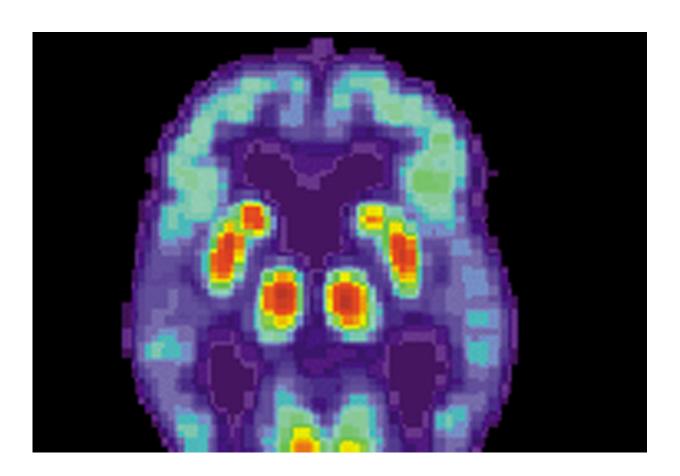


## Scientists discover why some people with brain markers of Alzheimer's have no dementia

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PET scan of a human brain with Alzheimer's disease. Credit: public domain

A new study from The University of Texas Medical Branch at Galveston



has uncovered why some people that have brain markers of Alzheimer's never develop the classic dementia that others do. The study is now available in the *Journal of Alzheimer's Disease*.

Alzheimer's disease, the most common form of dementia, affects more than 5 million Americans. People suffering from Alzheimer's develop a buildup of two proteins that impair communications between nerve cells in the brain—plaques made of <u>amyloid beta</u> proteins and <u>neurofibrillary tangles</u> made of tau proteins.

Intriguingly, not all people with those signs of Alzheimer's show any cognitive decline during their lifetime. The question became, what sets these people apart from those with the same plaques and tangles that develop the signature dementia?

"In previous studies, we found that while the non-demented people with Alzheimer's neuropathology had amyloid plaques and neurofibrillary tangles just like the demented people did, the toxic amyloid beta and tau proteins did not accumulate at synapses, the point of communication between nerve cells," said Giulio Taglialatela, director of the Mitchell Center for Neurodegenerative Diseases. "When nerve cells can't communicate because of the buildup of these toxic proteins that disrupt synapse, thought and memory become impaired. The next key question was then what makes the synapse of these resilient individuals capable of rejecting the dysfunctional binding of amyloid beta and tau?"

In order to answer this question, the researchers used high-throughput electrophoresis and mass spectrometry to analyze the protein composition of synapses isolated from frozen brain tissue donated by people who had participated in brain aging studies and received annual neurological and neuropsychological evaluations during their lifetime. The participants were divided into three groups—those with Alzheimer's dementia, those with Alzheimer's brain features but no signs of dementia



and those without any evidence of Alzheimer's.

The results showed that resilient individuals had a unique synaptic protein signature that set them apart from both demented AD patients and normal subjects with no AD pathology. Taglialatela said that this unique protein make-up may underscore the synaptic resistance to amyloid beta and tau, thus enabling these fortunate people to remain cognitively intact despite having Alzheimer's-like pathologies.

"We don't yet fully understand the exact mechanism(s) responsible for this protection," said Taglialatela. "Understanding such protective biological processes could reveal new targets for developing effective Alzheimer's treatments."

**More information:** Olga Zolochevska et al. Postsynaptic Proteome of Non-Demented Individuals with Alzheimer's Disease Neuropathology, *Journal of Alzheimer's Disease* (2018). DOI: 10.3233/JAD-180179

## Provided by University of Texas Medical Branch at Galveston

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