Presynaptic Receptors for Dopamine, Histamine, and Serotonin

Thomas J. Feuerstein

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Thomas J. Feuerstein
Neurochirurgische Universitätsklinik Breisacherstrasse 64 D - 79106 Freiburg, Germany
thomas.feuerstein@uniklinik-freiburg.de

T.C. Südhof, K. Staeke (eds.), Pharmacology of Neurotransmitter Release. 289
Handbook of Experimental Pharmacology 184.
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Presynaptic receptors for dopamine, histamine and serotonin that are located on dopaminergic, histaminergic and serotonergic axon terminals, respectively, function as autoreceptors. Presynaptic receptors also occur as heteroreceptors on other axon terminals. Auto- and heteroreceptors mainly affect Ca\textsuperscript{2+}-dependent exocytosis from the receptor-bearing nerve ending. Some additionally subserve other presynaptic functions.

Presynaptic dopamine, histamine and serotonin receptors are involved in various (patho)physiological conditions. Examples are the following:

Dopamine autoreceptors play a role in Parkinson’s disease, schizophrenia and drug addiction. Dopamine heteroreceptors affecting the release of acetylcholine and of amino acid neurotransmitters in the basal ganglia are also relevant for Parkinson’s disease. Peripheral dopamine heteroreceptors on postganglionic sympathetic terminals influence heart rate and vascular resistance through modulation of noradrenaline release.

Blockade of histamine autoreceptors increases histamine synthesis and release and may support higher CNS functions such as arousal, cognition and learning. Peripheral histamine heteroreceptors on C fiber and on postganglionic sympathetic fiber terminals diminish neuropeptide and noradrenaline release, respectively. Both inhibitory effects are beneficial in myocardial ischemia. The inhibition of neuropeptide release also explains the antimigraine effects of some agonists of presynaptic histamine receptors.

Upregulation of presynaptic serotonin autoreceptors is probably involved in the pathogenesis of major depression. Correspondingly, antidepressant treatments can be linked with a reduced density of 5-HT autoreceptors. 5-HT Heteroreceptor activation diminishes acetylcholine and GABA release and may therefore increase anxiety. In the periphery, presynaptic 5-HT heteroreceptor agonists shorten migraine attacks by inhibition of the release of neuropeptides from trigeminal afferents, apart from their constrictive action on meningeal vessels.

1 Introduction

Our knowledge of presynaptic dopamine and serotonin receptors dates back to the 1970s (Farnebo and Hamberger 1971). Presynaptic histamine receptors were discovered in 1983 (Arrang et al. 1983). Presynaptic dopamine receptors occur as autoreceptors, i.e., on dopaminergic axon terminals, and as heteroreceptors on nondopaminergic axon terminals. By analogy the same holds true for presynaptic histamine and serotonin receptors. The early days of the dopamine autoreceptors were stormy, but the controversies were finally solved (see Starke et al. 1989). The main function that presynaptic receptors affect is transmitter release, which in this article means Ca\textsuperscript{2+}-dependent exocytosis. However, some receptors discussed in