

Alzheimer's Cognitive Decline Slows in Advanced Age

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The greatest risk factor for Alzheimer's disease (AD) is advancing age. By age 85, the likelihood of developing the dreaded neurological disorder is roughly 50 percent. But researchers at the University of California, San Diego School of Medicine say AD hits hardest among the "younger elderly" – people in their 60s and 70s – who show faster rates of brain tissue loss and cognitive decline than AD patients 80 years and older.

The findings, reported online in the August 2, 2012 issue of the journal *PLOS One*, have profound implications for both diagnosing AD – which currently afflicts an estimated 5.6 million Americans, a number projected to triple by 2050 – and efforts to find new treatments. There is no cure for AD and existing therapies do not slow or stop disease progression.

"One of the key features for the clinical determination of AD is its relentless progressive course," said Dominic Holland, PhD, a researcher at the Department of Neurosciences at UC San Diego who led the study and is the paper's first author. "Patients typically show marked deterioration year after year. If older patients are not showing the same deterioration from one year to the next, doctors may be hesitant to diagnose AD, and thus these patients may not receive appropriate care, which can be very important for their quality of life."

Holland and colleagues used imaging and biomarker data from participants in the Alzheimer's Disease Neuroimaging Initiative, a multi-institution effort coordinated at UC San Diego. They examined 723 people, ages 65 to 90 years, who were categorized as either cognitively normal, with mild cognitive impairment (an intermediate stage between normal, age-related cognitive decline and dementia) or suffering from full-blown AD.

"We found that younger elderly show higher rates of cognitive decline and faster rates of tissue loss in brain regions that are vulnerable during the early stages of AD," said Holland. "Additionally cerebrospinal fluid biomarker levels indicate a greater disease burden in younger than in older individuals."

Holland said it's not clear why AD is more aggressive among younger elderly.

"It may be that patients who show onset of dementia at an older age, and are declining slowly, have been declining at that rate for a long time," said senior author Linda McEvoy, PhD, associate

professor of radiology. “But because of cognitive reserve or other still-unknown factors that provide ‘resistance’ against brain damage, clinical symptoms do not manifest till later age.”

Another possibility, according to Holland, is that older patients may be suffering from mixed dementia – a combination of AD pathology and other neurological conditions. These patients might withstand the effects of AD until other adverse factors, such as brain lesions caused by cerebrovascular disease, take hold. At the moment, AD can only be diagnosed definitively by an autopsy. “So we do not yet know the underlying neuropathology of participants in this study,” Holland said.

Clinical trials to find new treatments for AD may be impacted by the differing rates, researchers said. “Our results show that if clinical trials of candidate therapies predominately enroll older elderly, who show slower rates of change over time, the ability of a therapy to successfully slow disease progression may not be recognized, leading to failure of the clinical trial,” said Holland. “Thus, it’s critical to take into account age as a factor when enrolling subjects for AD clinical trials.”

The obvious downside of the findings is that younger patients with AD lose more of their productive years to the disease, Holland noted. “The good news in all of this is that our results indicate those who survive into the later years before showing symptoms of AD will experience a less aggressive form of the disease.”

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