Effects of the histamine H\textsubscript{3} receptor antagonist ABT-239 on cognition and nicotine-induced memory enhancement in mice

Marta Kruk\textsuperscript{1}, Joanna Miszkiel\textsuperscript{2}, Andrew C. McCreary\textsuperscript{3}, Edmund Przegaliński\textsuperscript{2}, Małgorzata Filip\textsuperscript{2,4}, Grażyna Biała\textsuperscript{1}

\textsuperscript{1}Department of Pharmacology and Pharmacodynamics, Medical University of Lublin, Chodzki 4A, PL 20-003 Lublin, Poland
\textsuperscript{2}Laboratory of Drug Addiction Pharmacology, Institute of Pharmacology, Polish Academy of Sciences, Śmigłona 12, PL 31-343 Kraków, Poland
\textsuperscript{3}BrainsOn-Line, de Mudder 16, 9747AW Groningen, The Netherlands
\textsuperscript{4}Department of Toxicology, Faculty of Pharmacy, Jagiellonian University, College of Medicine, Medycyna 9, PL 30-688 Kraków, Poland

Correspondence: Grażyna Biała, e-mail: grażyna.biła@umlub.pl

Abstract:

\textbf{Background:} The strong correlation between central histaminergic and cholinergic pathways on cognitive processes has been reported extensively. However, the role of histamine H\textsubscript{3} receptor mechanisms interacting with nicotinic mechanisms has not previously been extensively investigated.

\textbf{Methods:} The current study was conducted to determine the interactions of nicotinic and histamine H\textsubscript{3} receptor systems with regard to learning and memory function using a modified elevated plus-maze test in mice. In this test, the latency for mice to move from the open arm to the enclosed arm (i.e., transfer latency) was used as an index of memory. We tested whether ABT-239 (4-(2-{2-[2R]-2-methylpyrrolidinyl}ethyl)-benzofuran-5-yl), an H\textsubscript{3} receptor antagonist/inverse agonist, had influence on two different stages of memory, i.e., memory acquisition and consolidation (administered prior to or immediately after the first trial, respectively) and whether ABT-239 influenced nicotine-induced memory enhancement.

\textbf{Results:} Our results revealed that the acute administration of nicotine (0.035 and 0.175 mg/kg), but not of ABT-239 (0.1–3 mg/kg) reduced transfer latency in the acquisition and consolidation phases. In combination studies, concomitant administration of either ABT-239 (1 and 3 mg/kg) and nicotine (0.035 mg/kg), or ABT-239 (0.1 mg/kg) and nicotine (0.0175 mg/kg) further increased nicotine-induced improvement in both memory acquisition and consolidation.

\textbf{Conclusion:} The present data confirm an important role for H\textsubscript{3} receptors in regulating nicotine-induced mnemonic effects since inhibition of H\textsubscript{3} receptors augmented nicotine-induced memory enhancement in mice.

\textbf{Key words:} modified elevated plus maze, histamine3 receptor, nicotine, cognition