Untangling Alzheimer´s Disease Hallmarks in Sensory Systems of Rodent Models

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BACKGROUND

Alzheimer´s disease (AD) is the most common form of neurodegenerative dementia. Major hallmarks of the disease are: (1) extracellular plaque deposits of the β-amyloid peptide (Aβ) and (2) intracellular neurofibrillary tangles of phosphorylated tau. Published research suggests an association between AD and functional impairments of sensory systems. In fact, the occurrence of tau-mediated glaucoma has been reported, as well as AD protein-associated neuropathology in sensory systems.

MATERIALS and METHODS

To explore disease mechanisms and investigate features of AD-related pathological changes, we analyzed eyes from the rodent AD model TMHT and non-transgenic control mice, aged 6 and 12 months in order to address suitable biomarkers for early screening tests of AD.

RESULTS

Histological analyses of different neuronal and neuropathological markers showed mostly a signal increase in TMHT mice compared to ntg controls. Those markers include cholinergic neurons, astroglia, microglia and phosphorylated tau at Thr231. Furthermore, tyrosine hydroxylase signal was significantly reduced in 6 months old TMHT mice compared to non-transgenic controls, suggesting impaired chatecholaminergic function.

SUMMARY and CONCLUSION

The TMHT model employed in this study together with the specific antibodies tested, provide a powerful tool to analyze neuropathology in the retina of TMHT mice. In fact, this study shows alterations in the expression of various neurotransmitters and neuropathological markers analyzed in TMHT compared to non-transgenic mice, not only at the age of 6 but also at 12 months. Additionally, evaluation of the visual cortex of the same animals has been started in order to receive a detailed characterization of the visual system neuropathology.

Contact for more information about the models:
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RESULTS

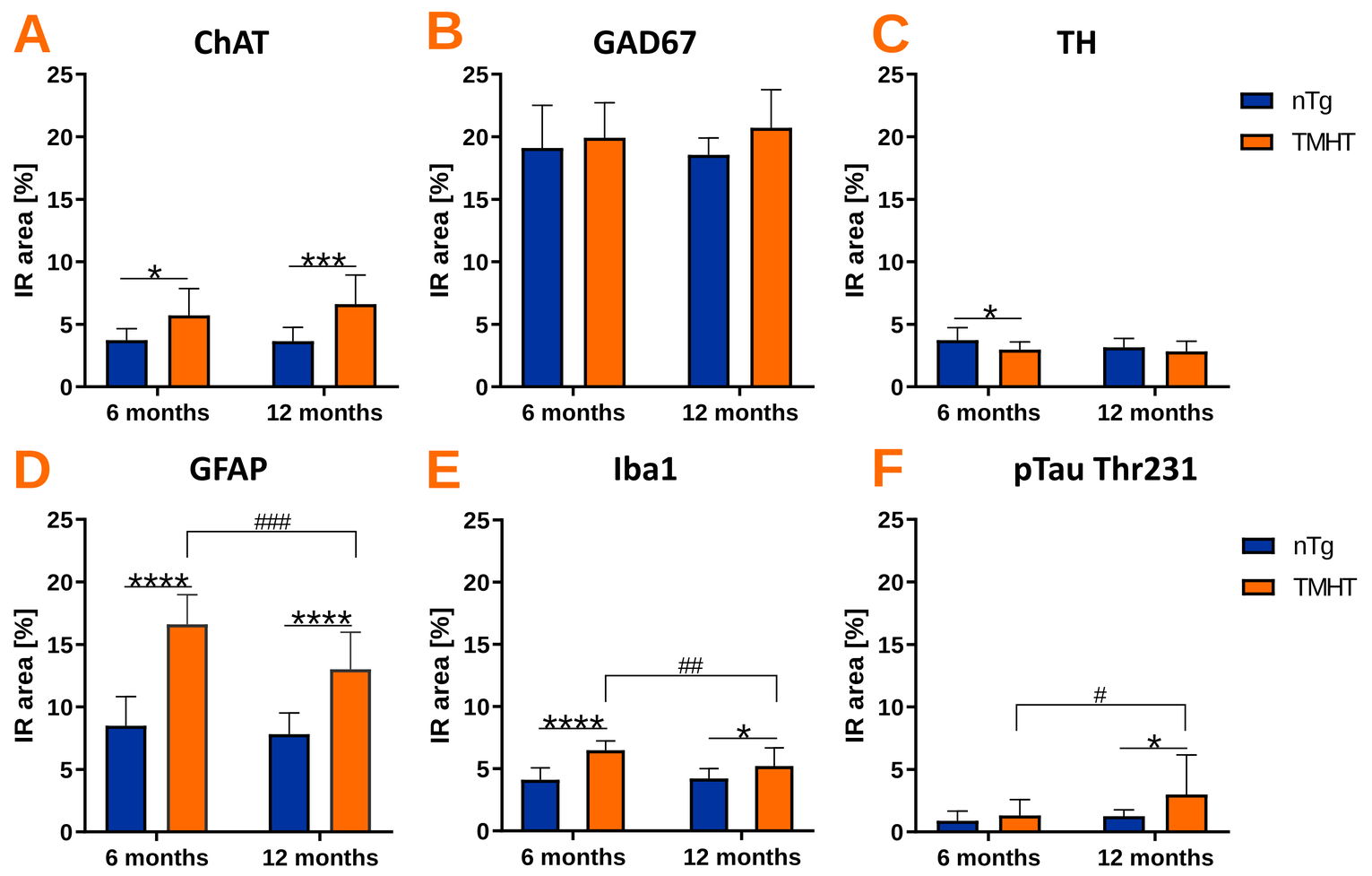

Figure 1. ChAT, GAD67, TH, GFAP, Iba1 and pTau Thr231 expression in the retina of TMHT mice: A: Choline acetyltransferase (ChAT) to label cholinergic cells; B: Glutamic acid decarboxylase 67 (GAD67) to label GABAergic cells; C: Tyrosine hydroxylase (TH) to label chatecholaminergic cells; D: Glial fibrillary acidic protein (GFAP) to label astroglia; E: Ionized calcium-binding adapter molecule 1 (Iba1) to label microglia; F: Phosphorylated Tau at Thr 231 (pTau Thr231). n = 12-19 per group; mean + SEM; A-F: Two-way-ANOVA followed by Sidak's multiple comparisons *posthoc* test.

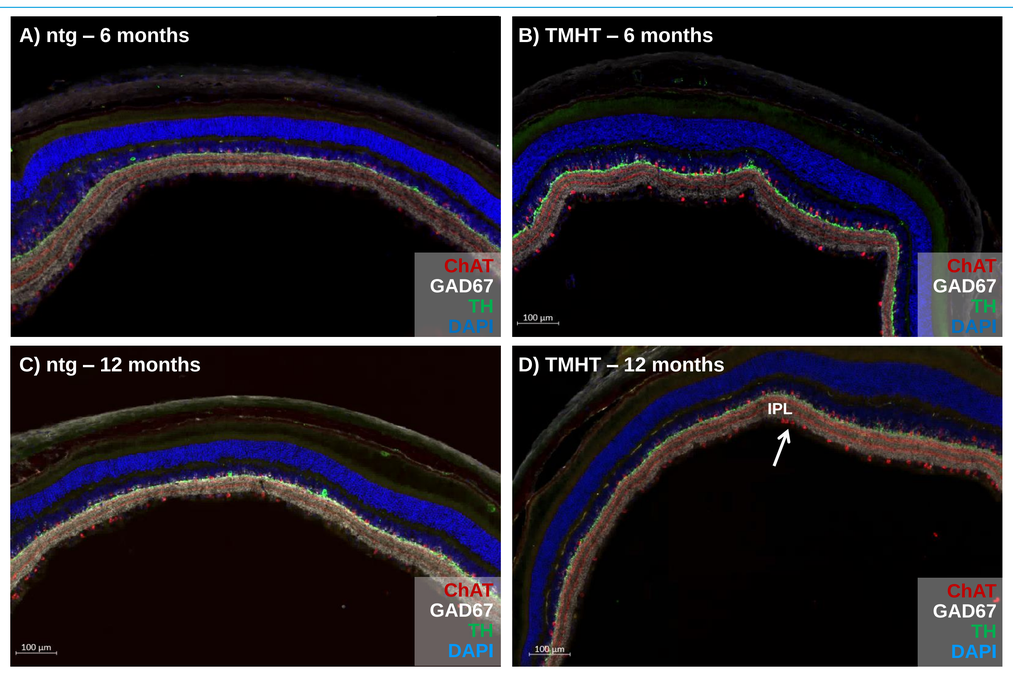

Figure 2: Detection of neurotransmitters in the retina of TMHT mice. Co-labeling of ChAT (red), GAD67 (white) and TH (green) in ntg (A,C) and TMHT mice (B,D). DAPI (blue) to stain cell nuclei. Peak expression of ChAT is observed in the inner plexiform layer (IPL) where cholinergic amacrine and ganglion cell dendrites form two distinct synaptic strata (white arrow in D). GAD67 signal is restricted to IPL. TH is observed in the inner nuclear layer (INL), stratifying mainly at the border to the IPL.

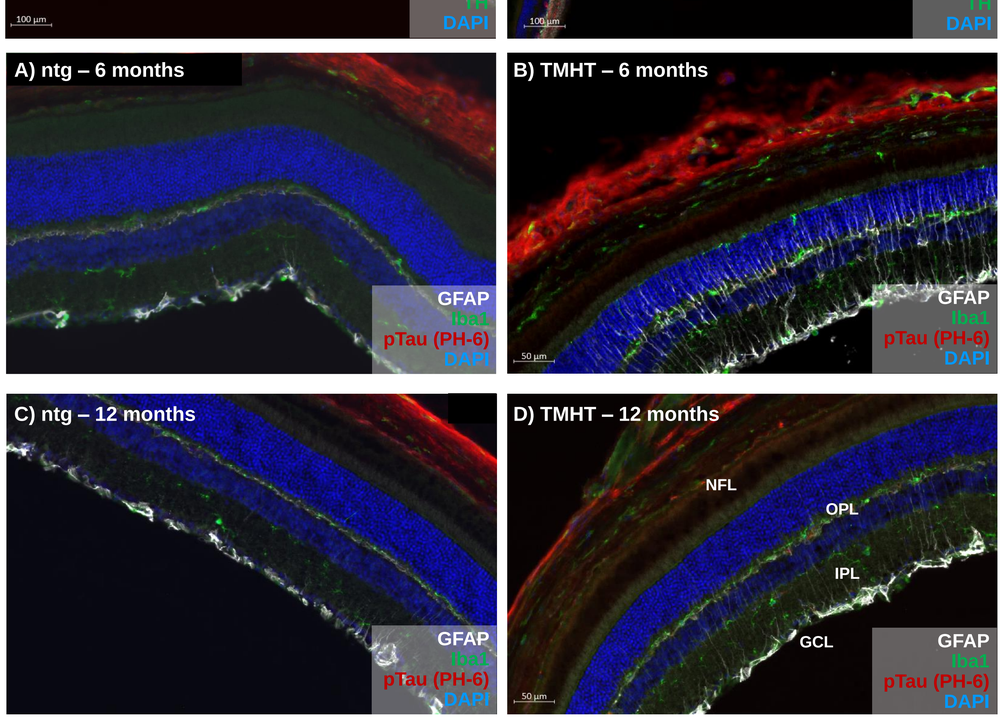

Figure 3: Detection of gliosis and tau in the retina of TMHT mice. Co-labeling of GFAP (white), Iba1 (green) and pTau Thr231 (red) in ntg (A,C) and TMHT mice (B,D). DAPI (blue) to stain cell nuclei. GFAP signal is restricted to ganglion cell layer (GCL) showing a significantly increased expression in TMHT mice. Iba1 (green) is expressed in the GCL, nerve fiber layer (NFL), and IPL and outer plexiform layer (OPL). The region labelled by pTau is the NFL.

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