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Visionary Insights: Assessing MS-Related Retinal Changes with Adaptive Optics

Announcer:
You're listening to *NeuroFrontiers* on ReachMD. On this episode, we'll discuss adaptive optics in multiple sclerosis with Dr. Daniel Harrison. Dr. Harrison is an Associate Professor of Neurology and the Director of the Division of Multiple Sclerosis and Neuroimmunology at the University of Maryland. He also presented a session on this exact topic at the 2024 ACTRIMS Forum. Let's hear from him now.

Dr. Harrison:
So I'll tell you a little bit about the session that I gave at the ACTRIMS meeting, which is a summary of adaptive optics and the applications of this towards retinal imaging for multiple sclerosis.

The optic nerve, which is a very important structure for multiple sclerosis, is the nerve that connects between the brain and the retina and is often affected in multiple sclerosis, and it can be affected by optic neuritis, which is direct inflammation of the optic nerve that causes demyelination and associated axonal loss, and then even a chronic optic neuropathy happens. All of these can indirectly affect evidence from previous histopathologic and other immunochemistry studies that have shown that there may even be direct inflammation within the retina itself that's happening in multiple sclerosis. So we really have an opportunity with the retina to very closely study multiple sclerosis. It's a portion of the nervous system that's directly accessible in a lot of ways with optical imaging. You don't have everything else in the way that you do with the brain, like the skull and all those other tissues.

So there has been a lot of work over the years to try and develop very good tools for visualizing what happens in the retina in multiple sclerosis, and some of the audience may be familiar with some of the current imaging methods for the retina. There are two that get used very routinely, often in unison. So there is scanning laser ophthalmoscopy and optical coherence tomography, and these are used by ophthalmologists to visualize the retina and make measurements of the retina. Particularly, optical coherence thermography, or OCT, is used currently to measure the thickness of various neuronal layers within the retina and it's begun to be used to assist with multiple sclerosis diagnostics. It has started to become integrated into some of the clinical trials.

So where does adaptive optics come in? Well, one of the limitations of doing any kind of visualization of the retina is you do have a few things in the way, some of which can cause some aberrations and distortions to the images, including things like the tear film, the cornea, and the lens, and that limits the resolution of some of these optical imaging techniques. So various adaptive optics techniques have been more recently applied to optical imaging, both for improving the resolution of images from scanning laser ophthalmoscopy, or SLO, and also for optical coherence tomography, which is OCT.

So adaptive optic scanning laser ophthalmoscopy has been briefly applied in a few small studies for multiple sclerosis, and some of the interesting findings have been visualizing reduced cone density, so measuring the rods and cones in the retina. Developing very high-resolution angiographic images also has been applied with scanning laser ophthalmoscopy with adaptive optics in the eye.

We're very excited about our work that we've been doing with adaptive optics OCT. And the real main advantage to using adaptive optics with OCT is that not only are we able to look at the thickness of various neuronal layers within the retina, but we're able to get resolution that is fine enough that we're able to get cellular-specific images. We're able to really zoom in and see individual cells within the retina. We did a small pilot project. We applied adaptive optics OCT to 10 patients with multiple sclerosis, some of whom had previously experienced optic neuritis, some of whom had not, and then we had nine healthy controls that we compared them to. And we obtained adaptive optics OCT images, and we focused on three particular cell types that we were able to measure. One was the retinal ganglion cells. We obtained images in the ganglion cell layer, where we were able to quantify directly the number, size, and shape of

those ganglion cells. We looked at the nerve fiber layer in the retina, and we were able to measure the size and the shape of axonal bundles within the nerve fiber layer. And then at the inner limiting membrane, we visualized cells, which we're calling macrophage-like cells, which are cells that have this appearance of processes extending outwards that do look very much like macrophage-like cells that may actually be microglia in the retina, and we are proposing that they are indeed microglia due to some of the activity and size and shape and confirmation of these cells. And what we were able to show in that study was that in this small group of patients, not only could we visualize those cells, which is a relatively novel finding for in-vivo imaging in a human, but we were able to see MS manifesting very clearly on a cellular basis.

So in the retinal ganglion cells, we saw a significant reduction in the number of retinal ganglion cells in the MS patients, particularly those who had a previous optic neuritis event. We saw a change in the size of the cells. In fact, we actually saw that the surviving cells increased in size, suggesting that there may be some hypertrophy of the remaining cells. In the retinal nerve fiber layer, we saw a significant reduction in the number of axonal bundles and the size of those axonal bundles. And again, that was worse in the patients who had previously experienced optic neuritis. And then, interestingly, these macrophage-like cells—which, again, we are proposing may actually be microglia—we saw an increase in the number of those cells in the MS patients, including and especially in those who had previously experienced optic neuritis. And this is very interesting in the sense that the patients we enrolled in this study had experienced optic neuritis a long time ago, so there was no active inflammation that's going on. Most of these patients had experienced optic neuritis many years in the past, yet we were seeing an increased number of inflammatory cells in that region. We also are able to record videos of those cells and measure the process motility, so the extension and retraction of various processes on those cells, and we were able to show that process motility in the macrophage-like cells in the patients with multiple sclerosis, especially those with optic neuritis, was faster, indicating that those cells are perhaps more active again, even in patients who have experienced optic neuritis many years ago.

Announcer:
That was Dr. Daniel Harrison talking about his presentation at the 2024 ACTRIMS Forum that focused on adaptive optics in 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!