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Beyond Guesswork: Validated Methods for MCI Assessment in Alzheimer's Diagnosis

Announcer:
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Dr. Hardy:
Hello, this is CME on ReachMD and I'm John Hardy. Today, we're going to discuss validated methods for an MCI in Alzheimer's disease. MCI refers to mild cognitive impairment, and the problem with that when it's used in that sense is that there are many reasons one might have mild cognitive impairment, and Alzheimer's disease is just one of those reasons. One might, for example, have depression, or one might be in the early stages of, for example, frontotemporal dementia, and so, a task that we need to do is to separate mild cognitive impairments, for many reasons, from mild cognitive impairment in Alzheimer's disease. And to do that, we need to go to biomarkers, really, and to say, using biomarkers, whether we can differentiate the Alzheimer cause of mild cognitive impairment from all the other causes of mild cognitive impairment. And basically, what you're doing in that case is getting a key to understand whether you have amyloid pathology. And how might you do that?

Well, there are a number of reasons, a number of ways. Classically, the way to do this is by PET scan. Can you see amyloid on a PET scan? If you've got mild cognitive impairment with amyloid on a PET scan, you're clearly in the early stages of Alzheimer's disease. The next historical way of doing it is by looking at the CSF measurements of amyloid related molecules. Most classically of this is A-beta 42, this is amyloid 42 amino acids long. And, counterintuitively what you're looking forin the CSF measurements is amyloid reductions indicate that amyloid is being deposited, because what happens is that amyloid, instead of getting into the CSF, is sticking to plaques. And so, what you see in the CSF is amyloid reductions.

More recently, and very excitingly, the field, has found a number of phosphorylated tau markers which indicate phospho tau, if you like, leakage, probably from around the plaques where you see the tau filaments. And you see that these tau markers, phospho-tau181, phospho-tau217, phospho-tau231, all rather similar species. You see these rise in CSF and they're an indirect plaque marker. And even more excitingly, and I think this is going to be of key importance over the next period, is we have now developed methods for finding these phospho-tau markers in the blood, and with new technology we can now detect these phospho-tau species, 181, 217, and 231 increasing in concentration in the blood. And these, too, are indirect measurements of amyloid deposition in the brain. So, really a time when we are now able, at least beginning to be able, to identify if somebody has MCI due to Alzheimer's disease by doing blood assays.

And how do these fit together? Well, there's been a number of studies and this study is one of them showing that, in fact, the amyloid in the brain, and here are the PET scans on the left correlate with the phospho-tau181 in this indication. And so, we're now in a period when we can see, measuring phospho-tau181, and other phospho-tau species, is going to be a way of using blood assays to tell if people have mild cognitive impairment due to amyloid deposition. So, we're really in a new era now of having blood biomarkers, which are just coming into acceptance as helping us make the diagnosis of Alzheimer's disease.

Thank you for listening.

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