Pathological changes to the visual system in Alzheimer’s Disease

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Understanding the mechanisms, timing, and progression of Alzheimer’s pathology in the visual system can help inform new, early interventions that may slow, stop, or reverse neurodegeneration. Research shows that visual deficits and accumulation of retinal amyloid beta and phosphorylated tau (ptau) pathologies may precede onset of cognitive decline in Alzheimer’s disease (AD). To elucidate the relationship between AD pathology and visual deficits, we examined two transgenic AD mouse models (Htau and 3xtg) and their respective controls (tau null and C57BLK6J) for visual deficits and pathological changes to brain regions that receive visual information. We assessed these variables across ages representing pre-pathological, emerging pathology, and progressing pathology disease states. Visual behavior tests were conducted using a fully-automated system to measure optomotor response in order to provide estimates of visual acuity. At pre-pathological ages, 3xtg mice had lower visual acuity than controls. With increasing age, both htau and 3xtg had reduced visual acuity compared to controls. There were no statistical differences between males and females of any strain in visual acuity at the ages tested; therefore, data are averaged across both sexes for each strain.

To assess brain pathology, immunofluorescent histological labeling techniques were used to identify amyloid beta, ptau, and inflammation in retinorecipient brain structures. Both htau and 3xTg mice show increased presence of Aβ, ptau and microglia inflammation in the SC at a prepathological age of 3 months compared to C57 and tau null mice. This supports literature that states retinal AD pathology precedes development of pathology in brain areas responsible for cognition—making visual disturbances and detection of retinal pathology potential early biomarkers for AD. Future work will characterize the progression of AD pathology in these mouse strains (and other AD models) throughout the central visual pathway in the brain.