

Combination of Available Tests Helps Predict Alzheimer's Disease Risk

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With age, forgetfulness and other signs of memory loss sometimes appear, prompting elderly individuals to seek a medical evaluation amid fears that they may be experiencing early symptoms of Alzheimer's disease (AD), the most common type of dementia among Americans aged 65 and older.

But even when early memory problems suggest the potential for impending AD, the actual risk is variable. Some patients are at high risk while others are not. The challenge for doctors has long been to differentiate that risk so they can determine the appropriate course of management.

In a paper to be published in the October 25 issue of the journal *Neurology*, a team of physicians and scientists from the University of California, San Diego School of Medicine and elsewhere describe using a combination of broadly available medical tests to produce a much improved predictive picture of the likelihood of impending AD in patients with mild cognitive impairment (MCI) - an intermediate stage between the expected cognitive decline of normal aging and the more pronounced decline of dementia.

"I'm extremely excited about these results," said neurologist James Brewer, MD, PhD, an associate professor of radiology and neurosciences and part of the Alzheimer's Disease Neuroimaging Initiative research team at UC San Diego. "The good news is that we can partially reassure those folks who are negative on these tests, at least regarding their next three years. We have never been able to do that before. These individuals, despite having a real memory problem, have no greater risk of near-term dementia than a similarly aged healthy person without a memory complaint."

To determine the likelihood of developing Alzheimer's disease, the UC San Diego researchers compared risk factors based on magnetic resonance imaging (MRI), cerebrospinal fluid (CSF) and neuropsychological testing. Unlike other efforts that have evaluated the predictive capabilities of research-based biomarkers, MRI, CSF and neuropsychological tests are all technologies widely available to clinicians.

The researchers found that these available biomarkers significantly improved accuracy in predicting near-term conversion to dementia. In combination, their prediction rate was almost perfect: None of the individuals who tested negative on all three measures went on to develop AD in the three-year follow-up. By comparison, almost 90 percent of individuals who tested positive on all three measures were demented at the end of three years.

The presence of medial temporal atrophy, determined by automated analysis of MRI using an FDA-approved software package, was associated with the likeliest chance of near-term dementia, with a median dementia-free survival time of only 15 months.

Brewer said the findings foretell a paradigm shift in the diagnosis of Alzheimer's disease.

"Instead of saying, 'Let's wait a year and see if this gets worse,' our neurologists can say, 'Let's get a volumetric MRI and check back in a month to see if your complaint is due to neurodegeneration.' That ability makes a huge difference in how we proceed. Maybe the memory complaint isn't due to neurodegeneration, but

rather it's a side effect of a medication, a sign of depression or someone is simply anxious and worried. Being able to reassure at least some patients that they are not at significant near-term risk of AD is something we never could do in the past, given the high prevalence of the disease."

Co-authors of the paper are David Heister and Linda K. McEvoy, department of Radiology, UC San Diego; Sebastian Magda, CorTechs Labs, La Jolla, CA; Kaj Blennow, Clinical Neurochemistry Laboratory, Sahlgrenska Academy, Goteborg University, Molndal, Sweden.

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