Effects of antioxidant in mouse model for Alzheimer’s: A behavioral phenotyping and microdialysis study


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1 INTRODUCTION

Evidence both supporting and refuting the benefits of antioxidants on Alzheimer’s disease and cognitive performance is abundant, leading to uncertainty in the field. In rodents, treatment with Sulforaphane inhibited Aβ plaque formation, reduced tau hyperphosphorylation, oxidative stress, and neuroinflammation, and prevented decline in spatial learning and memory in a mouse model for AD. It had similar effects in Aβ-depleted mice in a diabetes model (Hisu et al., 2018, Pu et al., 2018). On the other hand, exercise, but not antioxidants reversed impairments in Aβ mice (Chaudhuri et al., 2010). Evidence is inconstant in humans. Epidemiological studies suggest diets rich in antioxidants reduce risk of AD (Worrall, 2009), while clinical studies on AD patients treated with antioxidants have some functional improvement, but no cognitive benefits were observed (Sano et al., 1997, Petersen et al., 2000).

A randomized, double blind, placebo-controlled clinical trial in mild to moderate AD patients showed that antioxidant treatment did not influence CSF biomarkers related to amyloid or tau pathologies, but the treatment did reach its target, as it lowered CSF Aβ42/40 ratios in the brain, a biomarker for oxidative stress. However, the treatment may have caused better cognitive decline (Galasko et al., 2012).

In the current study, we attempted to elucidate whether chronic antioxidant treatment could impact AD biomarkers and cognitive performance in the Tg2576 mouse model for Alzheimer’s disease. To this aim, we treated 12-week-old female Tg2576 mice with saffron (50 mg/kg daily dose 5-7 days weekly for 17 weeks). Saffron, a potent antioxidant, has been shown to improve learning and memory in an opal mouse model (Papadakos et al., 2011), and the neuroprotective and antioxidant effects of saffron have been previously reported (Papadakos et al., 2011; Loring et al., 2012). After 12 weeks of treatment, behavioral phenotype was evaluated in the Y maze, open field, EPM, and LO box. Then, microdialysis was conducted in freely moving animals after 17 weeks of treatment. In dialysates, Aβ 41, 42, and 150 were measured, and the results showed that saffron treatment did not affect behavioral deficits or Aβ load, but may have influenced GABA and NE levels.

2 EXPERIMENTAL

Behavioral Parameters:

- **Age of animals:** 12 weeks old
- **Treatment:** Vehicle or Saffron (50 mg/kg daily dose 5-7 days weekly for 17 weeks)

Microdialysis Method Parameters:

- **Age of mice:** 12 weeks old
- **Treatment:** Vehicle or Saffron (50 mg/kg daily dose 5-7 days weekly for 17 weeks)

3 RESULTS

Figure 1: Levels of un-bound Aβ 1-40 and 1-42 (left to right) were significantly higher in transgenic mice than in their wild-type littermates at 38 weeks of age. Aβ 1-42 was higher but not significantly in Tg mice compared to WT (one-way ANOVA).

Figure 2: Tg2576 mice had significant reductions in the percent alternation (index of cognitive function) and an increase in total number of entries (index of locomotor activity) in the Y-Maze. (Two-way ANOVA)

4 CONCLUSION

Cognitive and anxiety-related deficits along with neurochemical changes in Aβ and NFT were observed in the Tg2576 mouse model for Alzheimer’s Disease. Chronic treatment with the antioxidant saffron did not affect behavioral deficits or Aβ load, but may have influenced GABA and NE levels.