

GS5-4 Donepezil-induced neuroprotection of acetylcholine neurons in mouse medial septum

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【Background】 In the Alzheimer's brain, degeneration of the cholinergic neurons projected to the hippocampus and cerebral cortex was found as well as accumulation of beta-amyloid protein. Donepezil, a potent acetylcholinesterase (AChE) inhibitor is reported to rescue neurons from excitotoxic injury in culture. However, there is no evidence to confirm its neuroprotective effect on ACh neurons *in vivo*. Using olfactory bulbectomy (OBX) mice, I will define the neuroprotective effect of donepezil on the medial septum cholinergic neurons with concomitant improvement of the impaired cognitive function. 【Methods】 Bilateral olfactory bulbs of DDY mouse were removed by surgery (1). After OBX, donepezil (1 or 3mg/kg/day) was administered for 15 days and mouse brain was fixed with paraformaldehyde perfusion at 18 days. Then, the neuroprotective effect of donepezil was evaluated by number of the ChAT positive neurons in the medial septum. 【Results】 The number of ChAT positive neurons in the medial septum was reduced by 40 % of that in sham-operated animals. The reduced ChAT positive neurons were restored by donepezil treatments. Consistent with these observations, the cognitive deficits observed in the OBX mice were significantly improved by the donepezil treatment. 【Discussion】 Taken together, donepezil treatment rescues the cholinergic neurons in the medial septum from the neurodegeneration by OBX. I will also discuss the mechanism underlying the donepezil-induced neuroprotection in the medial septum cholinergic neurons. (1) Han et al., Neuroscience 151:671-679 (2008)