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Brain May Shrink in Decade Before Alzheimer's Symptoms Appear

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Although study participants had no memory problems at first, the disease had taken a foothold



The brains of people diagnosed with Alzheimer's disease start shrinking up to a decade before symptoms appear, a new study finds.

Researchers from Rush University Medical Center in Chicago and Massachusetts General Hospital in Boston did brain imaging tests on older adults with no signs of memory loss.

Of the 33 people in the Mass General group, eight developed Alzheimer's over the course of 11 years. In the Rush group, seven of 32 people followed for an average of seven years developed the disease.

About 55 percent of those whose brains were in the upper tertile (third) of atrophy developed Alzheimer's, while none of those whose brains in the bottom tertile (little or no atrophy) developed Alzheimer's. Among those with moderate amounts of atrophy, about 20 percent developed the disease.

"We could differentiate those who would decline from those who would remain healthy," said senior study author Leyla deToledo-Morrell, director of the graduate program in neuroscience at Rush University Medical Center.

Based on the atrophy measurements, "we could even determine how quickly they were going to develop Alzheimer's disease," she added.

The study is published in the April 13 issue of *Neurology*.

Doctors have long known that Alzheimer's is an insidious disease, and that changes in the brain begin long before the first symptoms become evident, said Dr. Jeffrey Burns, director of the Alzheimer and Memory Program at University of Kansas Medical Center.

"This suggests, along with other studies, that Alzheimer's pathology is likely present years, if not decades, before the emergence of symptoms," Burns said.

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What's probably happening is that biochemical changes in the brain that are only partially understood cause degeneration of brain cells, said Dr. Steven DeKosky, vice president and dean of the University of Virginia School of Medicine. Over time, the cells begin to die off, leading to structural changes in the brain tissue, or atrophy.



Specifically, people in the study who would later be diagnosed with Alzheimer's disease were more likely to show cortical thinning, or shrinkage, in several brain regions, including the medial temporal lobe, temporal pole and the superior frontal gyrus, which prior research has implicated in the early stages of Alzheimer's.

"The amount of atrophy was much, much, much less than in a person with Alzheimer's disease," deToledo-Morrell said.

"But because each one who developed Alzheimer's disease showed it, the results are extremely significant," she added.

Eventually, the hope is that one day there will be drugs to slow the progression of the disease -- there are none currently available -- and being able to diagnosis Alzheimer's early would mean people could start treatment before they have experienced significant declines, she said.

"If we can identify people at risk of the disease, they would be at much greater benefit from receiving treatment, rather than people who have already developed Alzheimer's, who already have a certain amount of cell death and you can't really rescue those cells," she said.

Though the number of participants in the study was small and the findings need to be repeated in larger populations, it is "remarkable they saw changes this clear with this small number of cases," DeKosky said.

Still, it's doubtful that such a technique is specific enough to be used to predict Alzheimer's on an individual basis, the experts said, because not everyone who had higher levels of atrophy got Alzheimer's. "It's a ways away from being clinically useful," Burns said.

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But, a second study from the same journal may have practical applications immediately. The study found that vascular disease risk factors, such as hypertension, diabetes, cardiovascular disease and high cholesterol, may raise the risk of Alzheimer's disease.

The good news is that treating those conditions lowered the risk of Alzheimer's.

Chinese researchers followed 837 people over age 55 with mild cognitive impairment, which is often a precursor to Alzheimer's, for five years.



During that time, 298 developed Alzheimer's, while the others still had mild cognitive impairment but had not progressed to Alzheimer's.

People who were treated for all of their vascular disease risk factors were less likely to progress to Alzheimer's disease than those who weren't treated or who only had some of their risk factors treated, according to the study.

"That's a terrific study," Burns said. "It says vascular disease has a real effect on the manifestation of Alzheimer's disease. The vascular disease is damaging your brain and is probably causing you to have lowered resistance to the pathological effects of Alzheimer's disease."

Vascular disease can damage the blood vessels leading to and within the brain, he added. "With vascular disease, the brain is under attack two ways, so you develop Alzheimer's disease sooner."

Cholesterol-lowering medications, blood pressure medications and lifestyle changes such as losing weight and exercising can all help lower vascular disease risk factors, DeKosky said.

"If you aggressively treat vascular disease factors, you can delay the breakthrough of clinical symptoms of Alzheimer's," DeKosky said. "That's a pretty exciting finding."

More information

- The [U.S. National Institute on Aging](#) has more on Alzheimer's.

SOURCES: Leyla deToledo-Morrell, Ph.D., director, graduate program in neuroscience, Rush University Medical Center, Chicago; Jeffrey Burns, M.D., director, Alzheimer and Memory Program, University of Kansas Medical Center; Steven T. DeKosky, M.D., vice president and dean, University of Virginia School of Medicine; April 13, 2011, *Neurology*

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