COGNITIVE DECLINE AND TAU-ASSOCIATED PATHOLOGY WORSEN AFTER LATE-LIFE DEPRESSION IN P301S MICE

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Recent studies suggest that depression may be a crucial risk factor for the development of cognitive impairment and Alzheimer's disease (AD). In fact, there is a strong association between late-life depression and AD. The age of AD onset 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, the main toxic protein associated with AD 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, the induction of AD pathology due to a depressive process has not been studied under experimental conditions to emulate late-life depression as a risk factor for dementia. The objective of this study is to determine, by inducing unpredictable mild chronic stress (CUMS) in tau transgenic P301S mice, whether depression is a cause, rather than a consequence, of tau-associated pathology. The results of our study indicate that the induction of CUMS in transgenic animals accelerates tau pathology, synaptic impairment, elevates neuroinflammation, and triggers GABAergic alterations, in addition to worsen clinical signs. The findings generated in this project could provide solid evidence of depression as a risk factor for AD and other tauopathies.