

# Depression, tau deposits seen in subset of middle-aged persons

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Mitzi Gonzales, Ph.D., of The University of Texas Health Science Center at San Antonio, is lead author of a study suggesting that middle-aged people with depressive symptoms who carry a genetic variation called apolipoprotein (APOE)  $\epsilon 4$  may be more at risk to develop tau protein accumulations in the brain's emotion- and memory-controlling regions. Credit: UT Health San Antonio

Middle-aged people with depressive symptoms who carry a genetic

variation called apolipoprotein (APOE)  $\epsilon$ 4 may be more at risk to develop tau protein accumulations in the brain's emotion- and memory-controlling regions, a new study by researchers from The University of Texas Health Science Center at San Antonio (UT Health San Antonio) and collaborating institutions suggests.

*The Journal of Alzheimer's Disease* published the findings in its June 2021 print issue. The research is based on depression assessments and positron emission tomography (PET) imaging conducted among 201 participants in the multigenerational Framingham Heart Study. The mean age of these participants was 53.

## **Decades before diagnosis**

PET scans typically are conducted in older adults, so the Framingham PET studies in middle-aged persons are unique, said Mitzi M. Gonzales, Ph.D., lead author of the study and a neuropsychologist with the Glenn Biggs Institute for Alzheimer's and Neurodegenerative Diseases, which is part of UT Health San Antonio.

"This gives us an interesting opportunity to study people at midlife and get a sense of factors that might be associated with protein accumulations in individuals who are cognitively normal," Dr. Gonzales said. "These persons are likely decades before any type of dementia diagnosis, if they are to develop dementia in the future."

## **No associations found with amyloid beta**

Amyloid beta (amyloid- $\beta$ ) and tau are proteins that aggregate in the brains of people with Alzheimer's disease and also typically increase to a milder extent with normal aging. The study found no associations of [depressive symptoms](#) and depression with amyloid- $\beta$ . The only association was with tau, and only in APOE  $\epsilon$ 4 variant carriers. About

one-fourth of the participants (47 of 201) were  $\epsilon 4$  carriers, by virtue of having at least one copy of the  $\epsilon 4$  allele.

Having one copy of APOE  $\epsilon 4$  increases the risk of developing Alzheimer's by as much as two- to threefold, but some people with this variant live into their 80s and 90s and never develop the disease. "It's important to keep in mind that just because a person is identified as carrying the APOE  $\epsilon 4$  allele does not mean that he will develop dementia in the future," Dr. Gonzales said. "It just means that the risk is higher."

Depressive symptoms (and depression if symptoms were severe enough to reach that diagnostic threshold) were evaluated with the Center for Epidemiological Studies Depression Scale at the time of PET imaging, as well as eight years prior. Associations between depressive symptoms and depression with PET outcomes at both time points were evaluated, adjusting for age and sex.

## **Centers of emotion and cognition**

The study showed associations between depressive symptoms and increased tau in two brain regions, the [entorhinal cortex](#) and amygdala. "These associations do not infer that the tau accumulation causes the depressive symptoms, or vice versa," Dr. Gonzales said. "We only note that both are present in the  $\epsilon 4$  carriers."

The entorhinal cortex is important for memory consolidation and tends to be an area where protein deposition occurs early on, she noted. The amygdala, meanwhile, is considered the emotion center of the brain.

"Longitudinal studies are needed to further understand what is happening, but it is intriguing to think about the clinical significance of our findings in terms of cognition as well as emotional regulation," Dr. Gonzales said.

**More information:** Mitzi M. Gonzales et al, Association of Midlife Depressive Symptoms with Regional Amyloid- $\beta$  and Tau in the Framingham Heart Study, *Journal of Alzheimer's Disease* (2021). [DOI: 10.3233/JAD-210232](https://doi.org/10.3233/JAD-210232)

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