RHYTHM BINDING IN MEDULLARY RESPIRATORY NEURONS

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UDC 612.828:612.21

Spike activity of medullary respiratory neurons was investigated in experiments on cats under nembutal anesthesia in response to repeated stretching of the lungs at different frequencies and with different amplitudes of the respiratory volume.

The experimental results showed that inspiratory and expiratory neurons can begin to discharge in a new rhythm in response to repeated stretching of the lungs with a volume of air greater than the natural volume.

During repeated stretching of the lungs with a hypercapnic gas mixture, with the animal deeply anesthetized, the rhythm-binding ability of the respiratory neurons diminishes sharply and disappears completely after bilateral vagotomy.

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Synchronization of reflex discharges in the rhythm of stimulation of nervous centers has been observed by many investigators [1, 3-11]. Electromyographic studies by Marshak and Maeva [2] showed that in response to repeated reflex stimulation of the respiratory center the natural rhythm of volleys of spikes in the diaphragm disappears and a new rhythm develops, coinciding with the rhythm of adequate stimulation.

Continuing these investigations at the neuronal level, spike activity of medullary inspiratory and expiratory neurons was investigated during an artificially changed rate of respiration and with different amplitudes of the respiratory volume.

TABLE 1. Rhythm Binding in Respiratory Neurons during Repeated Stretching of the Lungs

Neurons	Number of neurons investigated	Number of cases of rhythm transformation	Artificial ventilation with air			Artificial ventilation with hypercapnic mixture	
			rhythm binding			rhythm binding	
			at once	after period of "conflict between rhythms"	absent	took place	absent
Inspiratory	48	6	21	16	5	6	28
Expiratory	27	2	12	10	3	5	23

EXPERIMENTAL METHOD

Experiments were carried out on 20 cats under nembutal anesthesia using stereotactic and microelectrode techniques. Spike activity of respiratory neurons was recorded extracellularly by means of metallic microelectrodes (tip 1-5 μ in diameter).

A new respiration rate was imposed by an apparatus which could vary the respiration rate from 16 to 44/min and the respiratory vovolume from 20-70 ml. Possible displacement of the brain during artificial inflation of the lungs with a large volume of air was prevented by flexing the animals' head through an angle of 45° and by stretching the animal as much as possible in a stereotactic apparatus. In separate experiments the surface of the exposed

Laboratory of Physiology and Pathology of Respiration and the Circulation, Institute of Normal and Pathological Physiology, Academy of Medical Sciences of the USSR, Moscow. (Presented by Academician V. V. Parin.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 68, No. 12, pp. 3-7, December, 1969. Original article submitted November 25, 1968.

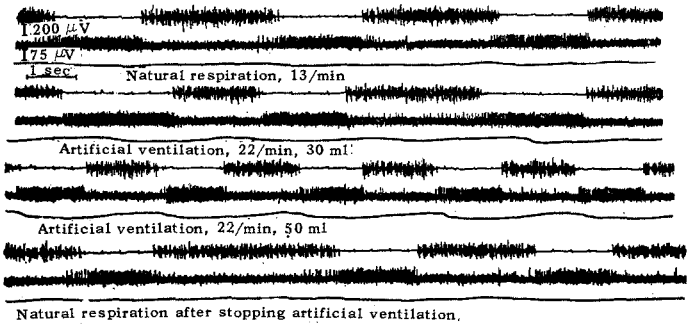

Fig. 1. Spike activity of expiratory neurons during artificial ventilation of the lungs at the same frequency, but with different respiratory volumes. Legend to recordings here and in Figs. 2 and 3 (from top to bottom): EMG of diaphragm, spike activity of medullary respiratory neurons, pneumogram.

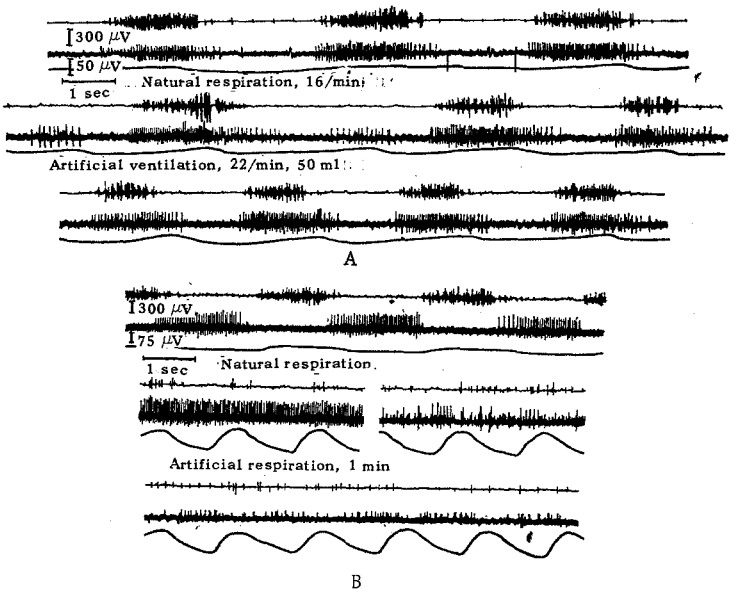

Fig. 2. "Conflict" between natural and artificial respiration rhythms. A) Mixture of natural and newly appearing volleys of inspiratory neurons of the respiratory center; B) continuous spike activity of expiratory neuron with increased frequency in phase of natural volley.

brain was irrigated with agar-agar solution. Atmospheric air and a hypercapnic mixture (3% CO_2 in air) were used for artificial respiration.

EXPERIMENTAL RESULTS

In experiments in which the frequency of artificial ventilation of the lungs varied from 16 to 44/min and the respiratory volume was 20-40 ml, the respiratory neurons most frequently continued to discharge in the rhythm of natural respiration (Table 1; Fig. 1). A new rhythm of volleys of spikes was observed only in 8 of the 75 investigated respiratory neurons, corresponding neither to natural nor the artificial rhythm, i.e., transformation of the rhythm of neurons in the respiratory center was observed.

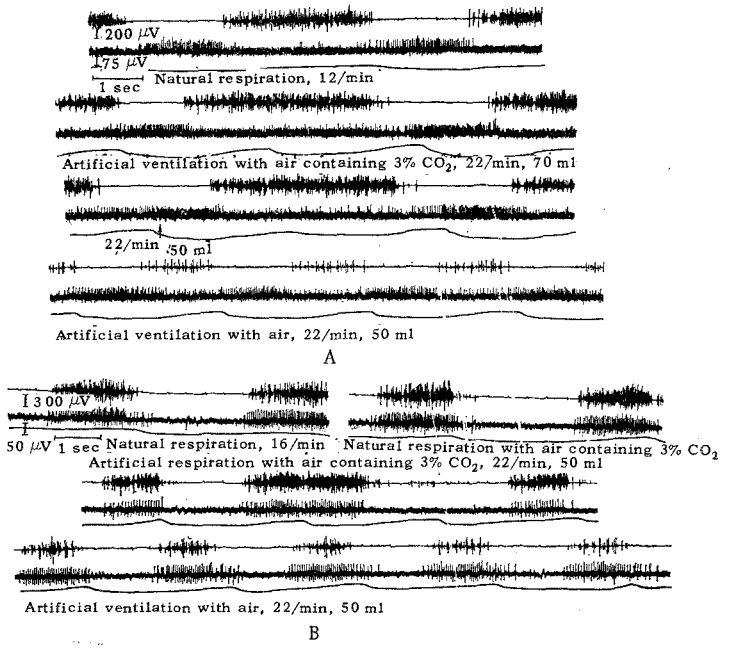

Fig. 3. Spike activity of respiratory neurons during repeated stretching of the lungs with a hypercapnic gas mixture from the beginning of artificial ventilation of the lungs (A) and during natural respiration followed by artificial ventilation of the lungs (B).

In subsequent tests the previous frequency of artificial respiration was preserved,but the respiratory volume was increased to 50-70 ml. It was found that after repeated and forced inflation of the lungs, most respiratory neurons were "bound" to the rhythm of artificial ventilation of the lungs, i.e., their volley activity coincided with the frequency of artificial respiration.

In some cases the binding of respiratory neurons to a new rhythm took place immediately after the animal was transferred to artificial respiration (Fig. 1; Table 1), while in other cases the rhythm binding was preceded by a definite "conflict" between the natural respiration rate and reflex stimulation of the respiratory center arising during artifical inflation of the lungs. This "conflict" between rhythms was manifested in various ways.

In some cases immediately after the animal was transferred to artificial respiration, besides the natural volleys of spike discharges from the respiratory neurons, newly appearing volleys were recorded from the inspiratory neurons corresponding to the rhythm of artificial respiration. The new volleys of the inspiratory neurons were less prolonged and were characterized by a low spike frequency (Fig. 2A). This mixture of rhythms was observed for only 10-15 sec, after which the natural rhythm of volley activity of the respiratory neurons disappeared, and subsequently the discharge of the respiratory neurons coincided with that of artificial respiration (Fig. 2A).

Cases were also observed in which, after the animal had been transferred to artificial ventilation for 30-60 sec, continuous spike activity was recorded with an increase in frequency during the phase of the natural volley of the neuron. New volleys of neurons appeared after 1-3 min, in time with the rhythm of artificial respiration (Fig. 2B).

Volley activity of the inspiratory and expiratory neurons at the new rhythm continued only for a short time. Repeated and forced inflation of the lungs led to the appearance of hypocapnia: the frequency and amplitude of spikes from the active neurons decreased. If the animal was transferred at this moment to ventilation with air containing 3% CO_2, activity of the respiratory neurons was restored and the previously bound rhythm was maintained throughout the period of artificial respiration.

In some experiments, to prevent the onset of hypocapnia, the animal was given the hypercapnic mixture from the beginning of artificial ventilation of the lungs. In most cases the respiratory neurons did not

bind the rhythm to which they were easily transferred when inhaling air before and after inhalation of the hypercapnic mixture (Fig. 3). This suggests that during artificial ventilation with a hypercapnic gas mixture, the respiratory neurons are less able to bind the rhythm of artificial respiration.

To confirm this hypothesis, a series of experiments was carried out in which artificial ventilation with the hypercapnic gas mixture was preceded by inhalation of the same mixture for 3-5 min during natural respiration. Under these conditions the respiratory neurons were completely unable to bind the rhythm of artificial respiration (Fig. 3). Rhythm binding by the respiratory neurons also was interferred with if the animals were deeply anesthetized, and it was completely absent in experiments with bilateral vagotomy.

The results thus show that respiratory neurons are capable of binding a new rhythm of volley activity. However, complete rhythm binding takes place only after repeated stretching of the lungs with a volume of air greater than the natural respiratory volume.

Rhythm binding is due to afferent impulses from receptors in the lungs generated during forced and repeated inflation of the lungs, and transmitted to the respiratory center along the vagus nerves.

There is reason to suppose that the absence of rhythm binding in respiratory neurons during inhalation of the hypercapnic mixture is due to the fact that during simultaneous action of two powerful stimuli (CO_2 and stretching of the lungs) on the respiratory center the respiratory neurons respond to the stronger of the two. Evidently in this case CO_2 is the stronger stimulus, for its reflex and direct action spreads not only to the respiratory center, but also to other structures in the reticular formation of the brain, influencing the respiratory center.

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