Anti-MOG Associated Disorder

Insights Into Neuroplasticity and Opportunities for Repair

You can view this presentation at: youtu.be/teCgjLuQOT8

[00:00:00] **Roberta Pesce:** Dr. Greenberg is staying on with us now to give us a little update on anti-MOG associated disorder, and insights on neuroplasticity and opportunities for repair, so over to you again, Dr. Greenberg.

[00:00:16] **Dr. Benjamin Greenberg:** So, in the next 10 minutes I want to give people a preview of the some of the work that's ongoing at UT Southwestern relative to anti-MOG associated disorder, and one of the questions that got asked on a prior talk was asked to Carlos Pardo about acute flaccid myelitis, there was a question about what are the chances of recovery over time in my child? And this gets into how does the nervous system functionally repair, and there are multiple ways a nervous system can repair. One is if there's been damage to the nervous system, you just repair the damage. But the second way is for the nervous system to reorganize what's called neuroplasticity and functionally repair, and what I want to present today is research we're doing here at UT on the neuroplasticity we've discovered in anti-MOG associated disorders.

[00:01:04] So first a very scientific slide, the MOG protein. What's shown here in that blue cell is a neuron wrapped in the yellow myelin, and that myelin is sandwich layers of lipids and proteins, one on top of the other making a spiral, and in that outermost portion of that rack around the axon is the MOG protein, and if you develop an antibody to this protein, you can have certain conditions. And this disease was very misunderstood over the years. On the next slide there are some titles from some publications going back 40 years, where we found these antibodies in lots of different people, but nothing made sense, it was all over the map. Some people had multiple sclerosis, some people had a diagnosis of ADEM, some people had a diagnosis of transverse myelitis, and none of the data made sense until, on the next slide a group out of Oxford figured out what was, we'll skip this slide in the interest of time. Roberta, I apologize, we'll go to the next one.

[00:02:07] A group out of Oxford discovered that the blood test was being done in a way that gave bad results. So, while we were detecting the antibody in some people, the test was saying it was positive, it really wasn't positive. They didn't have the antibody. And so, without a functioning test it made it very difficult to sort out what was this disease. So, on the next slide what we see is as the blood test was perfected, we understood that this disease presents differently depending on how old the person is. So, if you're a child below the age of 8, it usually presents with ADEM, inflammation of the brain, optic nerve, spinal cord. As you move to ages

8 to 12 you usually get optic neuritis, inflammation of the optic nerves. As you move to the teenage years and later you usually get transverse myelitis, and this curve isn't perfect.

[00:03:06] You can get any of these syndromes at any age, but as children develop, and this can affect adults as well, the way the immune system caused damage changed over time, and we were able to see that this disease was a distinct entity. And if we go to the next slide what we saw is you could have relapses over time. So, about half of individuals would have a relapse, but these relapses were spread out over time, and clinically, a lot of these patients looked like what we see in neuromyelitis optica. So, they had optic neuritis and transverse myelitis and relapses over time, but there were some distinct differences. So, on the next slide, if we compared individuals with the anti-MOG antibody to ones with the aquaporin-4 antibody, we found out some remarkable things.

[00:04:00] So number one, while they each were having optic neuritis and transverse myelitis, the disability rates between these two patient cohorts was completely different. Individuals with the aquaporin-4 antibody, despite having equal number of attacks, their disability was significantly greater. If we looked at visual acuity, the visual acuity of patients with anti-MOG associated disorder was better than those with anti-aquaporin-4 mediated disorders. And what I want to present to some of the data around the visual side of things that we published here out of UT. So, if we actually advance two slides, we'll go again.

[00:04:38] So I want to talk about unique features of MOG. So first, on the next slide, I want to talk about preserved vision in MOG, because this is what's giving us insight into this condition. So, on the next slide is a picture of a machine that does a test called optical coherence tomography, OCT. So, a patient will sit in front of a lens, which is on the left-hand side of the slide, nothing touches you, no eye drops are given, there's no puffs of air, and you just look through the lens and you'll see a laser light, either making lines or going in a circle, and you just have to stare. And on the next slide what you see is the image that the operator sees that white and black image that has the yellow circle drawn on it, that is the back of the retina, right where the optic nerve matures the retina. The wire that connects the eyeball to the brain, that's the connection point. And what we know when there's optic nerve inflammation is there can be damage to that optic nerve, to the wires that form the optic nerve.

[00:05:48] So why are we taking this picture? Well, the machine doesn't just get this black and white picture. This machine is able to separate out the layers of the retina into individual cell layers. So, on the next slide I'll show you an example of the image. So, these layers of white, black, grey, black, grey, each of those layers represents a different cellular layer. We can literally take a picture down to almost an individual cell width, and when there's optic neuritis what we have found is that that layer of wires of the optic nerve thins over time. So, the immune system comes in, chews on your optic nerve, and it gets thinner. And we now have a way to measure how thin it is.

[00:06:37] So you hear about, for example, in people with heart failure after a heart attack. They have a heart attack, it damages the heart muscle, we do an ultrasound, and we say your ejection fraction, the amount of blood you're pumping is lower than it should be, 30 percent, 20 percent, we give a number, and that number correlates with a person's function. The lower your ejection fraction the more shortness of breath you have because there's been more damage to the heart muscle. Very good correlation. And in optic neuritis when we take this measurement of the OCT and we measure the layer of wires that form the optic nerve, for years we have seen a very good correlation between how much damage is done and how much vision is lost after optic neuritis.

[00:07:26] So if I take somebody with multiple sclerosis, somebody with neuromyelitis optica, and they have 50 percent loss of the wires, they lose a certain number of letters on the visual chart. What we've found and

published out of UT was this correlation fails in individuals with anti-MOG associated disorder. And on the next slide, which is a complicated data slide, but I'm going to point out if you look to the right-hand part of the slide, the orange dots, each of those is an eye from somebody with anti-MOG associated disorder. And as you move to the left of that box, the optic nerve was getting thinner and thinner and thinner. And what you would expect would be the amount of vision would go down, down, down, down, down. That it would form a straight line.

[00:08:14] The better your optic nerve, the better your vision. The worse your optic nerve, the less vision you had. And in multiple sclerosis patients, that was true. In neuromyelitis optica patients that was true. In anti-MOG associated disorder patients, it's not true. Despite an equal amount of damage, and let me say that again, an equal amount of damage to the nervous system, our anti-MOG patients had better vision. How on Earth could this be true? Why is it that individuals with anti-MOG associated disorder could compensate for an amount of damage that our neuromyelitis optica or multiple sclerosis patients couldn't? Our theory is that it lies in neuroplasticity.

[00:09:00] So on the last slide I'll just introduce, we'll go one more, I'll introduce the study that we're doing here at Southwestern, which is an advanced imaging study using two different types of MRIs. To not just look at the structure of the brain but the function of the brain. And what our preliminary data suggests is that in anti-MOG associated patients, they have an ability to compensate for patients in a way different than multiple sclerosis and in a way different than neuromyelitis optica, and if we understand their biology better, we hope to identify opportunities to better treat patients with neuromyelitis optica or multiple sclerosis, or transverse myelitis, and tap into the inherent plasticity function that the nervous system has.

[00:09:48] And so we're actively doing this study now, and we've been inviting anti-MOG associated patients and patients with other disorders to take part in this study where they do scans separated by a couple of years and we track how their brain is functioning over time. So, it's just a glimpse, hopefully it gives you a sense of some of the work that's going on, and I'm happy to take any questions you might have about this.