Measuring Brain Atrophy in Patients with Mild Cognitive Impairment

New, automated way of measuring brain structures appears effective in predicting progression to Alzheimer's Disease

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Scientists at the University of California, San Diego School of Medicine have shown that a fully automated procedure called Volumetric MRI - which measures the "memory centers" of the brain and compares them to expected size - is effective in predicting the progression from mild cognitive impairment (MCI) to Alzheimer's disease. The procedure can be readily used in clinics to measure brain atrophy, and may help physicians to predict decline in MCI patients. Their study has been published in the June issue of the journal *Alzheimer Disease and Associated Disorders*.

"Use of this procedure is like bringing the experience of an expert neuro-radiologist to any clinic that has the right software," said James Brewer, MD, PhD, assistant professor in UC San Diego's Departments of Radiology and Neurosciences. "These fully automated and rapid methods of measuring medial temporal lobe volumes may help clinicians predict cognitive decline in their patients, and have the potential to influence how neurology is practiced."

Mild cognitive impairment (MCI) is considered a transitional stage between the forgetfulness associated with normal aging and Alzheimer's disease. Yet, many patients with MCI do not progress to Alzheimer's, and these individuals don't need treatments targeted to prevent or slow down neuro-degeneration. Therefore, objective measures are necessarily to distinguish MCI patients who will clinically decline from those who will remain stable.

"Our goal was to find neuroimaging measures of change that reflected more than merely a person's advancing age, but instead correlated tightly with how a person's cognitive status worsens over time," said co-author Michael Rafii, MD, PhD, assistant professor of neurosciences at UC San Diego. "It's too early to draw a definitive comparison, but it appears that these early changes - especially shrinking of the hippocampus - may offer a robust biological marker for change."

Medial temporal lobe atrophy has been associated with increased risk for conversion of MCI to Alzheimer's disease. However, until now, studies have focused only on measurements of the brain's hippocampus. The extent to which volumes of the amygdala - the section of the brain associated with emotions - and the nearby temporal horn could predict cognitive decline was unknown.

In addition, methods to measure these parts of the brain relied on subjective assessments of MRIs using a "tracing technique" that literally required a drawing of these portions of the brain - a technique that isn't practical or possible in most clinical settings.

For more than a year, researchers at the Memory Disorders Clinic at UC San Diego Medical Center have been successfully using a fully computerized procedure that takes images from the MRI scanner and translates them into quantitative values, according to Rafii, the clinic's director. UC San Diego was the first clinic site to use this technology, which is now starting to be used in other clinical settings throughout the country.

The study looked at the fully automated volume measures of 269 MCI patients over a six-month interval. Baseline volume measurements of the hippocampus, amygdala and temporal horn were evaluated as predictors of cognitive change as measured by two commonly used instruments for screening cognitive function and dementia. Patients with smaller volumes of the hippocampus and amygdala showed more rapid clinical decline on these tests.

"These values objectively measure the hippocampus and amydala, and early data confirm previous findings that these brain areas may atrophy early in Alzheimer's disease and can offer a clinical marker for change," said Rafii. The fluid-filled temporal horn increases as the hippocampus shrinks, and these complementary measurements may correlate closely with how a patient's cognitive status worsens over time, he added.

The study is part of the Alzheimer Disease Neuroimaging Initiative (ADNI), the largest Alzheimer's disease study ever funded by the National Institutes of Health. Announced in October 2004 and set to run until 2010, this public-private consortium has engaged 59 research centers in the U.S. and Canada in a massive effort to follow 821 research volunteers for three years. One of its main goals is to develop biomarkers that can ultimately be approved by the FDA to substitute for cognitive measures in Alzheimer's disease clinical trials.

Sanja Kovacevic, PhD, UC San Diego Department of Radiology, also contributed to this study, which was supported by the National Institute of Neurological Disorders and Stroke, part of the National Institutes of Health, and the Alzheimer's Disease Neuroimaging Initiative, funded by the National Institute on Aging, the National Institute of Biomedical Imaging and Bioengineering and the Food and Drug Administration. Principle investigator of ADNI is Michael W. Weiner, MD, VA Medical Center and University of California, San Francisco.

Scanner images were processed using the NeuroQuant software package produced by CorTechs Labs, Inc. of La Jolla, California. Images were downloaded from the ADNI image depository at the Laboratory of Neuroimaging at UCLA.

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