1. **No.**

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2. **Title**

   Effectiveness of Galantamine Treatment in Normal Cognition Phase of APPswe/PS1dE9 mice

3. **Period**

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4. **Summary**

Alzheimer's disease (AD) is a common neurodegenerative disease that progressively impairs memory and cognition. Deposition of amyloid-β (Aβ) peptides is the most important pathophysiological hallmark of AD. Oxidative stress induced by generation of reactive oxygen species (ROS) is a prominent phenomenon in AD and known to occur early in the course of AD. Galantamine is an acetylcholinesterase inhibitor and has been reported to have an oxidative stress inhibitory function. We used APPswe/PS1dE9 mice (AD mice) and their littermates (Wild mice) in this study. Galantamine was administered orally to AD model mice from before the appearance of Aβ plaques (preplaque phase). We measured the amount of Aβ and the levels of malondialdehyde as marker of oxidative stress in the brain. Then we performed pathological evaluation (Iba1， GFAP) by immunohistochemistry. Galantamine administration enhanced microglial function to promote Aβ clearance, reducing the Aβ-positive area in the cortex and amount of insoluble Aβ in the brain. In contrast, galantamine treatment from the preplaque phase suppressed the production of proinflammatory cytokines through neurotoxic microglial activity. And oxidative stress in the brain was suppressed in the AD mouse brain treated with galantamine for 6 months compared with the AD mouse brain in the control group. We showed that galantamine administration from the preplaque phase results in the improvement of cognitive function and suppresses the oxidative stress and the progression of pathological findings in AD mice. Our data may reveal the importance of early stage treatment by galantamine.