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VISCERAL ADIPOSE TISSUE TRIGGERS TAU PATHOGENESIS IN TRANSGENIC MICE TROUGH CDK5/P25 PATHWAY

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Abstract Body

Alzheimer's disease (AD) is a complex disorder and multiple molecular mechanisms are involved in AD onset and progression. Recent evidences have suggested that metabolic alterations are an important pathological feature in this disease progression. Likewise, diabetes and obesity, two mayor metabolic illnesses, are risk factors for AD. These two overwhelming diseases are associated with a significant expansion of visceral adipose tissue (VAT). Here, we hypothesize that the VAT may serve as a key communicator organ between the brain and peripheral metabolic illnesses and affecting both types of disorders.

We used histological stains, immunohistochemistry and biochemical means to determine changes in the visceral adipose tissue from WT and db/db mice. Moreover, similar techniques were used in 3xTg-AD mice that received white fat pads from WT and db/db donors to determine any changes in amyloid and tau pathology.

Our study shows that recipient 3xTg-AD mice from db/db mice fat pads develop profound changes in tau pathology due to increased CDK5 expression compared to 3xTg-AD mice that received fat pads from WT mice. This increment in tau level was associated with elevated levels in IL-1β and profound microglia activation. Moreover, we found the opposite effect on amyloid pathology, in which insoluble Aβ levels and Thioflavin positive plaques were reduced in recipient 3xTg-AD mice from db/db fat pads compared to 3xTg-AD mice that received fad pads from WT mice. These reduction in Aβ levels were correlated with an increment in microglia phagocytic capacity.

Overall, our study demonstrate a novel important crosstalk between Alzheimer´s disease and obesity/diabetes type II through visceral adipose cells and a differential effect on tau and Aβ pathology mediated by an activated immune response.

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