LITERATURE CITED

1. E. V. Gubler, Computerized Methods of Analysis and Diagnosis of Pathological Processes [in Russian], Leningrad (1978).
2. A. M. Dygai, E. V. Kirienkova, A. V. Mikhlenko, et al., Byull. Éksp. Biol. Med., No. 4, 397 (1986).
3. N. A. Kraskina, V. M. Man'ko, and M. S. Blyakher, Advances in Immunology, ed. by O. V. Baroyan [in Russian], Moscow (1977), pp. 103-108.
4. A. Ya. Fridenshtein and E. A. Luriya, Cellular Basis of the Hematopoietic Microenvironment [in Russian], Moscow (1980).
5. F. G. J. Hayhoe and D. Quaglino, Hematological Cytochemistry [Russian translation], Moscow (1983).
6. I. L. Chertkov and O. A. Gurevich, The Hematopoietic Stem Cell and its Microenvironment [in Russian], Moscow (1984).
7. V. P. Shakhov, G. K. Popov, L. V. Portnaya, and T. A. Suslova, Gematol. Transfuziol., No. 10, 55 (1985).
8. V. P. Shakhov, A. M. Dygai, A. V. Mikhlenko, et al., Patol. Fiziol., No. 5, 24 (1985).
9. A. Piersma, K. Brockbank, R. Ploemacher, et al., Exp. Hemat., 13, 237 (1985).
10. M. Tavassoli, A. Maniatis, and W. Crosby, Proc. Soc. Exp. Biol. (New York), 13, 878 (1970).

ROLE OF CARDIOVASCULAR NEURONS OF THE BULBAR CARDIOVASCULAR CENTER IN ADAPTIVE RESPONSES OF THE CIRCULATORY SYSTEM TO CHANGES IN COMPOSITION OF THE INSPIRED AIR

S. D. Mikhailova, T. M. Semushkina,
I. Fitze, and G. I. Kositskii

UDC 612.13.014.49-06:
612.282-06:612.223

KEY WORDS: cardiovascular neurons; bulbar cardiovascular center; changes in blood gas composition.

Changes in composition of the inspired air lead to appreciable changes in cardiac activity, vascular tone, and the respiratory system, and in the case of prolonged exposures, changes in hematopoiesis also. Most attention in the study of mechanisms of adaptive responses is currently being paid to the respiratory centers [2, 7, 9, 11], whereas the role of the cardiovascular neurons of the cardiovascular center in these responses has not yet been explained.

The aim of the present investigation was to study the latent period and character of changes in the firing pattern of the cardiovascular neurons of the bulbar cardiovascular center during changes in the O_2 and CO_2 concentrations in the inspired air.

EXPERIMENTAL METHOD

Experiments were carried out on 48 rabbits weighing 3-4 kg under pento-barbital anesthesia (60 mg/kg intraperitoneally). Electrical activity of the bulbar cardiovascular neurons was recorded extracellularly with glass microelectrodes with a tip 1 μ in diameter, and filled with 2.5 M KCl. The neurons were identified by means of stereotaxic coordinates in the region of the nucleus of the tractus solitarius (2 mm rostrally and caudally to the obex). The functional group to which the cardiovascular neurons belonged was determined by means of criteria described previously [3, 4, 6, 12]. The ECG in standard lead I or II, and the blood pressure in the carotid artery, by a direct method using the ÉMT-35 electromanometer, were recorded continuously during all experiments. The parameters recorded were amplified by means of an M-42 four-channel myograph.

N. I. Pirogov Second Moscow Medical Institute.

Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 105, No. 3, pp. 272-274, March, 1988. Original article submitted June 19, 1986.

0007-4888/88/0003-0314$12.50

© 1988 Plenum Publishing Corporation

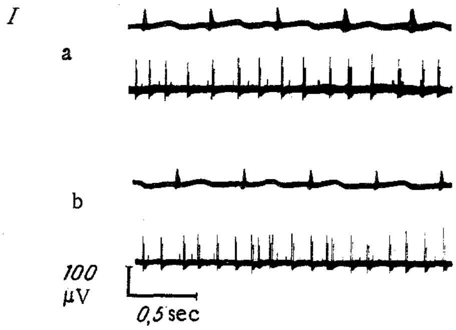

Fig. 1. Spike discharge of cardiovascular interneuron during inhalation of a hypoxic mixture. a) Spontaneous activity of neuron; b) activity during and after exposure. From top to bottom: ECG, neuronal spike discharge.

The blood gas composition was determined by means of a Radelkis biological microanalyzer. Different gas mixtures were produced by means of cylinders of N_2, O_2, and CO_2 connected to artificial respiration apparatus through a system of dosimeters. The animals received the following gas mixtures for 40 sec: hypoxic (5% O_2 in nitrogen), hyperoxic (100% O_2), and hypercapnic (8% CO_2 in air). Hypocapnia was induced by hyperventilation of the animal for 2 min. A special series of experiments was devoted to studying the reaction of bulbar cardiovascular neurons to the same gas mixtures under the condition of cutting of the carotid sinus nerves. We analyzed the activity of 142 bulbar cardiovascular neurons. In all the series of experiments the statistical reliability of the results was estimated by the χ^2 criterion.

EXPERIMENTAL RESULTS

In the experiments of series I activity of 25 afferent cardiovascular neurons and 57 cardiovascular interneurons of the bulbar cardiovascular center was analyzed during inhalation of various gas mixtures. The afferent neurons did not change their spike activity before a change in the heart rate and blood pressure, either in response to a decrease ($p < 0.01$) or to an increase ($p < 0.001$) in the O_2 concentration in the inspired air. With an increase in the in the CO_2 concentration in the inspired air 31% of afferent neurons altered their discharges before the development of hemodynamic changes: 23% of neurons reduced their firing rate and 8% increased it; the latent periods of the response varied from 15 to 35 sec. During hypocapnia 69% of afferent neurons had no change in their firing pattern, but in 31% of cases slowing or quickening of their activity was observed equally often ($p > 0.5$).

Cardiovascular interneurons, unlike the afferent neurons, were highly sensitive to O_2 insufficiency ($p < 0.01$; Fig. 1). Changes in discharges of neurons of this type to hypoxia took place equally often in the form of an increase or decrease in firing rate between 5 and 30 sec after the beginning of exposure. A response to an increase in the O_2 concentration in the inspired air before the development of hemodynamic changes was given by 52% of neurons: 29% responded with a decrease, 23% with an increase in the firing rate; the latent periods of response varied from 9 to 32 sec. Slowing of the spike discharge of the neurons in response to an increase in the CO_2 concentration in the inspired air to 8% was significant ($p < 0.01$; Fig. 2). The latent periods of their response were 6-34 sec. Before the development of hemodynamic changes neurons of this type responded to CO_2 deficiency in 63% of cases: 45% by slowing and 18% by quickening of the spike discharge.

Thus a change in the spike discharge of cardiovascular neurons of the bulbar cardiovascular center was preceded by a change in the hemodynamic parameters (pulse rate and blood pressure). This indicates that changes in the spike discharge of the cardiovascular neurons are primary relative to the hemodynamic changes.

A change in the gas composition of the inspired air led to changes in the blood gas concentrations [5, 8]. In ten experiments on rabbits, with a decrease in the O_2 concentration in the inspired air, the partial pressure of O_2 in the blood 5 sec after the beginning of inhalation was reduced by 3 mm Hg, and after 35 sec it was reduced by 53 mm Hg; with an increase in the O_2 concentration in the inspired air the partial pressure of O_2 in the blood rose at the 5th second by 5 mm Hg and at the 35th second by 192 mm Hg; with an increase in

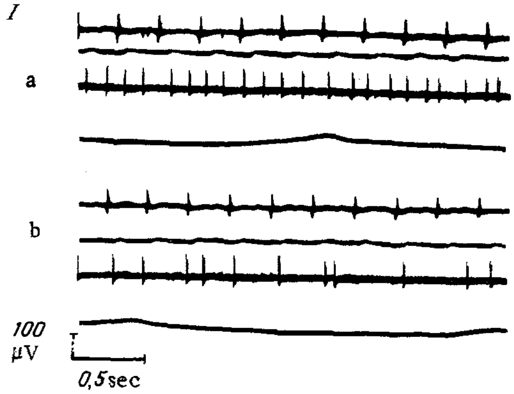

Fig. 2. Spike discharge of cardiovascular interneuron during inhalation of hypercapnic gas mixture. a, b) See Fig. 1. From top to bottom: ECG, blood pressure, spike discharge of neuron, pneumogram.

the CO_2 concentration in the inspired air by 8%, at the 5th second after exposure the partial pressure of CO_2 in the blood was increased by 5 mm Hg, and at the 35th second it was increased by 32 mm Hg. Comparison of the different durations of latent periods of changes in the firing pattern of the neurons during inhalation of gas mixtures with the changes in partial pressure of the blood gases suggests that different types of cardiovascular neurons of the bulbar cardiovascular center differ in their sensitivity to the gas composition of the blood. Afferent neurons and interneurons play different roles in adaptive responses of the circulatory system to changes in the composition of the inspired air. Cardiovascular interneurons, highly sensitive to O_2 deficiency and CO_2 excess, are most active in this process.

Changes in the blood gas composition are detected by arterial chemoreceptors. These include the carotid sinus and aortic chemoreceptive regions, and in rabbits the leading role is played by the carotid sinus reflexogenic zone [1, 10]. To determine the role of the carotid sinus reflexogenic zone in the change in firing pattern of the neuron a series of experiments was carried out to study activity of cardiovascular neurons of the bulbar cardiovascular center after division of Hering's nerves, which carry information from the chemoreceptors of these zones to the medulla.

In this series of experiments spike activity of 18 afferent neurons and 22 interneurons of the bulbar cardiovascular center was analyzed during inhalation of the same gas mixtures. Afferent cardiovascular neurons did not change their spike activity either during hypoxia ($p < 0.1$) or during hyperoxia ($p < 0.001$). In response to hypercapnia 37% of afferent neurons modified their discharge pattern (30% reduced and 7% increased their firing rate), whereas during hypocapnia 45% of neurons increased or decreased their firing rate equally.

Cardiovascular interneurons did not respond to an increase in the O_2 concentration in the inspired air ($p < 0.1$), and in 52% of cases they did not respond to a decrease. With an excess of CO_2 in the inspired air, activity of 36% of neurons changed before any change in the hemodynamics (an increase or decrease in firing rate took place equally often; the latent periods of response ranged from 9 to 39 sec), whereas during CO_2 deficiency 30% of cardiovascular neurons quickened their firing rate.

The results are thus evidence that there is no difference in the response of afferent neurons to changes in the O_2 and CO_2 concentrations in the inspired air whether the carotid sinus nerves are intact or divided. This evidently indicates that the carotid sinus reflexogenic zone does not play an essential role in the activity of the afferent cardiovascular neurons studied. The responses of these neurons only to a change in pCO_2 in the blood may be connected with excitation of central chemoreceptive structures, sensitive to changes in the partial pressure of CO_2 in the blood.

Interneurons which modify their firing pattern in response to hypoxic and hypercapnic gas mixtures in the control series of experiments responded to these factors after division of the carotid sinus nerves in only 48 and 36% of cases, respectively. A significant difference was found in the response of these neurons to an increase in the O_2 concentration in the inspired air ($p < 0.1$). It may accordingly be supposed that these interneurons receive information about changes in the blood gas composition mainly from the carotid sinus reflexogenic zone, which is sensitive to a deficiency and excess not only of CO_2, but also of O_2.

It can thus be concluded that bulbar cardiovascular afferent neurons and interneurons differ in their sensitivity to the gas composition of the blood. Reflex influences on the hemodynamics with a change in the gas composition of the inspired air may be affected from the carotid sinus reflexogenic zone, not only through bulbar respiratory neurons, but also through the system of interneurons of the bulbar cardiovascular center.

LITERATURE CITED

1. L. N. Ardashnikova, The Oxygen Balance of the Body and its Regulation [in Russian], Kiev, (1966), p. 37.
2. I. S. Breslav and V. D. Glebovskii, The Regulation of Respiration [in Russian], Leningrad (1981).
3. G. I. Kositskii, S. D. Mikhailova, S. V. Putygin, and I. N. D'yakonova, Patol. Fiziol., No. 6, 31 (1980).
4. G. I. Kositskii, S. D. Mikhailova, and S. V. Putygin, Abstracts of Proceedings of the 11th All-Union Conference on Physiology and Pathology of Cortico-Visceral Interrelations [in Russian], Leningrad (1981), p. 115.
5. A. M. Kulik and L. N. Kondrat'eva, Byull. Éksp. Biol. Med., No. 4, 39 (1975).
6. S. V. Putygin, S. D. Mikhailova, and G. I. Kositskii, Characteristics of Neurons of the Bulbar Cardiovascular Center [in Russian], Moscow (1985), p. 4. Abstract lodged with the All-Union Institute of Scientific and Technical Information, March 10, 1986, No. 1633-V86.
7. V. A. Safonov, V. N. Efimov, and A. A. Chumachenko, The Neurophysiology of Respiration [in Russian], Moscow (1980).
8. S. I. Frankshtein, T. I. Sergeeva, Z. N. Sergeeva, and E. S. Ivanova, Byull. Éksp. Biol. Med., No. 11 (1972).
9. R. Baumgarten, Pflüg. Arch. ges. Physiol., 262, 573 (1956).
10. C. Eyzaguirre and L. Monti-Bloch, Fed. Proc., 39, 2653 (1980).
11. H. Gauter and M. Bonora, Proceedings of the 28th International Congress of Physiological Science, Budapest (1981), pp. 573-578.
12. G. I. Kositskii (G. I. Kositsky), S. D. Mikhailova (S. D. Mikailova), and S. V. Putygin, Sudden Cardiac Death, ed. by L. Szekers, J. G. Papp, and I. Takats, Budapest (1981), pp. 43-46.