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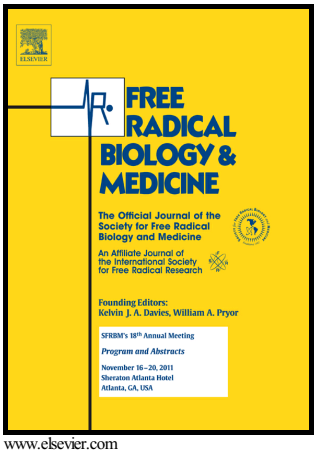

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Chronic vitamin E deficiency impairs cognitive function in adult zebrafish via dysregulation of brain lipids and energy metabolism

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Abstract

Zebrafish (*Danio rerio*) are a recognized model for studying the pathogenesis of cognitive deficits and the mechanisms underlying behavioral impairments, including the consequences of increased oxidative stress within the brain. The lipophilic antioxidant vitamin E (α-tocopherol; VitE) has an established role in neurological health and cognitive function, but the biological rationale for this action remains unknown. In the present study, we investigated behavioral perturbations due to chronic VitE deficiency in adult zebrafish fed from 45 days to 18-months of age diets that were either VitE-deficient (E–) or sufficient (E+). We hypothesized that E– zebrafish would display cognitive impairments associated with elevated lipid peroxidation and metabolic disruptions in the brain. Quantified VitE levels at 18-months in E– brains (5.7 ± 0.1 nmol/g tissue) were ~22-times lower than in E+ (122.8 ± 1.1; *n*= 10/group). Using assays of both associative (avoidance conditioning) and non-associative (habituation) learning, we found E– vs E+ fish were learning impaired. These functional deficits occurred concomitantly with the following observations in adult E– brains: decreased concentrations of and increased