Research Week 2022

Effect of Hormone Replacement Therapy on Amyloid Beta Expression in the Amygdala of Aged Rhesus Macaques

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Keywords

Amyloid, estrogen, macaque, amygdala, Alzehimer's Disease

Abstract

Amyloid beta (Aβ) plaques represent one of the classic hallmarks of Alzheimer's disease (AD) pathology in the brain. In rhesus macaques, these plaques start becoming prominent when the animals are 20+ years old, although the underlying cause(s) are unclear. In the present study, our goal was to test the hypothesis that exposure to a Western-style, high-fat, high-sugar diet (WSD) and/or loss of ovarian steroids would advance the development of this histological marker of AD pathology. Specifically, we used immunohistochemistry to compare the expression of Aβ plaques in the amygdala of old female macaques, that were either maintained on a regular diet or exposed for 30 months to a WSD. Furthermore, to more closely mimic the hormonal status of post-menopausal women, all of the animals were ovariectomized (Ovx) and either received continuous estradiol hormone replacement therapy (Ovx+E) via a subcutaneous elastomer implant, or served as untreated controls. Overall, there was no obvious effect of dietary treatment on Aβ plaque deposition. However, there was a marked difference in the number of animals showing a high level of Aβ plaque deposition (i.e., >0.1% of amygdala area) between the Ovx and Ovx+E groups. Seven of the 12 (58%) Ovx controls showed this high level of Aβ plaque deposition compared to only 1 of 15 (7%) Ovx+E animals. Although it remains unclear if exposure to a WSD advances the onset of Aβ pathology, the data demonstrate that rhesus macaques, like humans, show an increased incidence of Aβ plaques during old age. Moreover, they suggest that estradiol supplementation may significantly delay or block AB plaque deposition in postmenopausal women.