Olfactory performance and neuropathology in the Tg6799 strain of Alzheimer's disease model mice

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Olfactory impairment is an early symptom of Alzheimer's disease (AD) and is used as a preclinical marker in humans - but is this behavioral symptom also developed by the transgenic AD model mouse strain Tg6799? And if it is, does it precede other behavioral symptoms and how does it correlate to neuropathologic amyloid-β plaque load?

Behavioral Testing

Tg6799 mice (2-3 months and 8-10 months of age) were trained to discriminate between monomolecular odorants using an automated liquid dilution olfactometer. Olfactory impairment compared to control mice was detected at 2-3 months of age. Using a simple spatial learning test, also spatial learning impairment was detected at 2-3 months of age.

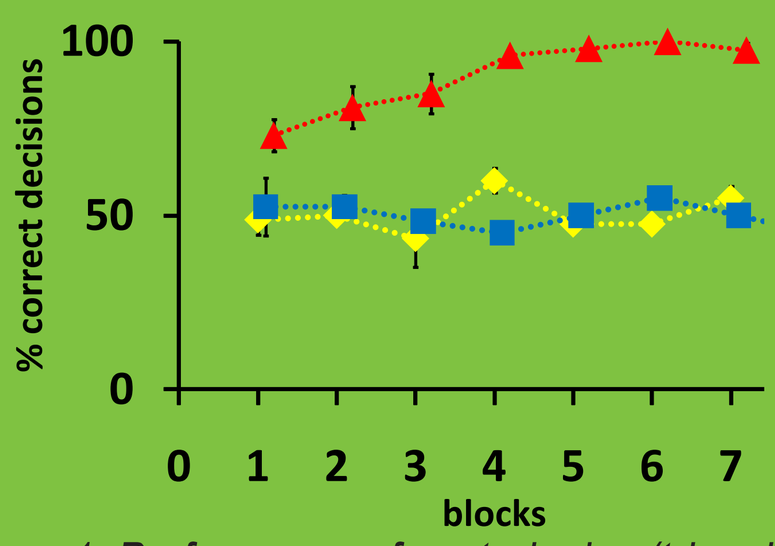

Figure 1. Performance of control mice (triangles), 2-3 month old (squares) and 8-10 month old 5xFAD mice (diamonds) in discriminating a monomolecular odorant pair at 0.01 ppm. Each data point represents 20 decisions.

Histology

Brains were sectioned at 50 μm and histochemically stained with Thioflavin T which binds to the amyloid-β plaques. Control mice were clear of plaques and Tg6799 mice developed plaques mainly between 3 and 8 months. Thus behavioral symptoms preceded plaque development.

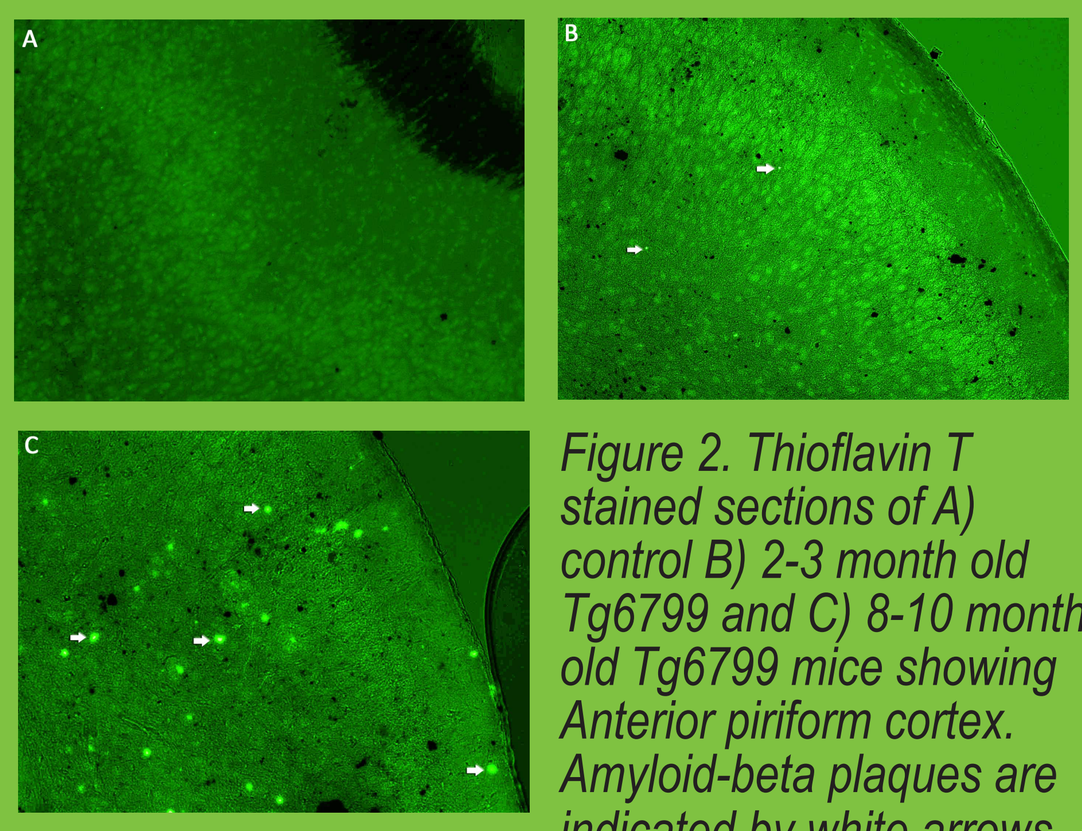

Figure 2. Thioflavin T stained sections of A) control B) 2-3 month old Tg6799 and C) 8-10 month old Tg6799 mice showing Anterior piriform cortex. Amyloid-beta plaques are indicated by white arrows.

Olfactory impairments and spatial learning deficits were shown at the same early age in the Tg6799 mice. Thus the olfactory deficits do not precede other behavioral symptoms, according to the data obtained. Histological data implicates that soluble amyloid-β rather than plaques is responsible for the first behavioral symptoms.

To determine the value of the Tg6799 strain to research on human AD more research is needed, but results are promising and the strain is suitable for research on olfactory impairment

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