

## **Study shows brain structures make some people resilient to Alzheimer's disease**

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Top image: dendritic spines of control group. Middle image: spines of the 'pathology without disease' group". Bottom image: Alzheimer's disease group. Credit: University of Alabama at Birmingham

The size, shape and number of dendritic spines in the brain may play a major role in whether someone gets Alzheimer's disease, according to new research from the University of Alabama at Birmingham. Dendritic



spines are sub-units of neurons that act as the connector to other neurons.

In findings published Oct. 24 in the *Annals of Neurology*, the research team showed, for the first time, that the presence of healthy <u>dendritic</u> <u>spines</u> conveyed a protective effect against Alzheimer's in people whose brains had proteins associated with the <u>disease</u>.

"One of the precursors of Alzheimer's is the development in the brain of proteins called amyloid and tau, which we refer to as the pathology of Alzheimer's," said Jeremy Herskowitz, Ph.D., assistant professor in the Department of Neurology, School of Medicine and lead author of the study. "However, about 30 percent of the aging population have amyloid and tau buildup but never develop dementia. Our study showed that these individuals had larger, more numerous dendritic spines than those with dementia, indicating that spine health plays a major role in the onset of disease."

Neurons are constantly sending out long, thin dendritic spines in search of other <u>neurons</u>. When they connect, a synapse, or exchange of information between neurons, occurs. This is the basis for memory and learning.

"One obvious culprit in Alzheimer's disease is the loss of dendritic spines and thus the loss of synapses," said Herskowitz, who is the Patsy W. and Charles A. Collat Scholar in Neuroscience. "This would impair the ability to think, so the assumption has been that those without dementia had healthy spines and those with dementia did not. But no one had gone in to see if that was true."

Herskowitz's team studied brain samples from patients at memory clinics at Emory University. The control group did not have the Alzheimer's pathology of <u>amyloid plaques</u> and tau tangles and never developed



dementia. A second group had the Alzheimer's pathology and progressed to the disease. The third group had the pathology, but no disease.

The researchers took thousands of microscopy images of the subject brains. Those images were then turned into 3-D images using novel, exclusive software. This allowed the team to look more fully at the shape and dimensions of each image.

"We first noted that the control group had more dendritic spines than the group with Alzheimer's, which matched beautifully with existing historical data," Herskowitz said. "But we also saw that the group with Alzheimer's pathology but no disease also had more spines than the Alzheimer's group. In fact, they had roughly the same spine density as the control group. What is even more exciting is that the 'pathology but no disease' group had very long spines, longer than both the <u>control group</u> and the disease group."

Herskowitz says the longer spines demonstrated great plasticity, or ability to move. This indicates that they could navigate around or through amyloid plaques or <u>tau tangles</u> in their efforts to connect with other neurons.

"This provides an explanation of why some people are cognitively resilient to Alzheimer's disease, even if they possess the typical Alzheimer's pathology," he said.

Herskowitz says that the high plasticity and density of dendritic spines in this population could be genetic. Another theory suggests that it could be the result of healthy lifestyle behaviors, such as good diet and exercise, which are known to be protective against dementia. It may be that the reason these behaviors are protective is that they help maintain spine health, plasticity and density.



The findings also offer a new target for slowing or preventing Alzheimer's in the first place, Herskowitz says.

"This provides a target for drugs that would be designed to support and maintain dendritic spine health in an effort to rebuild neurons or prevent their loss," he said. "This data suggests that rebuilding neurons is possible. And as we are better able to identify the increase of amyloid and tau early in the progression of the disease, even before symptoms arise, we might be able to one day offer a medication that can contribute to maintaining healthy dendritic spines in those with the Alzheimer's pathology."

Herskowitz credits the innovative 3-D imaging system used in the study to groundbreaking work done by UAB science and technology honors student Benjamin Boros.

**More information:** Benjamin D. Boros et al. Dendritic spines provide cognitive resilience against Alzheimer's disease, *Annals of Neurology* (2017). DOI: 10.1002/ana.25049

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