Chronic treatment with the tetrahydrofuran derivative ANAVEX2-73, a mixed muscarinic cholinergic and sigma-1 ligand, alleviates pathology in Tg2576 mice, a transgenic Alzheimer’s disease model

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ABSTRACT

• Tg2576 mice exhibit a great increase in the amyloid precursor protein β and 315-317 signal peptide levels in the hippocampus, as well as increased levels of Aβ42, Aβ40, and Aβ25-35 as compared to controls. In particular, the drug attenuated the oxidative stress, caspase 3/caspase 9 induction, Bax/Bcl2, autophagy induction, and neuronal caspase 3 induction.

• In the present study, we started to address this question by administering chronically ANAVEX2-73 (3 mg/kg/day) in drinking bottle to 10 month-old Tg2576 and WT male mice. Water-treated Tg2576 showed significant alternation in the Y-maze test after 2 months of p.o. treatment with ANAVEX2-73 (3 mg/kg/day).

• The results suggest that ANAVEX2-73 has a therapeutic effect in preventing the progression of the disease in Tg2576 mice.

MATERIALS AND METHODS

• Tg2576 mice were administered ANAVEX2-73 (3 mg/kg/day) for 2 months in drinking bottle and water-treated Tg2576 mice were administered with tap water. The compound protected against both Aβ seeding and GSK-3β activation, p < 0.05 for the interaction, in (a); p < 0.01, #p > 0.05 for the genotype, F(1,33) = 11.98, p < 0.0001 for the genotype, F(1,33) = 2.65, p > 0.05 for the genotype.

DISCUSSION

• ANAVEX2-73 has been shown to alleviate the toxicity and functional deficits induced by our model of AD. The results suggest that the treatment could be a potential treatment for AD, as it has been shown to protect against both Aβ seeding and GSK-3β activation.

• The results suggest that ANAVEX2-73 has a therapeutic effect in preventing the progression of the disease in Tg2576 mice.

REFERENCES