The therapeutic effect of J4 in sporadic Alzheimer's disease mice

Objective

Alzheimer's disease (AD) is the most common neurodegenerative disorder characterized by memory loss and cognitive dysfunction. Adenosine levels are decreased in AD patients, and equilibrative nucleoside transporter 1 (ENT1) inhibitors, such as J4, have been reported to improve cognitive performance in AD mouse models. This study aims to investigate the therapeutic effects of J4 in sporadic AD mouse models, with a particular focus on sleep regulation.

Methods

A sporadic AD model was established by intracerebroventricular injection of streptozotocin (STZ) and intrahippocampal injection of $A\beta_{1\text{-}42}$ to induce AD-like pathologies, including cognitive deficits and sleep disturbances. Stereotaxic surgery was performed to implant electrodes for electrocorticography (ECoG) recordings. Sleep architecture was analyzed using ICELUS software. Cognitive performance was further assessed with behavioral tests, including the novel object recognition (NOR) and the Morris water maze (MWM).

Results

J4 administration improved behavioral and sleep outcomes in sporadic AD mice. At a dose of 6 mg/kg, J4 significantly ameliorated learning and memory impairments and restored sleep architecture, whereas 1 mg/kg showed no noticeable effect. These findings suggest that J4 not only prevents neurocognitive decline but also alleviates sleep dysfunction associated with AD.

Conclusion

J4, an ENT1 inhibitor that elevates extracellular adenosine concentration, exerts therapeutic benefits in sporadic AD mice. By counteracting the neurocognitive and sleep-related deficits induced by STZ and Aβ1-42, J4 demonstrates potential as a preventive and therapeutic strategy for sporadic Alzheimer's disease.

中文題目：**J4 在偶發型阿茲海默症小鼠模型中的治療效果**

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