrodes that are placed in different specific regions of the brain, spinal cord, or peripheral nervous system. Or in some cases, it can be administered noninvasively through the skin to access more superficial nerves in the body. And the beauty of neuromodulation is that it can be very precise, both in location—you can put your electrode exactly where you want to stimulate—and also in terms of time, so you can stimulate right at the moment that you want that region of the nervous system to be activated.

Neuromodulation hasn't been explored extensively in the context of myelin loss or multiple sclerosis, but in our research lab, we decided to investigate if neuromodulation could be used to actually restore and repair the myelin state of the nervous system. We used an animal model of demyelination called a cuprizone model. That is a drug that targets oligodendrocytes, which are the myelinating cells of the nervous system. And so when we administer this agent to animals, oligodendrocytes die, much like you might observe in patients with multiple sclerosis. What we found is that after this demyelinating event, if we then applied a neuromodulation technology—and in our case, we were using a technology called vagus nerve stimulation, which is electrical stimulation of the vagus nerve through the region in the neck, the cervical region of the vagus nerve—we found that we could increase the amount of remyelination that occurs after demyelinating injury by up to 40 percent.

We're still exploring how vagus nerve stimulation could lead to remyelination and myelin repair, but we think that it may have to do with the fact that stimulating the vagus nerve causes an activation of neurotransmitters in the brain, including acetylcholine and noradrenaline. And these neurotransmitters have been linked to regulating the proliferation, differentiation, and maturation of oligodendrocytes into mature myelinating oligodendrocytes.

There's very limited literature to suggest that neuromodulation could promote remyelination. There has been a little bit of work done exploring a different type of noninvasive neuromodulation technology called transcutaneous magnetic stimulation, or TMS, with some evidence for oligodendrocyte proliferation in that context. But really, our studies are some of the first that give a true demonstration of the remyelinating potential of neuromodulation technologies.

Some of the challenges that can be a part of neuromodulation include that some of these devices are implanted in the body, which isn't inherently a challenge—they actually have a very well-established safety profile, but of course, anything that requires surgery poses a little bit of risk. Not all patients might be comfortable with the idea of having a stimulating electrode implanted in the body so that is one potential limitation to the use of an implanted vagus nerve stimulation technology for remyelination. However, there are opportunities to stimulate the nervous system, even the vagus nerve noninvasively, and so we're exploring those approaches as well.

There's actually some vagus nerve endings in the inner ear, and it's possible to activate those nerve endings via stimulation applied through the skin, so you don't have to implant or inject anything to activate those nerves. And surprisingly, we found that in our animal

model, when we noninvasively stimulate the vagus nerve endings in the ear, we found similar recovery of myelin after demyelinating injury as to when we stimulated with an implanted vagus nerve stimulator. And so we're very excited about the opportunities to perhaps provide noninvasive vagal nerve stimulation.

How can you pair neuromodulation technology with, perhaps, pharmaceutical agents to accelerate these effects? There isn't published literature that explores this yet, but it is something that we would very much like to explore. It's in our pipeline. We have proposed this in some grant applications to perhaps pair vagus nerve stimulation with a remyelinating agent, such as clemastine. We think it's a very promising path forward, and it points to one of the one of the key advantages of neuromodulation: it can be safely combined with pharmaceutical strategies. So it really allows for this multimodal approach to remyelination, which is absolutely something that we'd like to pursue.

Announcer:
That was Dr. Cristin Welle discussing how neuromodulation can play a role in myelin repair. 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!