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Brain inflammation links memory impairment and depressive-like behavior induced by Alzheimer’s Aβ oligomers in rodents

Sergio T. Ferreira
Institute of Medical Biochemistry, Federal University of Rio de Janeiro, Brazil

Considerable clinical and epidemiological evidence connects Alzheimer’s disease (AD) to depression. However, the molecular/cellular mechanisms underlying this association have only recently begun to be unraveled. In recent studies, we found that Aβ oligomers (AβOs), toxins that accumulate in the AD brain and are increasingly thought to cause synapse failure, activate pro-inflammatory and neuronal stress response pathways that lead to memory impairment. AβOs further induce depressive-like behavior in rodents, also found to be associated with brain inflammation and gliosis. More recently, we found that AβOs instigate microglial activation and inhibition of serotonergic signaling, and that microglial-derived TNF-α mediates behavioral alterations induced by oligomers. Current findings establish that oligomer-induced microglial activation and TNF-α release link memory impairment and depressive-like behavior in mice, providing support to clinical evidence connecting AD and depression. Results further suggest a mechanism by which elevated brain levels of AβOs may be linked to changes in cognition and mood in AD.