Transcript Details
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MS in Children: A Look into Research on a New Biomarker

Announcer:
You're listening to *NeuroFrontiers* on ReachMD. On this episode, we'll hear from Dr. Ahmed Abdelhak, who's the clinical instructor of neurology at the University of California San Francisco School of Medicine, to discuss his research on a new biomarker for multiple sclerosis in children.

Let's hear from him now.

Dr. Abdelhak:
So neurofilaments in general are proteins that we find in the axons of neurons, so they are part of the so-called cytoskeleton of neurons, which maintain their trait. The neurofilament light chain is one of those proteins, and over the last years, with the introduction of new technologies that allows for ultrasensitive measurements in the blood, we were able to measure those neurofilament chains in the blood of our patients, and we take that as a robust marker for the pathology that's affecting the axons. If we see high neurofilament in the blood, we anticipate that axonal are in an unhealthy state. So earlier, we were able to measure those neurofilaments in the CSF, and now with the newer assays coming to the market, we are able to measure them in the blood. We are still in the process of bringing those neurofilaments to the clinic. So far, they are not approved by the FDA to be used for clinical scenarios, but we think they provide great additional information to the clinician beside the usual investigations we are doing, like the MRI and CT scans, and the context of use in every disease will also differ, and that's what the research is focused on now.

And like this paper is one of the essential papers that can bring this assay to the clinic. This paper contained amazing international collaboration that was conducted in UCSF at the University of Basel and University of Regensburg in Germany. At every site, there was a multisite cohort. In Germany, it was a cohort that was established with the coronavirus pandemic to study the effect of coronavirus on CNS health in young children. At UCSF, we have the US multiple sclerosis pediatric cohort, which also has healthy participants in it. And in Basel we have done the biomarker measurements. So from those two cohorts, the one in Southern Germany and the one in the US, we collected the samples from healthy children and younger adults, and we measured the levels of neurofilament light chain in Basel. We have in total around 2,667 participants, and following having all those NfL data from our patients, we tried to correlate the NfL data with the basic clinical demographics, particularly with age. So we know from other studies that age is by far the strongest factor that can impact NfL values. And a normal NfL value in someone who is, for example, 60 years old can be considered severely elevated in someone who's 20 years old. The main aim of this study was to really look for how age can impact the NfL concentration in this age range that we investigated here, which was from zero until 20 years old.

The findings we had were very interesting in the fact that compared to adults, NfL dynamics in children and younger adults were completely different. So in adults, we know that the older the people get the higher the NfL values are. In children, the pattern was different. So we saw that after birth, and particularly in the first 10 years, NfL values are really high. They decrease with age until the age of 10 year, and then they stay almost flat until the age of 20. After the age of 20, or maybe even 22, we start seeing this pattern I was talking about in adult that with increasing age, NfL increases.

That was, I think, the key finding from the paper regarding the impact of age on NfL, which is indeed very important because that would mean a high NfL value in neonate or a child that's five years old can still be normal if we don't evaluate the effect of age on those low concentrations.

Over the last years, there has been a massive expansion in the number of available biomarkers that we can use. One of them is called

GFAP, which we are also working on heavily, and another protein, called UCHL1. Those two proteins reflect different components of the CNS pathology. So NfL, on the other hand, is measuring probably something different, and that is the advantage of having many biomarkers because then if you do an MRI, for example, you see a lesion, but you don't really know from the MRI what's happening inside this lesion. Do you have damage to the neuron? Do you have astrocyte injury or astrogliosis? But if you have biomarkers that you can measure in the blood that can directly reflect if one of those components is affected, you have a much, much better picture about the underlying pathophysiology.

So NfL is so far the most well-established and validated biomarker to reflect the damage that's happening to the axons, either in the brain or in the spinal cord, but even also in the periphery, which means it has applications in any CNS and peripheral disease, and also diseases of the peripheral nervous.

There are two NfL assays now that has received the FDA breakthrough designation, which means they are undergoing accelerated approval process, and one of them is for detecting MS activity. We give our MS patients now really effective treatments, and usually, those treatments can eliminate the occurrence of MRI lesions or relapses, but we still see sometimes those lesions happening or relapses taking place. And NfL is a great tool to predict the occurrence of that, and also is a great tool to predict the treatment response, so if our patients are getting good treatment, you will see NfL values to be low. So I anticipate it to come to the clinic soon, but still we don't have complete FDA approval.

Announcer:
That was Dr. Ahmed Abdelhak discussing new biomarkers for multiple sclerosis in children. To access this and more episodes on our series, visit *NeuroFrontiers* on ReachMD dot com, where you can Be Part of the Knowledge. Thanks for listening.