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2. Title

Studies on Cholinergic Functions in Neocortex, Hippocampus and Olfactory Bulb toward to Establish Methods for Preventing Dementia

3. Period

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4. Summary

Olfaction is a potential biomarker for early diagnosis of Alzheimer's disease, because patients with Alzheimer's disease exhibit olfactory dysfunction before impairments of memory and other cognitive function. The olfactory bulb receives cholinergic basal forebrain inputs, as does the neocortex and hippocampus contributing cognition and memory, respectively. This study aimed to clarify the contribution of cholinergic inputs, especially nicotinic acetylcholine receptors (nAChRs) in the regulation of olfactory processing in the olfactory bulb, by comparing the neocortex.

First, we showed that in urethane anesthetized rats, intravenous injection of nicotine (30 μg/kg) increased blood flow in the neocortex, via activation of α4β2-like nAChRs, while the nicotine did not alter the blood flow in the olfactory bulb. This nicotine-induced increase in blood flow in the neocortex was attenuated in rats anesthetized by clinically used inhalation anesthetics (isoflurane, sevoflurane) or intravenous anesthetics (propofol). Second, we showed that olfactory stimulation increased blood flow in the olfactory bulb, while the stimulation did not alter blood flow in the neocortex. This olfactory stimulation-induced increase in blood flow in the olfactory bulb was augmented by nicotine (30 μg/kg) via activation of α4β2-like nAChRs. We speculate that olfactory dysfunction in the early Alzheimer's disease may be caused by the decline of α4β2-like nAChR function.