Why “Subjective Cognitive Decline” Is Important

By David Hsu, MD [6]

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The pace of Alzheimer disease (AD) research is fast moving, and the prize of finding the cure seems tantalizingly close. We have the target protein, the antibody to knock out the protein, and the imaging test locating the protein in the brain, but there still remains one problem . . . Who should receive the antibody?

Researchers from around the world came together recently for the Alzheimer’s Association International Conference in Boston and presented the latest findings in trying to answer that very question. The conference made headlines in The New York Times and yielded multiple letters to the editor.³ A group from Germany led by Dr Frank Jessen presented strong evidence that maybe people with “subjective cognitive decline” (SCD) should be the ones to be given the antibody first.

The phenomenon of SCD occurs when patients who do not have cognitive impairment but who nevertheless present to their physician with cognitive concerns. To be clear, these patients score within the normal range of standard cognitive instruments, such as the Folstein Mini-Mental State Examination, and do not have any functional deficits. They also do not fall within the realms of “mild cognitive impairment (MCI).” Persons with SCD just notice that their minds are “not as sharp” as before, which may get in the way of daily tasks (like remembering to buy groceries). Research presented at the Boston meeting also suggests that those with SCD have more build-up of the protein likely to cause AD. Thus far, the Alzheimer research community seems to be excited about the SCD hypothesis and will likely pursue this further.

All this focus on SCD hopes to further define “preclinical AD.” Studies tell us that beta amyloid, the main protein causing AD, start to accumulate in brains up to a decade before clinical AD.²,³ The trials last year testing solanezumab and bapineuzumab started too late, although patients had a mild reduction of cognitive symptoms and reduced amyloid. Researchers now want to test patients much earlier (ie, those who have MCI or normal cognition). The first trial to do that has started already in Colombia through Genentech, Banner Alzheimer Institute, and the National Institutes of Health, with the antibody crenezumab.

SCD brings up several research questions, as well as potentially complicated ethical questions. Can
patients reliably assess their cognitive decline? Findings from Jessen and other groups suggest that the answer is yes. Future studies will need to better assess whether certain cognitive domains are more predictive than others and whether SCD can be reproducible in the lay population. Participants in clinical research are often “cleaner” and do not represent the people who have multiple co-morbidities or come from various socioeconomic backgrounds. What if a 40-year-old man comes into clinic with SCD? Would a doctor order a PET scan and potentially give the antibody? How about someone with Down syndrome, a previous head injury, or a history of stroke?

However, the larger question for me is: What then constitutes normal cognition if SCD can predict AD? One future scenario is for AD to develop in a patient at the “right” age. Her doctor wants to get a PET scan and start the antibody right away. Technically, the doctor would be treating AD as defined as amyloid build-up in the brain. Would she then be deemed to have AD? Should she quit her job or stop driving? Would her health insurance cover treatment for this “disease,” and should she tell her life-insurance company? Would Medicare pay for the antibody as “preventive care,” just like for hypertension and hyperlipidemia? What if the patient were actually undergoing a major depressive episode with cognitive deficits and got better after starting an antidepressant? Should she continue getting the antibody treatment even though her cognition improved?

I guess we’ll just have to cross that bridge when we get there.

Disclosures:
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Disclaimer: The above perspective is the opinion of the author and does not necessarily reflect the view of the Partners HealthCare system or Harvard Medical School.

References:


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