Involvement of cholinergic receptors in the different stages of memory measured in the modified elevated plus maze test in mice

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Background and Methods: Several lines of evidence support a strong relationship between cholinergic pathways and memory. The aim of our experiments was to examine the mechanisms involved in the formation of different memory stages, to evaluate the impact of substances, which affect the cholinergic system in mice, with an employment of the modified elevated plus maze (MEPM) test. This test allows examining different processes of memory (acquisition, consolidation and retrieval), depending on the time of drug treatment. The time period, necessary for the mouse to move from the opened arm to the enclosed arm (i.e., transfer latency, TL) was used as an index of memory.

Results: Our findings revealed that in both memory acquisition and consolidation, nicotine, an agonist of cholinergic receptors (0.035 and 0.175 mg/kg, free base, sc), reduced TL on the second day of the experiment (TL2), thus improving memory. In turn, scopolamine, an antagonist of cholinergic receptors (0.3 and 1.0 mg/kg, ip), significantly increased TL2 values, impairing cognition. Subsequently, we evaluated the influence of mecamylamine, a non-selective antagonist of nicotinic cholinergic receptors (nAChRs) and of varanicline, an α4β2 partial nAChRs agonist, on memory-related behaviors induced by nicotine and scopolamine. Acute injections of mecamylamine (0.5 and 1.0 mg/kg, ip) and varanicline (0.5 and 1.0 mg/kg, ip), prior to the injections of nicotine (0.035 mg/kg) or scopolamine (1.0 mg/kg), significantly suppressed nicotine-induced memory improvement or scopolamine-induced memory impairment.

Conclusion: Our studies indicate that the cholinergic system plays a crucial role in memory processes. Pharmacological manipulation of cholinergic transmission can be the base to develop more effective pharmacotherapies for these memory disturbances in which cholinergic receptors are involved.

Key words: nicotine, scopolamine, mecamylamine, varanicline, memory and learning, modified elevated plus maze