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EFFECT OF STIMULATION OF THE MEDIAL AND LATERAL ZONES OF THE RESPIRATORY CENTER ON ELECTRICAL ACTIVITY OF THE DIAPHRAGM, INTERCOSTAL MUSCLES, AND PHRENIC NEURONS

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Experiments on cats showed that the nucleus of the tractus solitarius contains zones during stimulation of which electrical activity of the phrenic neurons and diaphragm is selectively stimulated or inhibited. Stimulation of inspiratory and expiratory zones of the nucleus ambiguus influences the electrical activity of the external intercostal muscles. During stimulation of the corresponding zones in the gigantocellular nucleus electrical activity is changed in both groups of inspiratory muscles simultaneously. It is postulated that the action of stimulation of the zones of the gigantocellular nucleus on both groups of inspiratory muscles is indirect in its mechanism, through neurons of the nucleus of the tractus solitarius and nucleus ambiguus.

KEY WORDS: respiratory center; phrenic neurons; diaphragm; intercostal muscles.

The respiratory center contains groups of neurons connected selectively with centers for the phrenic and intercostal nerves [1,5-6, 8, 10]. Without their connections with the respiratory center, the latter cannot maintain the rhythmic alternation of phases of the respiratory cycle [3, 4, 7, 10].

This paper gives the results of observations on responses of the phrenic neurons, diaphragm, and intercostal muscles to electrical stimulation of the nucleus of the tractus solitarius, nucleus ambiguus, and gigantocellular nucleus in order to compare the effects of such stimulation. The first two nuclei lie in the lateral zone and the third in the medial zone of the respiratory center.

EXPERIMENTAL METHOD

Observations were made on 74 anesthetized (pentobarbital, 40 mg/kg, intraperitoneally) cats. The animals were fixed in a stereotaxic apparatus. The medulla and cervical part of the spinal cord were exposed from the dorsal aspect. Stimulation by square pulses (1-6 V, 5 msec, 100-200 Hz) was applied through bipolar electrodes (distance between them 150 μ) inserted into the brain in accordance with coordinates of a stereotaxic atlas [12]. Action potentials of the respiratory muscles were recorded with bipolar electrodes. Spike discharges of the neurons were recorded by glass microelectrodes with a tip not more than 8 μ in diameter, filled with 3 M KCl solution. Respiration was recorded by means of the MT-54 microthermistor, mounted in the tracheotomy tube.

EXPERIMENTAL RESULTS

Altogether 96 respiratory neurons were recorded in 4-6 cervical segments (70 inspiratory, 24 expiratory, 2 combined inspiratory–expiratory) at a depth of 3-5 mm and situated 1-1.4 mm from the midline. Probing of the nuclei at intervals of 0.5 mm in three planes revealed zones whose stimulation evoked activation or

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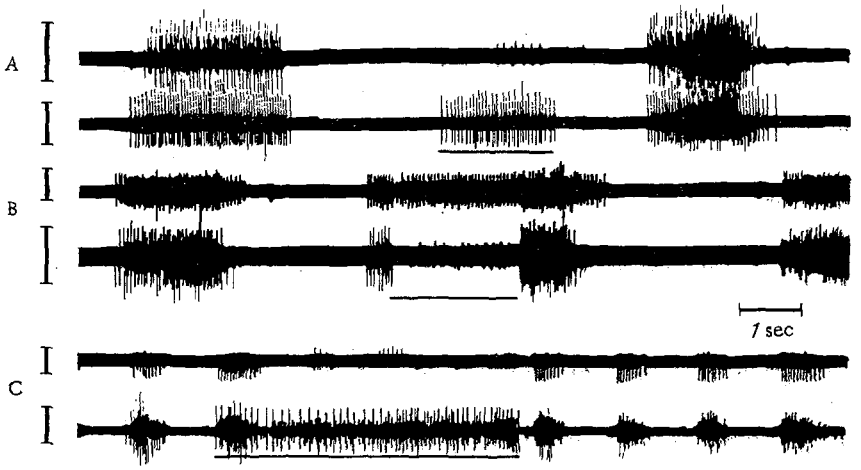

Fig. 1. Selective action of stimulation of nuclei of lateral zone on electrical activity of diaphragm and intercostal muscles. A) Inhibition of combined electrical activity on diaphragm during stimulation of nucleus of tractus solitarius in zone 5 mm rostrally to obex, 2 mm laterally to midline, and at a depth of 2.5 mm from dorsal surface of medulla (calibration 200 μV); B) inhibition of combined electrical activity of inspiratory intercostal muscles during stimulation of nucleus ambiguus in zone 5 mm rostrally to obex and 3.5 mm laterally to midline (calibration 100 and 180 μV); C) increase in electrical activity of inspiratory intercostal muscles during stimulation of nucleus ambiguus in zone 2 mm rostrally to obex and 3.5 mm laterally to midline (calibration 100 and 120 μV). Top record in A, B, and C represents combined electrical activity of diaphragm, bottom record the same of inspiratory intercostal muscles, with marker of stimulation below.

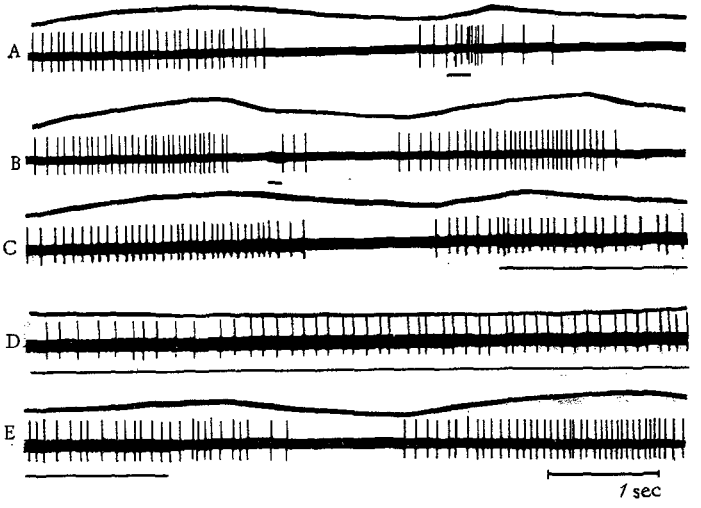

Fig. 2. Responses of inspiratory phrenic neuron to electrical stimulation of nucleus of tractus solitarius and gigantocellular nucleus. A) Respiration and unit activity during stimulation of nucleus of tractus solitarius in zone 3 mm rostrally to obex, 2.5 mm laterally to midline, and at depth of 2.5 mm; B) stimulation of unit activity during brief stimulation of gigantocellular nucleus in zone located 2.5 mm rostrally to obex, 1.5 mm laterally to midline, at depth of 3 mm; C, D, E) respiration and unit activity during prolonged stimulation of same zone. Top record in A-E represents pneumogram, bottom record activity of inspiratory neuron, with marker of stimulation below.

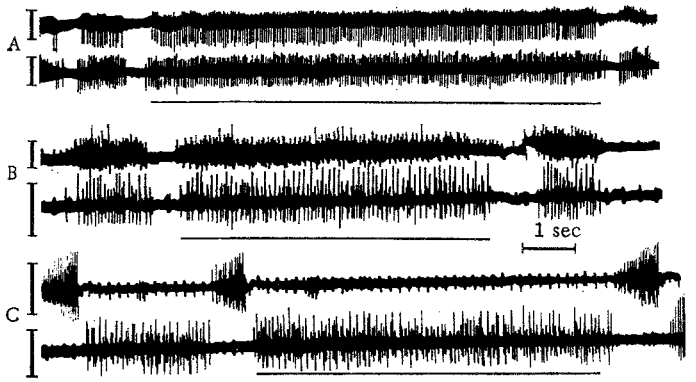

Fig. 3. Effect of stimulation of gigantocellular nucleus on electrical activity of diaphragm and intercostal muscles. A) Stimulation of zone located 3 mm rostrally to obex, 2 mm laterally to midline, and at depth of 4 mm (calibration 100 μV); B) stimulation of zone located 4 mm rostrally to obex, 0.5 mm laterally to midline, and at depth of 3.5 mm (calibration 100 and 200 μV); C) stimulation of zone located 2.5 mm rostrally to obex, 1.5 mm laterally to midline, and at depth of 3.5 mm (calibration 100 μV). Top record in A-C represents combined electrical activity of diaphragm, bottom record the same of intercostal muscles, with marker of stimulation below.

inhibition of the peripheral component of the respiratory system. In the nuclei of the lateral region 22 such zones were found, some of them with a selective influence on the phrenic neurons and disphragm (located mainly in the nucleus of the tractus solitarius; Figs. 1A and 2A), zones whose stimulation evoked a response of the intercostal muscles (located in the region of the nucleus ambiguus; Fig. 1B, C), and zones whose stimulation was accompanied by responses of the diaphragm and intercostal muscles in the same direction. These zones were found over the whole area of the nuclei of the lateral region. Zones whose stimulation evoked activating and inhibitory responses were most numerous at the level of the obex and 3 mm rostrally to it. The mean discharge frequency in the volley from the inspiratory neurons of the diaphragm during stimulation of the nucleus of the tractus solitarius at this level was increased in 42.6% of observations (Fig. 2A) by 63.5 ± 17.9% ($P < 0.01$), in 45.7% of observations it was reduced by 33.6 ± 5.0% ($P < 0.001$), and in 11.7% of observations it was unchanged. The spike discharge of the expiratory neurons was increased in 23.5% of observations by 97.0 ± 49.4% ($P > 0.05$), in 58% of observations it was reduced by 53.1 ± 10.8% ($P < 0.001$), and in 18.5% of observations it was unchanged. In the more rostral region of the nucleus there were significantly fewer such zones. In about half of the observations the combined electrical activity of the external intercostal muscles in response to stimulation of the nucleus of the tractus solitarius was increased or reduced. During stimulation of the nucleus ambiguus in the zone of the obex and 2 mm rostrally to it, the combined electrical activity of the inspiratory intercostal muscles was selectively increased and activity of the diaphragm (Fig. 1C) and of its inspiratory neurons (64.2%) was depressed by 52.8 ± 10.1%. In the other observations the mean discharge frequency in the volley of these neurons was unchanged. In response to stimulation of more rostral regions of the nucleus ambiguus combined activity of the external intercostal muscles was inhibited (Fig. 1B). The combined activity of the diaphragm in this case was reduced in 80% of observations and in the rest it was unchanged.

Stimulation of five zones of the gigantocellular nucleus had a selective action on discharges of the diaphragm, intercostal muscles, and phrenic neurons. The responses were manifested as activation of both groups of inspiratory muscles in response to stimulation of the inspiratory zones (Fig. 3A, B). Stimulation of the expiratory zone caused an increase in the combined spike activity of the internal intercostal muscles and depression of activity of the disphragm and external intercostal muscles (Fig. 3C). Inspiratory zones were found 4 mm rostrally to the obex, 0.5 mm laterally to the midline, and at depths of 3.5 and 4 mm, as well as 2 mm rostrally and at depths of 4 and 4.5 mm, and 2 mm laterally to the midline. The expiratory zone was located 2.5 mm rostrally to the obex, 1.5 mm laterally to the midline, and at a depth of 3.5 mm. In one case stimulation of the expiratory zone evoked expiratory apnea and continuous activity of a phrenic inspiratory neuron (Fig. 2B, C, D, E). The volume of the zones of the gigantocellular nucleus was greater than the volume of the zones of the lateral region whose stimulation evoked responses of the diaphragm and intercostal muscles in the same direction; the intensity of the responses to stimulation of the corresponding zones of the gigantocellular nucleus also was greater.

The latent period of response of the respiratory neurons of the lateral zone evoked by stimulation of the gigantocellular nucleus varied from 5 to 50 msec but was always shorter than the latent period of the phrenic neurons.

The results of these observations confirm several facts discovered by other workers [2, 6-11]. At the same time, new data were obtained on the effects of structures of the respiratory center on the motor mechanism of the respiratory movements. A specific effect followed stimulation not of the whole nucleus of the tractus solitarius, nucleus ambiguus, and gigantocellular nucleus, but only of certain zones of them. These medullary nuclei are thus functionally heterogeneous. Each of them contains zones whose stimulation evokes no responses of the neuromotor apparatus of the respiratory system. In the nuclei of the lateral region there are structures whose stimulation is accompanied by responses of activation and depression of the activity of different groups of inspiratory muscles (diaphragm and intercostal). Finally, structures whose stimulation is accompanied by a clearly selective action were found in the nuclei of the lateral region. Special attention must evidently be paid to the fact that stimulation of particular zones of the gigantocellular nucleus regularly evokes a coordinated increase in electrical activity of the diaphragm and intercostal muscles. The action of stimulation of the inspiratory and expiratory zones of the gigantocellular nucleus suggests that these zones differ in their physiological role from the other zones of the gigantocellular nucleus. In the writers' view, these are "integrating" zones of the respiratory center.

It can be concluded from the results of this comparison of the latent periods of responses of neurons in the lateral region and of phrenic neurons to stimulation of the gigantocellular nucleus that the action of that nucleus on the spinal efferent mechanism is exerted indirectly, through neurons of the lateral region of the respiratory center.

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