Alterations of Phrenic Nerve Activity Caused by Stimulation of Neuronal Structures in Rostral Area of Ventral Surface of the Medulla Oblongata

V. F. Pyatin, O. L. Nikitin, and V. S. Tatarnikov

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Electrical stimulation of neuronal structures in a rostral area of the ventral bulbar surface alters central inspiratory activity in anesthetized rats, augmenting the amplitude and velocity of this activity during the periods of its increase and plateau. The reactions are more pronounced in rats with transected vagal nerves. Blockade of pulmonary mechanoreceptors eliminates the influence of rostral neuronal structures only on the temporal parameters of the plateau. Bilateral cooling of neuronal structures to 20°C results in complete block of central inspiratory activity.

Key Words: *rostral region of ventral bulbar structure; central inspiratory activity; respiratory center*

Central inspiratory activity (CIA) of the respiratory center forms under the influence of specific afferent pulses from chemo- and mechanoreceptors [6,7]. The role of central chemoreceptors in this activity remains unclear because these receptors have not been identified. Recent studies have shown that neuronal structures located in the rostral region of the ventral surface of medulla oblongata (ventral bulbar surface, VBS) probably fulfil a chemosensory function and exert a complex effect on the respiratory center [2,4]. The mechanism of this effect is poorly understood. The purpose of the present study was to evaluate the role of the rostral region of the VBS in the mechanisms through which the CIA of the respiratory center is formed.

MATERIALS AND METHODS

The study was carried out on 58 Nembutal-anesthetized (35 mg/kg) rats (body weight 200-250 g) with intact (n=36) or cut (n=22) vagal nerves. The VBS was exposed from the C1 level to the level of exit of roots of cranial nerves VI-VII and 4.0-4.5 mm lateral to the midline. Rostral neuronal structures of the VBS were stimulated via bipolar electrodes (interelectrode distance 100 μ) with square pulses (100 Hz, 1 msec, 0.5-20 μA) delivered by an ESU-2 electrostimulator. Neuronal structures were cooled to 20°C unilaterally or bilaterally with a thermode. Electrical activity of the phrenic nerve was measured with bipolar silver electrodes, amplified, and integrated using standard equipment [1]. Arterial blood pressure was recorded with an ID-2I apparatus. The results were statistically analyzed by Student's t test with comparison of the means.

RESULTS

Neuronal structures of the VBS were electrically stimulated, with a step of 1 mm, at levels from the middle of cranial nerve XII roots to the exit of nerve VI roots (Fig. 1). A neurogram with its envelope showing variations of the phrenic nerve activity (PNA) before and after electrical stimulation is shown in Fig. 2. This activity changed upon stimulation of a limited zone within the rostral region of the VBS.

Department of Normal Physiology, State Medical University, Samara

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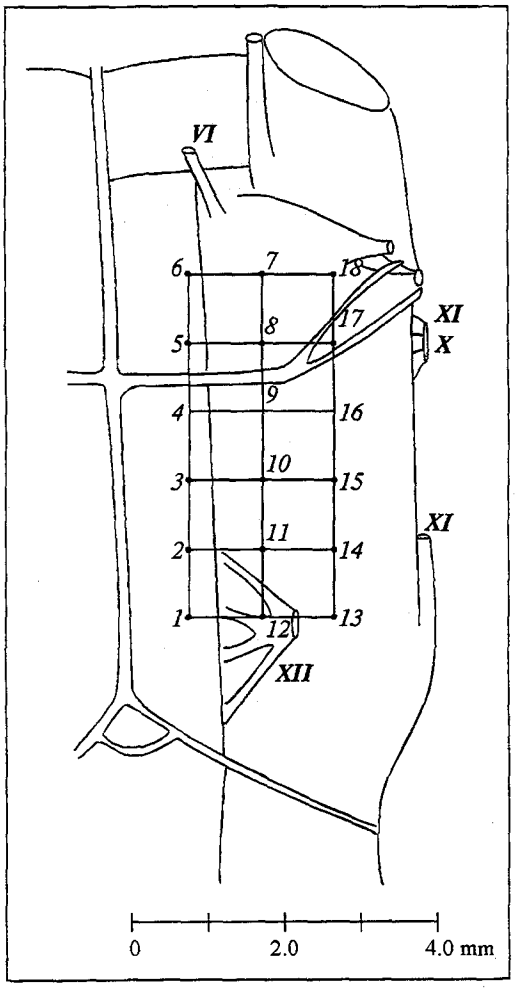

Fig. 1. Diagram of the ventral bulbar surface of rat brain showing the topography of electrically stimulated points.

This zone was located 3.5-4.5 mm rostral to the middle of sublingual nerve roots and 2.5-3.5 mm lateral to the midline of the brain. In rats with intact vagal nerves, stimulation of neuronal structures in this zone reduced the respiration period by 13.1±2.8% relative to baseline due to equal decreases of the inspiratory and expiratory phases, and it also shortened the time of PNA increase to the maximum amplitude by 14.7±1.6% and the time of the PNA plateau by 18.7±2.9%. The PNA amplitude at the beginning and the end of inspiratory discharge increased by 18.4±3.1% and 13.5±2.3%, respectively; the PNA amplitude at the beginning of postinspiratory phase increased by 13.8±2.3%. The duration of the so-called "useful" respiratory cycle slightly decreased (by 9.3±1.1%). The velocity parameters of PNA changed considerably. The ratio of the initial PNA amplitude to the time of its rise to the maximum increased by 41.9±5.6%, while the ratio of the amplitude to time of the PNA plateau increased by 40.5±5.7% (Fig. 3).

In vagotomized rats, electrical stimulation of neuronal structures in the above-mentioned zone of the VBS produced effects that differed markedly from those in rats with intact vagal nerves (Fig. 3). The respiration period decreased by 21.8±4.3%, with a 19.0±2.8% reduction of the inspiratory phase and a 26.4±4.8% reduction of the expiratory phase. The time of PNA increase to its maximum amplitude became shorter by 30.3±3.4%, whereas the time of the PNA plateau remained almost unchanged. The postinspiratory phase became longer by nearly 10%. The PNA amplitude at the beginning and the end of the inspiratory discharge increased by 53.0±5.7% and 24.9±2.7%, respectively. The amplitude of the postinspiratory PNA discharge increased by 23.8±4.7%, while the "useful" cycle remained unchanged. The rate of increase in the CIA of the respiratory center was two times as high as in the intact rats (i.e., the ratio of the initial PNA amplitude to the time of its rise to the maximum was 83.9±9.4% above baseline *vs.* 41.9±5.6%).

Unilateral cooling to 20°C of neuronal structures in the rostral zone of the VBS reduced the total PNA, while their bilateral cooling to this temperature completely blocked the CIA of the respiratory center. This area contains structures stimulation of which in isolated brain from neonatal rats generates phasic

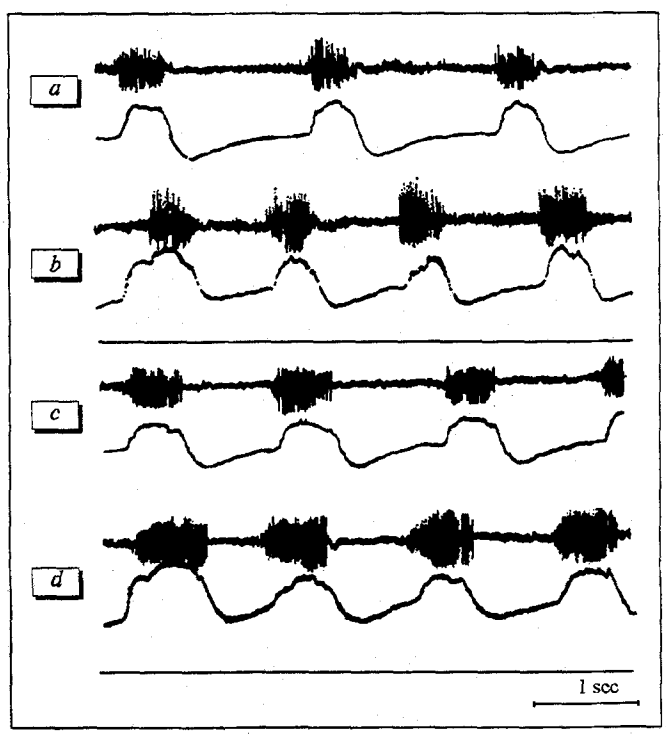

Fig. 2. Neurogram and its envelope showing variations of phrenic nerve activity before and during electrical stimulation of neuronal structures in the rostral region of the ventral bulbar surface before (*a* and *b*) and after (*c* and *d*) vagotomy. *a* and *c*) before stimulation; *b* and *d*) during stimulation.

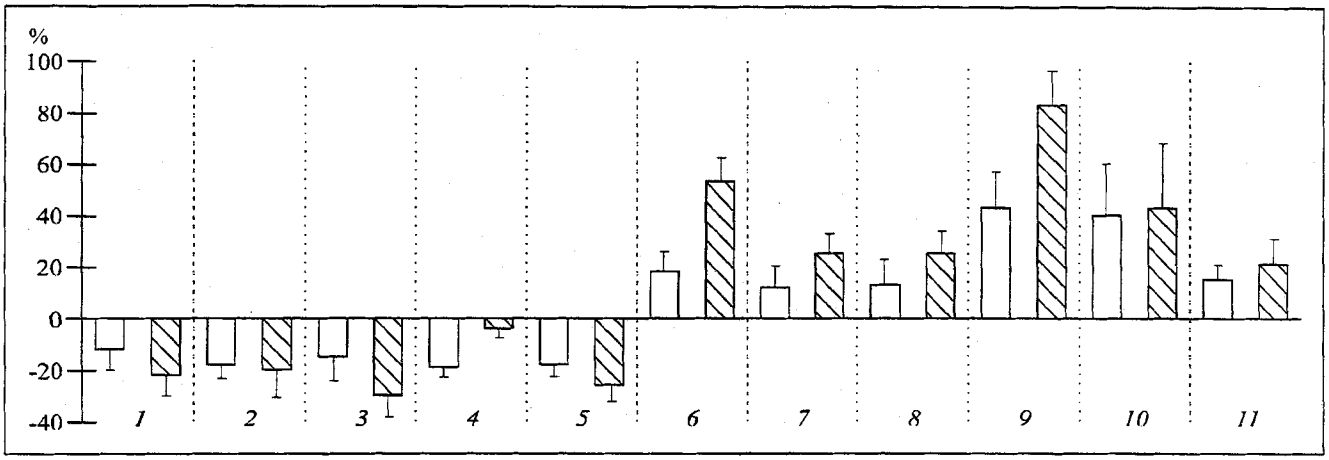

Fig. 3. Alterations in phrenic nerve activity (PNA) relative to its baseline level in response to electrical stimulation of neuronal structures in the rostral region of the ventral bulbar surface before (white bars) and after (hatched bars) vagotomy. *1*) duration of respiration; *2*) inspiratory phase time; *3*) time of PNA increase to its maximum amplitude; *4*) time of the PNA plateau; *5*) expiratory phase time; *6*) amplitude at the beginning of PNA discharge; *7*) amplitude of the PNA plateau; *8*) amplitude of postinspiratory PNA discharge; *9*) ratio of the initial PNA amplitude to the time of its rise to the maximum (reflecting the rate of increase in central inspiratory activity of the respiratory center); *10*) ratio of the amplitude to time of the PNA plateau; *11*) ratio of the maximum amplitude of the postinspiratory discharge to its time.

inspiratory activity in the phrenic nerve [5]. In our study, electrostimulation of neuronal structures in the rostral zone of the VBS elevated arterial blood pressure by an average of 12.3% in both intact and vagotomized rats, and PNA parameters began to alter immediately after the stimulation was started, whereas the arterial pressure rose after a latent period of 1.2 to 1.8 sec. Arterial pressure returned to baseline 45-60 sec after the stimulation was stopped. Cooling the studied neuronal structures to 20°C lowered arterial pressure by 20.5% with of normalization 90-120 sec after cooling. Interestingly, in cats the response of arterial pressure to stimulation of rostral structures in the VBS developed separately from that of respiration [3].

Thus, neuronal structures in rostral VBS enhance generation of CIA during its increase and plateau in rats with preserved afferent inputs from pulmonary mechanoreceptors. In bilaterally vagotomized rats, these neuronal structures strongly increase the initial (i.e., velocity-related) processes of CIA formation as well as the amplitude of this activity, but have little or no effect on the duration of PNA plateau. It can be concluded that neuronal structures in the rostral region of the VBS and pulmonary afferent pulses influence various components of the mechanism by which CIA is formed.

REFERENCES

1. L. I. Kalakutskii, V. F. Pyatin, and O. L. Nikitin, *Fiziol. Zh. SSSR*, **77**, No. 5, 611 (1991).
2. B. Ya. Peskov and V. F. Pyatin, *Fiziol. Zh. SSSR*, **34**, No. 1, 101-110 (1988).
3. K. Budzinska, C. von Eluer, F. F. Kao, *et al.*, *Acta Physiol. Scand.*, **124**, 329-340 (1985).
4. T. Chonan, E. M. Adams, C. von Euler, *et al.*, *Respir. Physiol.*, **80**, No. 1, 45-54 (1990).
5. H. Onimaru, A. Arata, and J. Homma, *Neurosci. Res. Suppl.*, No. 5, 21 (1987).
6. D. W. Richter, *J. Exp. Biol.*, **100**, 93-107 (1982).
7. C. von Euler, *J. Appl. Physiol.*, **55**, No. 6, 1647-1659 (1983).