Miconazole promotes cooperative ability of a mouse model of Alzheimer's disease

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Abstract

Background and Purpose: Cooperative defect is one of the earliest manifestations of patients with Alzheimer's disease (AD), but the underlying mechanism remains unclear. The purpose of the current study was to address this issue. Experimental Approach: The cooperative function of APP/PS1 transgenic AD model mice at ages 2, 5 and 8 months was evaluated by a cooperative drinking task. Neuropathological changes were examined in the medial prefrontal cortex (mPFC), a key brain area regulating social behavior. Another experiment was designed to observe whether miconazole, a drug has a protective effect on myelin sheath, could promote cooperative ability of APP/PS1 mice in the early AD-like stage. The protective effects of miconazole on cultured mouse cortical oligodendrocytes exposed to human amyloid β peptide (Aβ1-42) peptide were also investigated. Key Results: There was an age-dependent impairment of cooperative drinking water behavior in APP/PS1 mice. AD mice with cooperative dysfunction showed decreases in myelin sheath thickness, oligodendrocyte nuclear heterochromatin percentage and myelin basic protein expression levels in the mPFC. The cooperative ability was significantly improved in APP/PS1 mice treated with miconazole. Consistently, miconazole increased oligodendrocyte maturation and myelin sheath thickness, without reducing Aβ plaque deposition in the mPFC. Miconazole protected cultured oligodendrocytes from the toxicity of Aβ1-42. Conclusions and Implications: These results demonstrate that mPFC myelin hypomyelination is involved in cooperative deficits of APP/PS1 mice. Improving myelination via miconazole therapy may offer a potential therapeutic approach for early intervention of AD.

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