PHARMACOLOGICAL ANALYSIS OF THE HYPOTHERMIC EFFECTS OF NAN-190 AND ITS ANALOGS, POSTSYNAPTIC 5-HT$_{1A}$ RECEPTOR ANTAGONISTS, IN MICE

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In this study, we examined the role of 5-hydroxytryptamine (5-HT) and $\alpha_1$-adrenergic receptors in the hypothermia induced by 1-(2-methoxyphenyl)-4-[4-(2-phthalimido)butyl]-piperazine (NAN-190) and its analogs, 1-(2-methoxyphenyl)-4-[4-(4-succinimido)butyl]piperazine (MM77) and trans-1-(2-methoxyphenyl)-4-[4-(2-phthalimido)cyclohexyl]piperazine (MP245), which – like NAN-190 – showed a high affinity for 5-HT$_{1A}$ and $\alpha_1$-adrenoceptors. Administration of NAN-190 (a partial agonist of presynaptic and an antagonist of postsynaptic 5-HT$_{1A}$ receptors and $\alpha_1$-adrenoceptors), MM77 and MP245 (antagonists of postsynaptic 5-HT$_{1A}$ receptors), as well as 8-OH-DPAT (a 5-HT$_{1A}$ agonist) and prazosin (an $\alpha_1$-adrenoceptor antagonist) induced a dose-dependent hypothermia in mice. The silent antagonist of 5-HT$_{1A}$ receptors, WAY 100635, which abolished the hypothermic effect of 8-OH-DPAT, inhibited the hypothermia induced by NAN-190 administered at a dose of 1 mg/kg (but not 2 mg/kg) and by MP245 (0.5 and 1 mg/kg), but failed to change the MM77 (1 and 4 mg/kg)-induced decrease in body temperature in mice. The $\alpha_1$-adrenoceptor agonist St 587, which reduced the hypothermic effect of prazosin, inhibited the decrease in body temperature evoked by NAN-190 at the higher dose and by MP245 at both the doses used, but did not affect the MM77-induced hypothermia in mice.

The obtained results suggest that the hypothermia in mice induced by NAN-190 and its constrained analog MP245 is connected with stimulation of 5-HT$_{1A}$ receptors and with blockade of $\alpha_1$-adrenoceptors, participation of these receptors not being equivalent, though. The origin of the hypothermia evoked by MM77 is still unknown.

Key words: NAN-190 and its analogs, 5-HT$_{1A}$ receptor ligands, $\alpha_1$-adrenoceptor ligands, body temperature, mice

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