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Endogenous GABAergic Mechanisms in the Medulla and the Regulation of Blood Pressure[1]

ROBERT N. WILLETTE, PETER P. BARCAS, ABBOTT J. KRIEGER and HREDAY N. SAPRU

Section of Neurological Surgery, Veterans Administration Medical Center, East Orange, New Jersey, and the Section of Neurological Surgery and the Department of Pharmacology, University of Medicine and Dentistry of New Jersey, Newark, New Jersey

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ABSTRACT

In the present study, the γ-aminobutyric acid receptor antagonist, bicuculline methiodide (BMI), was used to explore the role of endogenous medullary GABAergic mechanisms in the neural control of circulation. In urethane-anesthetized rats, microinjections of the neuroexcitatory amino acid, L-glutamate (150–300 ng/site) were used to functionally identify rostral ventrolateral vasopressor neuron pools (VLPA) and caudal ventrolateral vasodepressor neuron pools (VLDA). The bilateral microinjection of BMI into the ventrolateral vasodepressor neuron pool caused a dose-related (0.1–100.0 ng/site) decrease in blood pressure (BP), pulse pressure and heart rate (HR). Maximum decreases in BP and HR were 51 ± 2 mm Hg and 245 ± 9 beats/min, respectively. In the VLPA, BMI caused a dose-related (0.1–100.0 ng/site) increase in BP, HR and pulse pressure. Maximum increases in BP and HR were 88 ± 3 mm Hg and 73 ± 4 beats/min, respectively. In the VLPA, BMI also caused a 40% increase in the carotid artery occlusion response and a 48% reduction in the aortic depressor nerve response. It seems plausible that GABAergic mechanisms in both the caudal and rostral ventrolateral medulla are tonically involved with the maintenance and reflex regulation of vasomotor activity. Medullary γ-aminobutyric acid may provide a reciprocal inhibition between rostral vasopressor and caudal vasodepressor neuron pools.

Neuron pools in the ventrolateral medulla play an important role in the maintenance and reflex regulation of BP and HR (Guertzenstein, 1973; Dampney, 1981; Blessing *et al.*, 1981; Willette *et al.*, 1983a). Rostral ventrolateral neuron pools are involved with the generation of tonic vasomotor activity (Dampney, 1981; Willette *et al.*, 1983b). Stimulation of this VLPA with the neuroexcitatory amino acid, L-Glu, causes an increase in BP and HR; while inhibition of neuronal activity in the VLPA with the GABA receptor agonist, muscimol, results in a decreased BP and HR. Tonic activity in caudal ventrolateral neuron pools exerts an opposing action on BP and HR (Blessing and Reis, 1982; Willette *et. al.*, 1983b). Stimulation of neurons in this VLDA with L-Glu causes a decrease in BP and HR; inhibition with muscimol results in an increase in BP and HR. Neuronal activity in the VLDA also seems to be necessary for the proper processing of afferent information in the aortic depressor nerve and pulmonary J-fibers (Pulmonary C-fibers; Willette *et al.*, 1983b).

VLDA and VLPA are potentially important sites for the neurochemical control of circulation. As indicated above, stimulation of GABA receptors in these two areas elicits profound and opposing effects on BP and HR. *In the present study*, experiments were performed in an effort to determine whether GABA receptors in the VLPA and VLDA receive a tonic inhibitory GABAergic innervation. Microinjections of BMI were used to antagonize GABA receptors in each area (Andrews and Johnston, 1981).

Methods

Surgical preparation. All experiments were carried out in urethane-anesthetized (1.2 g/kg i.p.) male Wistar rats (Royal Hart Farms, Middletown, NY) weighing 250 to 350 g. In these animals, the trachea and the left femoral artery and vein were cannulated. Each animal was then placed in a stereotaxic instrument (David Kopf Instruments, Tujunga, CA) in a supine position with the upper incisor bar at the level of the interaural line. The upper trachea, larynx, esophagus, surrounding musculature and the longus capitis muscles were removed, exposing the occipital foramen and the basal aspect of the occipital bone was then carefully removed, creating a ventral window approximately 5 mm wide and 6 mm in length. The rostrocaudal, mediolateral and dorsoventral stereotaxic coordinates were in reference to the most caudal aspect of the occipital foramen, midline and ventral surface of the medulla, respectively.

In two groups of animals, the effects of GABA receptor antagonism (in the VLPA) on the cardiovascular reflexes elicited by carotid occlu-

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ABBREVIATIONS: BP, blood pressure; HR, heart rate; VLPA, ventrolateral pressor area; GABA, γ-aminobutyric acid; VLDA, ventrolateral vasodepressor area; L-Glu, L-glutamate monosodium; BMI, bicuculline methiodide; ANS, aortic nerve stimulation; COR, carotid occlusion response.