COOPERATIVE CONTRIBUTION OF PRESYNAPTIC NICOTINIC AND NMDA RECEPTORS IN THE MODULATION OF NORADRENALINE RELEASE FROM HIPPOCAMPAL NERVE ENDINGS

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Receptor-receptor interaction has been reported to be present at the presynaptic receptor level. In the present study we examined the interaction between nicotine and N-Methyl-D-aspartic acid (NMDA) receptors which modulate noradrenaline (NA) release from hippocampal nerve terminals prelabeled with [^{3}H]-NA.
Nicotine (100 mM) enhanced the basal release of [^{3}H]-NA while the glutamate receptor agonist NMDA (100 mM) did not enhance [^{3}H]-NA release in presence of physiological concentration of Mg^{2+} but was effective only when the ion was removed from the perfusion medium.
However, in the presence of Mg^{2+}, the NMDA channel blockade could be overcome when nicotine was added to the medium together with NMDA, the result being a potentiation of the nicotine evoked [^{3}H]-NA release, which was counteracted by CGS 19755 (cis-4[Phosphomethyl]-2-piperidinecarboxylic acid) (10 mM) an inhibitor of the NMDA receptor. This potentiation was also antagonized by the protein kinase C inhibitor staurosporine (0.01 mM). The nicotinic evoked [^{3}H]-NA release elicited in presence of NMDA was totally counteracted by dihydrobetaerythroidine (10 mM) and mecamylamine (100 mM). No synergistic response was observed when nicotine was applied with NMDA in absence of magnesium.
In conclusion nicotinic and NMDA receptors coexist on noradrenergic terminals and the synergistic effect of nicotine plus NMDA on NA release seem to be due to a permissive effect of nicotine on the NMDA response resulting in the removal of the magnesium block due probably to the nicotinic activation of the protein kinase C.