COEXISTENCE AND FUNCTIONAL INTERACTION BETWEEN PRESYNAPTIC NICOTINIC AND MUSCARINIC RECEPTORS THAT MODULATE NEUROTRANSMITTERS RELEASE FROM STRIATAL SYNAPTOSOMES

Massimo Grilli,[1] Laura Patti,[1] Federica Robino,[1] Stefania Zappettini,[1] Ioannis Sofianos,[1]Maurizio Raiteri,[1,2] and Mario Marchi[1,2]

[1]Section of Pharmacology and Toxicology, Department of Experimental Medicine, University of Genoa, Italy and [2]Center of Excellence for Biomedical Research, University of Genoa, Italy

Receptor-receptor interaction has been reported to be present at the presynaptic level.
Recent data from our laboratory have shown functional interactions between nAChRs and NMDA receptors, mGluRs, purinergic receptors which coexist on the same noradrenergic or glutamatergic nerve endings.
It is well known that nAChRs are also present on dopaminergic and gabaergic nerve endings of different brain areas and it is accepted that dopaminergic system plays an important role in the reinforcing effect of drugs of abuse and among them also of nicotine.
The cholinergic system is able to modulate both dopamine and GABA release also by activating muscarinic receptors (1).
In the present study we demonstrate that nicotinic and muscarinic presynaptic receptors collaborate in the modulation of dopamine and GABA release from isolated nerve terminals of c. striatum or n. accumbens. In particular when Acetylcholine 100 µM is administered to the synaptosomal preparation we measure an effect that is partially due to the activation of muscarinic receptors (see block with atropine 30nM).
Interestingly mecamylamine 20 µM, a non subtype selective nicotinic receptors antagonist with no effect for muscarinic receptors, completely blocks the acetylcholine evoked dopamine release. Similarly when nicotine 100 µM is added with oxotremorine 30 µM, a muscarinic receptors agonist ineffective at this concentration, we show an over addictive effect that was selectively blocked with atropine 30 nM. The activation of muscarinic receptors on gabaergic nerve endings modulates negatively the nicotine evoked GABA overflow. This effect is blocked by himbacine 10nM indicating that this inhibition is mediated by a muscarinic receptor subtype different from that one present on dopaminergic nerve endings.
Taken together, our results suggest that nicotinic and muscarinic receptors coexist on the same nerve endings and sinergically modulate dopamine and GABA release.

(1) Marchi M., Paudice P., Bonanno G., Raiteri M. Neurochem International 1985 Jan 7; 137-141.

This work was supported by a MIUR Network grant