Am J Physiol Heart Circ Physiol. 2006 Dec;291(6):H2847-56. doi: 10.1152/ajpheart.00625.2005. Epub 2006 Jul 28.

Interaction between glutamate and GABA systems in the integration of sympathetic outflow by the paraventricular nucleus of the hypothalamus

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PMID: 16877560 DOI: 10.1152/ajpheart.00625.2005

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Abstract

The paraventricular nucleus (PVN) of the hypothalamus is a central site known to modulate sympathetic outflow. Excitatory and inhibitory neurotransmitters within the PVN dictate final outflow. The goal of the present study was to examine the role of the interaction between the excitatory neurotransmitter glutamate and the inhibitory neurotransmitter GABA in the regulation of sympathetic activity. In alpha-chloralose- and urethane-anesthetized rats, microinjection of glutamate and N-methyl-D-aspartate (NMDA; 50, 100, and 200 pmol) into the PVN produced dose-dependent increases in renal sympathetic nerve activity, blood pressure, and heart rate. These responses were blocked by the NMDA receptor antagonist DL-2-amino-5-phosphonovaleric acid (AP-5). Microinjection of bicuculline, a GABA(A) receptor antagonist, into the PVN (50, 100, and 200 pmol) also produced significant, dose-dependent increases in renal sympathetic nerve activity, blood pressure, and heart rate; AP-5 also blocked these responses. Using microdialysis and HPLC/electrochemical detection techniques, we observed that bicuculline infusion into the PVN increased glutamate release. Using an in vitro hypothalamic slice preparation, we found that bicuculline increased the frequency of glutamate-mediated excitatory postsynaptic currents in PVN-rostral ventrolateral medullary projecting neurons, supporting a GABA(A)-mediated tonic inhibition of this excitatory input into these neurons. Together, these data indicate that 1) glutamate, via NMDA receptors, excites the presympathetic neurons within the PVN and increases sympathetic outflow and 2) this glutamate excitatory input is tonically inhibited by a GABA(A)-mediated mechanism.

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