

# PULSED ACTIVITY OF INSPIRATORY AND EXPIRATORY NEURONS OF THE MEDULLA IN HYPOXIA AND HYPEROXIA

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Studies of the electrical activity of the inspiratory and expiratory neurons of the reticular formation in the medulla [4, 5, 8-14, 21-23] have shown that reciprocal relationships exist between them.

Similar relationships between the electrical activity of the inspiratory and expiratory muscles and nerves in response to various procedures were described by Marshak and Maeva [2, 3] in acute experiments on animals and by Kulik [1] in observations on man.

In the present investigation the dynamics of the pulsed activity of the inspiratory and expiratory neurons was studied during hypoxia and hyperoxia.

## EXPERIMENTAL METHOD

Investigations were carried out on 42 cats, weighing 2-3 kg, anesthetized with Nembutal (50 mg/kg body weight intraperitoneally).

The pulsed activity was detected by means of metallic microelectrodes (diameter of point 1-5  $\mu$ ) and recorded on a "Disa" electromyograph. A unipolar method of recording was used. The indifferent electrode was a silver plate 2  $\times$  2 cm in size, placed on the skull in the region of the frontal sinuses. The active electrode was inserted into the medulla through the cerebellum by means of a Horsley-Clark stereotaxic apparatus in accordance with the coordinates of Szentagothai's atlas. The respiratory center was stimulated by using 10% oxygen in nitrogen and 100% oxygen. For control purposes, the electrical activity of the muscle of the diaphragm and the pneumogram were recorded in step with the pulsed activity of the respiratory neurons.

## EXPERIMENTAL RESULTS AND DISCUSSION

Only those neurons giving volleys of impulses either in step with volleys of impulses of the diaphragm (inspiratory neurons) or during the period of rest of the diaphragm (expiratory neurons) were regarded as respiratory neurons. The view is held that the inspiratory and expiratory neurons are localized separately in the medulla [5-9, 12, 14, 19, 21], although Gesell suggested as long ago as in 1936 that the inspiratory and expiratory neurons are not spatially separable. This view is now held by many investigators [13, 18, 20, 22, 23].

Expiratory and inspiratory neurons were found with the same coordinates. Moreover, action potentials from one inspiratory and a group of expiratory neurons and vice versa were frequently recorded by the same microelectrode.

Examples of the different electrical activity of the expiratory and inspiratory neurons are shown in Fig. 1. Volleys of individual neurons differed considerably in the duration and frequency of the impulses. However, for each neuron they remained constant during inhalation of air.

When the gaseous composition was changed, obvious changes very quickly appeared in the pulsed activity of the inspiratory and expiratory neurons. These changes were seen particularly clearly in experiments in which the pulsed activity was recorded by the same microelectrode from the inspiratory and

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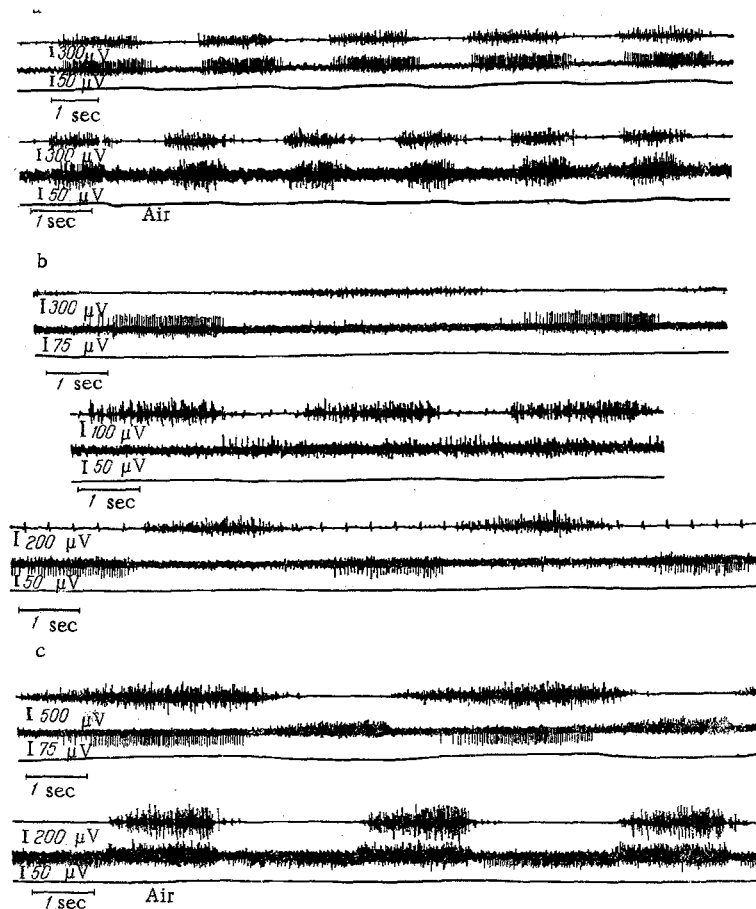


Fig. 1. Pulsed activity of the respiratory neurons of the medulla during inhalation of atmospheric air. a) Inspiratory; b) expiratory; c) inspiratory and expiratory neurons; a-c (from top to bottom): EMG of diaphragm, pulsed activity of respiratory neurons, pneumogram.

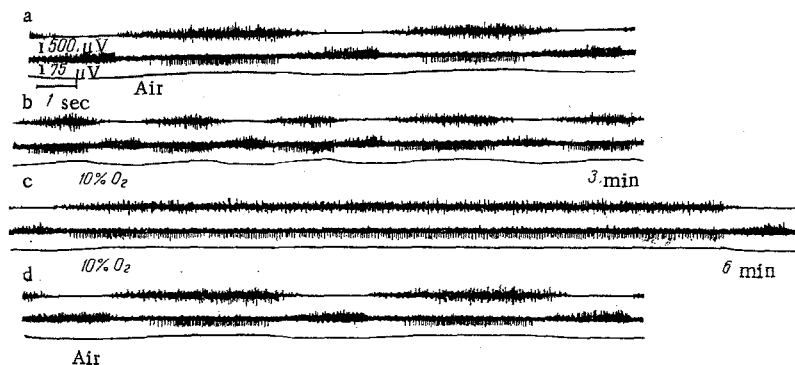


Fig. 2. Pulsed activity of a single inspiratory neuron and a group of expiratory neurons during hypoxia. a) Inhalation of atmospheric air; b) gas mixture containing 10% oxygen; c) inspiratory apnea; d) recovery (after inhalation of atmospheric air for 6 min).

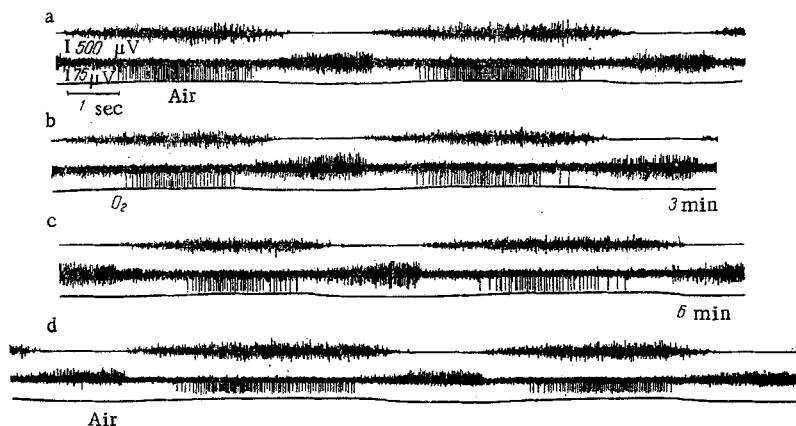


Fig. 3. Pulsed activity of a single inspiratory neuron and a group of expiratory neurons during hyperoxia. a) Inhalation of atmospheric air; b) after inhalation of oxygen for 3 min; c) after inhalation of oxygen for 6 min; d) recovery (after inhalation of atmospheric air for 6 min).

expiratory neurons. For example, inhalation of 10% oxygen for 3-6 min in most cases caused an increase in the frequency of the impulses in the volleys of the inspiratory neurons and a decrease of their frequency in the volleys of the expiratory neurons. The duration of the volleys was reduced (Fig. 2b), and this led to an increase in the respiration rate and in the minute volume of pulmonary ventilation.

In some experiments longer inhalation of a gas mixture poor in oxygen led to disturbance of the respiratory movements and produced inspiratory apnea. During this state the pulsed activity of the inspiratory neurons became continuous (Fig. 2c). With the change of the inspiratory neurons to continuous impulsion, continuous activity also developed in the muscle of the diaphragm (Fig. 2c). With the resumption of rhythmic activity of the respiratory neurons, spontaneous respiration was restored (Fig. 2d).

The appearance of continuous activity of the inspiratory neurons in acute hypoxia may be considered to be associated with the flushing out of carbon dioxide [3]. The ability of the inspiratory neurons to carry out continuous activity was emphasized by Dirken and Woldring (1951). Later, Baumgarten postulated that the activity of the inspiratory neurons is itself continuous, but is periodically inhibited by the expiratory neurons.

During inhalation of pure oxygen for 3-6 min, the pulsed activity of the respiratory neurons changed in the opposite direction: the frequency of the impulses was reduced and the time of the volley of the inspiratory neurons was diminished, while the frequency and amplitude of the impulses in the group volley of the expiratory neurons were increased, indicating the bringing of new active expiratory neurons into play (Fig. 3). The duration of the volley was increased, so that the respiration became slower. Hence, in hypoxia and hyperoxia, reciprocal relationships were clearly revealed between the inspiratory and expiratory neurons.

Similar results in analogous conditions were obtained by Baumgarten [8]. He considers that the changes in the pulsed activity of the expiratory neurons during inhalation of oxygen are not reflected at the periphery, i.e., they do not modify the electrical activity of the expiratory muscles, and that the main function of the expiratory neurons is to inhibit the inspiratory neurons. However, reciprocal changes of electrical activity were found in the authors' laboratory in investigations carried out on the respiratory muscles and also on the phrenic and intercostal nerves [1, 3] in hypoxia and hyperoxia. This suggests that the changes in the pulsed activity of the expiratory neurons during hyperoxia modify the electrical activity of the expiratory muscles.

#### LITERATURE CITED

1. A. M. Kulik, in the book: *Problems in the Physiology and Pathology of the Nervous System*, Moscow (1962), p. 105.
2. M. E. Marshak, *The Regulation of Respiration in Man*, Moscow (1961).

3. M. E. Marshak and T. A. Maeva, *Fiziol. Zh. SSSR*, No. 8, 1052 (1964).
4. O. Achard, V. M. Bucher, *Helv. physiol. pharmacol. Acta*, 12, 265 (1954).
5. E. C. Amoroso, J. G. Bainbridge, F. R. Bell et al., *Nature*, 167, 603 (1951).
6. H. Batsel, *Exp. Neurol.*, 9, 410 (1964).
7. Idem., *Ibid.*, 11, 341 (1965).
8. R. von Baumgarten, *Pflüg. Arch. ges. Physiol.*, 262, 573 (1956).
9. R. von Baumgarten, A. von Baumgarten, and K. P. Shaefer, *Ibid.*, 264, 217 (1957).
10. R. von Baumgarten and E. Kanzow, *Arch. ital. Biol.*, 96, 361 (1958).
11. R. von Baumgarten, H. P. Koepchen, and L. Aranda, *Verh. dtsh. Ges. Kresil.-Forsch.*, 25, 170 (1959).
12. R. von Baumgarten, K. Baltasar, and H. P. Koepchen, *Pflüg. Arch. ges. Physiol.*, 270, 504 (1960).
13. B. D. Burns and G. C. Salmoiraghi, *J. Neurophysiol.*, 23, 27 (1960).
14. M. N. Dirken and S. Woldring, *J. Neurophysiol.*, 14, 211 (1951).
15. C. von Euler and U. Soderberg, *J. Physiol. (London)*, 118, 545 (1952).
16. C. Eyzaguirre and J. R. Taylor, *J. Neurophysiol.*, 26, 61 (1963).
17. R. Gesell, L. Bricker, and C. Magee, *Am. J. Physiol.*, 117, 423 (1936).
18. R. Gesell, *Ergebn. Physiol.*, 43, 477 (1940).
19. E. Haber, K. W. Kohn, S. H. Ngai, et al., *Am. J. Physiol.*, 190, 350 (1957).
20. T. Hukuhara, S. Nakayma, et al., *Jap. J. Physiol.*, 4, 145 (1954).
21. J. R. Nelson, *J. Neurophysiol.*, 22, 590 (1959).
22. G. C. Salmoiraghi and B. D. Burns., *Ibid.*, 23, 2 (1960).
23. Idem., *Ibid.*, p. 14.