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Dual Effects of Norepinephrine on $GABA_A$-Mediated Spontaneous Postsynaptic Currents in the Rat Hypothalamic Paraventricular Neurons.

Seong Kyu Han*, Pan Dong Ryu
Dept. of Pharmacol., Coll. of Vet. Med., Seoul Nat'l Univ., Suwon, 441-744

The paraventricular nucleus (PVN) is a complex structure comprised of several different populations of cells divided into two main groups, the magnocellular (type I) neurons which secrete vasopressin and oxytocin and the parvocellular (type II) neurons which regulate hormone secretion from the anterior pituitary. PVN receives dense noradrenergic innervations from lower brain stem nuclei. However, little is known about the role of the norepinephrine (NE) on synaptic transmission in the PVN.

In this work, the effects of NE on spontaneous synaptic currents to Type II neurons of the rat PVN were studied using whole cell patch clamp technique in coronal slice preparations. The pipette solution contained (mM): KCl 140, $CaCl_2$ 0.5, EGTA 5, HEPES 20, MgATP 5 and biocytin (0.1%) (pH 7.2). Neurons were classified by the presence of rebound action potentials in response to hyperpolarizing current pulses. The spontaneous synaptic currents were blocked by bicuculline, a $GABA_A$ receptor antagonist, but not by excitatory amino acid receptor blockers, CNQX and kynurenic acid or tetrodotoxin (TTX), suggesting that they are spontaneous inhibitory postsynaptic currents (sIPSC).

NE (10~100 μM) induced both stimulatory and inhibitory effects on sIPSC. The NE-induced increase in the frequency and amplitude of sIPSC was reversible and was blocked by TTX (1 μM), but not by the propranolol (20 μM), a β-adrenergic antagonist or yohimbine (20 μM), a α_2-adrenergic antagonist. The stimulatory effects of NE were mimicked by phenylephrine (100 μM), an α_1-adrenergic agonist. NE-induced decrease in the frequency of sIPSC was observed only in the presence of TTX or prazosin (20 μM), an α_1-adrenergic antagonist. Such inhibitory effect of NE was mimicked by clonidine (50 μM), an α_2-adrenergic agonist.

These results suggest that NE can enhance the synaptic release of GABA by activation of α_1-adrenoceptors of presynaptic GABAergic cell soma, but decrease the release of GABA by activating α_2-adrenoceptors on the nerve terminal in PVN of the rat hypothalamus.