α-Tocopherol suppresses lipid peroxidation and behavioral and cognitive impairments in the Ts65Dn mouse model of Down syndrome.

Shichiri M, Yoshida Y, Ishida N, Hagihara Y, Iwahashi H, Tamai H, Niki E.

Health Research Institute, National Institute of Advanced Industrial Science and Technology, Ikeda, Osaka 563-8577, Japan.

OBJECTIVE: It is widely accepted that oxidative stress is involved in the pathogenesis of Down syndrome, but the effectiveness of antioxidant treatment remains inconclusive. We tested whether chronic administration of α-tocopherol ameliorates the cognitive deficits exhibited by Ts65Dn mice, a mouse model of Down syndrome.

METHODS: α-Tocopherol was administered to pregnant Ts65Dn females, from the day of conception throughout the pregnancy, and to pups over their entire lifetime, from birth to the end of the behavioral testing period.

RESULTS: Cognitive deficits were confirmed for Ts65Dn mice fed a control diet, revealing reduced anxiety or regardlessness in the elevated-plus maze task test and spatial learning deficits in the Morris water maze test. However, supplementation with α-tocopherol attenuated both cognitive impairments. In addition, we found that levels of 8-iso-prostaglandin F(2α) in brain tissue and hydroxyoctadecadienoic acid and 7-hydroxycholesterol in the plasma of Ts65Dn mice were higher than those of control mice. Supplementation with α-tocopherol decreased levels of lipid peroxidation products in Ts65Dn mice. Furthermore, we found out that α-tocopherol improved hypocellularity in the hippocampal dentate gyrus of Ts65Dn mice.

CONCLUSIONS: These results imply that α-tocopherol supplementation from an early stage may be an effective treatment for the cognitive deficits associated with Down syndrome.

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