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[Lab. of Molecular Biology]

Oral Administration of Propentofylline, a Stimulator of Nerve Growth Factor (NGF) Synthesis, Recovers Cholinergic Neuronal Dysfunction Induced by the Infusion of Anti-NGF Antibody into the Rat Septum.

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We have reported that the continuous infusion of anti-nerve growth factor (NGF) monoclonal antibody into the septum of rats produces an impairment of memory and a decrease in choline acetyltransferase (ChAT) and cholinesterase (ChE) activities in the hippocampus. To investigate the pharmacological effects of propentofylline *in vivo*, we induced amnesia in rats by infusion anti-NGF antibody into the septum for 16 days. In the treated amnesic rats, learning and memory in the 3 tasks and ChAT and ChE activity were reduced compared to values in control rats. The administration of propentofylline recovered the decreased learning capacity and the deficit in cholinergic marker enzyme activity. These results suggest that the use of NGF stimulatory may provide a new approach to the treatment of dementia.

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[Lab. of Molecular Biology]

Effects of Metrifonate on Impairment of Learning and Dysfunction of Cholinergic Neuronal System in Basal Forebrain-lesioned Rats.

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In this study, we investigated the effects of MTF on the impairment of learning and memory, decreased ChE activity and extracellular acetylcholine (ACh) levels in basal forebrain (BF)-lesioned rats. The oral administration of MTF improved the BF-lesion-induced impairment of performance on passive avoidance task. Further, MTF reduced ChE activity in the cerebral cortex. *In vivo* brain microdialysis studies showed that MTF significantly increased the release of ACh. This suggested that MTF may be useful as a therapeutic drug for Alzheimer's disease.

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[Lab. of Molecular Biology]

Orally Active NGF Synthesis Stimulators: Potential Therapeutic Agents in Alzheimer's Disease.

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Since NGF plays an important role in the survival and maintenance of cholinergic neurons, this factor may have some beneficial effects on the cognitive impairment observed in patients with AD. However since NGF does not cross the blood-brain barrier and is easily metabolized when administered peripherally, it can only be used when directly injected into the brain. In this study we show that oral administration of NGF synthesis stimulators. These compounds recovered the learning ability and cholinergic activity. These results suggest that the use of NGF synthesis stimulators may provide a novel therapeutic approach to cholinergic dysfunction.

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[Lab. of Molecular Biology]

Effects of Metrifonate on Memory Impairment and Cholinergic Dysfunction in Rats.

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Metrifonate is an organophosphorous compound that has been used in the treatment of schistosomiasis. In this study, we investigated the effects of metrifonate on the impairment of learning and central cholinergic dysfunction in scopolamine-treated and basal forebrain-lesioned rats. Metrifonate ameliorated the learning impairment in these amnesia models. These findings suggest the usefulness of metrifonate for the therapy of Alzheimer's disease.