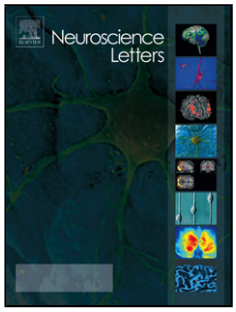

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Upregulated BMP6 pathway involved in the pathogenesis of Aβ toxicity *in vivo*

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Highlights

1. BMP6 was upregulated in the hippocampus in APP/PS1 mice.

2. The endogenous BMP6 is mainly expressed in the cytoplasm of neuron and nuclear of microglia, not in astrocyte in APP/PS1 mice.

3. BMP6 supplementation did not benefit transgenic (CL2006) *C. elegans*, even toxic at certain concentrations, and antagonizing BMP downstream pathways including Smad and LIMK1 could alleviate the toxicity caused by excessive BMP6.

Abstract

In our previous work, we demonstrated the protective effect of BMP6 on neuron against Aβ toxicity *in vitro*. In the present study, our aim was to determine the effects of BMP6 in Aβ toxicity *in vivo*. Firstly, we evaluated the levels and localization of endogenous BMP6 in APP/PS1 transgenic mice. Secondly, dose-response effects of exogenous BMP6 and BMP6 pathway antagonists were tested in transgenic CL2006 *C. elegans* (expressing Aβ3-42) lifespan and locomotor activity. We have three findings: 1) BMP6 was upregulated in the hippocampus in APP/PS1 mice. 2) The endogenous BMP6 is mainly expressed in the cytoplasm of neuron and nuclear of microglia, not in astrocyte in APP/PS1 mice. 3) BMP6 supplementation did not benefit transgenic worms, even toxic at certain concentrations, and antagonizing BMP downstream pathways including Smad and LIMK1 could alleviate the toxicity caused by 0.1μg/ml BMP6. The results suggest there is elevated BMP6