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Late-life depression accelerates cognitive decline in a tauopathy mouse model

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Background: Clinical studies suggest that depressive symptoms could be considered an important risk factor for the future development of cognitive impairment and even Alzheimer's disease (AD). In fact, there is a strong association between depression in later life and AD. The age of onset of AD has been shown to be accelerated in patients with mild cognitive impairment (MCI) with a history of depression, and women appear to be particularly more vulnerable to this condition. In addition, individuals with MCI who present depressive symptoms have an elevated burden of amyloid-beta, one of the featured toxic proteins associated with Alzheimer's pathology, and a higher risk of developing AD compared to non-depressed MCI patients. Although it has been described that some transgenic models of AD can develop signs similar to depression in advanced stages, it is unknown whether late-life depression can accelerate tau-associated pathology and, therefore, acting as a risk factor for AD.

Method: In this study, we induced chronic unpredictable mild stress (CUMS) in P301S tau transgenic mice to determine whether depression is a cause, rather than a consequence, of the development of AD.

Result: The results of our study indicate that the induction of CUMS in transgenic animals induces phenotypic changes related to a depressive state.

Conclusion: The findings obtained after inducing late-life depression-like in P301S mice indicate that depression could be considered a risk factor for AD, by accelerating tau aggregation and worsening clinical signs.