

Hyperactivated astrocytic TGF- β signaling event in 5xFAD mice

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Transforming growth factor- β (TGF- β) is a pleiotropic cytokine that regulates a myriad of cellular processes, and dysregulation of TGF- β signaling has implications in aging-associated disorders, including Alzheimer's disease (AD). However, the role of TGF- β signaling in astrocytes altering brain function in aging and AD pathogenesis is not clear. Here, we investigated the changes of astrocytic TGF- β signaling events using aged mice and a mouse model of AD (5xFAD mice, Jackson lab). We found that TGF- β levels and linked signaling cascades were increased in astrocytes but not in neurons and microglia in aging and in an AD mouse model. Furthermore, inhibition of TGF- β activity disrupted glucose uptake, glycolysis, and mitochondrial function, resulting in reduced ATP and lactate production. These studies suggest that the activation of the TGF- β signaling pathway in astrocytes may play a critical role in aging and AD pathogenesis.

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