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Researchers image earliest signs of Alzheimer's, before symptoms appear

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(PhysOrg.com) -- Estimates are that some 10 percent of people over the age of 65 will develop Alzheimer's disease, the scourge that robs people of their memories and, ultimately, their lives.

While researchers race to find both the cause and the cure, others are moving just as fast to find the earliest signs that will predict an eventual onset of the disease, well before any outward symptoms. The reason is simple: The earlier the diagnosis, the earlier treatments can be applied.

Now, through the use of sophisticated brain-imaging techniques, researchers at UCLA have been able to predict a brain's progression to Alzheimer's by measuring subtle changes in brain structure over time, changes that occur long before symptoms can be seen. The research appears in two separate papers currently available online and scheduled for future print publication.

In the first study, which appears in the online edition of the journal Human Brain Mapping, UCLA assistant clinical professor of neurology Liana Apostolova and colleagues tracked 169 people over three years who had been diagnosed with mild cognitive impairment (MCI), a condition that causes memory problems greater than those expected for an individual's age — but not the personality or cognitive changes that define Alzheimer's. They found that after three years, those who went on to be diagnosed with Alzheimer's disease showed a 10 to 30 percent greater atrophy in two specific locations within the brain's hippocampus, a part of the brain known to be critical for long-term memory.

In the second study, which appears in the online edition of the journal Neurobiology of Aging, the researchers looked at 10 cognitively normal elderly people and compared their brain scans with those of seven other elderly people who were later diagnosed with MCI and then Alzheimer's. Again, they found that the group that went on to be diagnosed with Alzheimer's showed the same pattern of atrophy in the same regions of the hippocampus.

This shows, Apostolova said, that excess atrophy is present in cognitively normal individuals who are predestined to develop MCI. Further, that atrophy ultimately cascades across the entire hippocampus of the brain, leading to Alzheimer's disease.

"We feel this is an important finding because it is in living humans," said Apostolova, senior author of both papers and a member of the UCLA Laboratory of Neuro Imaging. "Now we have a sensitive technique that shows the 'invisible' — that is, the progression of a disease before symptoms appear."

In the first study, the researchers wanted to track disease progression in the hippocampus. In earlier work, Apostolova's lab had shown that greater atrophy can be documented in the living brain and that it can predict conversion from MCI to Alzheimer's. The researchers looked at two areas within the hippocampus: the CA1 (cornu ammonis) and the subiculum. In this study, they tracked atrophy from the CA1 as it spread to the subiculum, which matched disease progression from the MCI state to a diagnosis of Alzheimer's.

They split the MCI subjects into those who had no noticeable hippocampal atrophy other then what is expected from normal aging alone, and those who had atrophy greater than expected for normal aging. Three years later, the researchers followed up and compared the MCI group with no visual change to the one with premature change.

They found 10 to 30 percent greater atrophy in the CA1 and subiculum of those MCI patients with premature atrophy who were later diagnosed with Alzheimer's.

"In looking at the longitudinal changes, we could see there was definitive evidence of a progression from the CA1 to the subiculum region, and on to the other regions of the hippocampus," Apostolova said.

The second, much smaller study of 17 individuals confirmed the findings of the larger study, but this time in people who were cognitively healthy. Here, the researchers looked at 10 cognitively normal elderly subjects who remained normal at three-year and six-year follow-ups, and at seven cognitively normal elderly subjects who were diagnosed with MCI between two and three years after their initial brain scan and with Alzheimer's approximately seven years after the initial scan.

Again, excessive atrophy in the CA1 and subicular regions was present in cognitively normal individuals who went on to be diagnosed with MCI, and a slow progression of atrophy beyond the CA1 and subiculum to other regions was evident in those ultimately diagnosed with Alzheimer's.

Apostolova noted that the degree of atrophy is not easily visible in the brain scans and that very sensitive techniques are required to show its progression.

"We can't see the pathologic changes, but we clearly see the neurodegenerative atrophy associated with MCI and AD, and how it spreads through the hippocampus," she said. "This is exactly what a biomarker, being an indirect measure of disease progression, is supposed to do."

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