Respiratory Effects of Sensorimotor Cortex and Their Mechanisms in Rats

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Acute experiments on anesthetized rats showed differential effect of various areas of the sensorimotor cortex on activity of the respiratory center. It is hypothesized that GABAergic structures of the solitary tract nucleus play an important role in the mechanisms of respiratory effects of the sensorimotor cortex.

Key Words: *sensorimotor cortex of the brain; respiratory center; nucleus of solitary tract; GABAergic system*

It is believed that any suprabulbar regions of the brain can participate in the regulation of respiration. This participation is provided by the formation of functional complexes of the nervous centers, which include the respiratory center (RC) [5]. Cerebral cortex occupies a special place in the hierarchy of suprabulbar structures participating in the central mechanisms of regulation [1,2,4,6]. However, neurochemical mechanisms of respiration regulation by structurally and functionally different cortical areas (in particular, rat sensorimotor cortex) remain unstudied. Neuroanatomical and physiological experiments revealed direct projections from the sensorimotor cortex to the nucleus of the solitary tract (NST) [11,12], whose ventrolateral subnucleus is a component of the dorsal respiratory group [7]. The key role of GABA and other elements of GABAergic system in the functioning of this RC region was shown [3,8].

The purpose of the present study was to examine respiratory influences of various areas of the sensorimotor cortex and to elucidate the role of GABAergic structures of NST in the mechanisms of modulation of RC activity.

MATERIALS AND METHODS

Outbred male and female rats (n=68) weighing 210-265 g were anesthetized with urethane (1.5-1.8 g/kg intraperitoneally). Craniotomy above the sensorimotor cortex (3 mm rostrally and 5 mm caudally to the coronal suture, 4 mm laterally from the sagittal suture) of the right hemisphere was performed according to the rat brain map [9]. Monopolar electrostimulation (80-250 μA, 50 Hz, 0.5 sec impulse duration) was performed with a surface ball electrode (200 μ active surface). Indifferent electrode was fixed to nasal bones.

For elucidation of the neurochemical mechanisms of regulation of respiration by the sensorimotor cortex, the stimulation was carried out before and after microinjections of GABA (10^{-3} M, 0.2 μl) or specific $GABA_A$ receptor blocker bicuculline (10^{-3} M, 0.2 μl) into NST. Control rats received the same volume of cerebrospinal fluid. Microinjections were performed according to the atlas of rat brain [10].

Respiration and activity of inspiratory muscles were evaluated by spirograms and electromyograms (EMG) of the diaphragm. Respiration volume and frequency and minute volume of respiration were evaluated by spirograms. Bioelectrical activity from the diaphragm was recorded bipolarly via needle electrodes. The duration of burst activity, burst intervals, frequency and mean amplitude of oscillations in the bursts were estimated on EMG. Experimental curves were obtained on an H-338 recorder. The body temperature during the experiment was maintained at 37.0±0.5°C.

The results were processed statistically using Student's t test.

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RESULTS

Electrostimulation of different areas of the sensorimotor cortex caused pronounced changes in respiration pattern and bioelectrical activity of the diaphragm. The respiratory responses depended on the location of stimulating electrodes and parameters of stimulating pulses (Fig. 1). Stimulation of the rostral areas of the sensorimotor cortex (0.2-3.0 mm rostrally from the coronal suture and 1-4 mm laterally from the sagittal suture) caused maximum changes in activity of the bulbar RC. Stimulation of these areas with low amplitude current (100 μA, 50 Hz, 0.5 msec) insignificantly inhibited rhythmogenic function of RC: the frequency and duration of respiratory bursts decreased by 15.8 and 10.4%, respectively ($p<0.05$). The respiration frequency and minute respiration volume decreased by 13.7 and 16.3% ($p<0.05$), respectively. Increasing the current amplitude to 150 μA (unchanged frequency) potentiated the respiratory effects: the interburst intervals increased by 31.2% ($p<0.01$), respiration frequency decreased by 29.4% ($p<0.01$), mean frequency and amplitude of burst activity of the respiratory muscles decreased by 22.7 and 18.7%, respectively ($p<0.01$ and $p<0.05$, respectively), and volume component of the respiration pattern decreased by 21.7% ($p<0.05$). Suprathreshold stimulation (250 μA, 50 Hz) of rostral areas of the sensorimotor cortex sharply inhibited respiration. This respiration pattern was characterized by irregular interburst intervals and respiration attests (in 12.4% animals). Respiratory responses to stimulation of the sensorimotor cortex 2.5-3.0 mm caudally to the coronal suture were characterized by a higher threshold: changes in RC activity were recorded only at a current strength of 140 μA (50 Hz, 0.5 msec). Similar to stimulation of rostral areas, the changes in respiration pattern and bioelectrical activity of the diaphragm attested to inhibitory influence of caudal areas of the sensorimotor cortex on temporal parameters of the respiration rhythm. At the same time, changes in frequency and amplitude parameters of diaphragm burst activity and respiration volume were insignificant.

The most active respiratory areas topically correspond to motor representation of forelimbs and vibrissae. This cortical area is probably a focus of functional integration of projections from the respiratory and motor systems.

For evaluation of neurochemical mechanisms of the regulatory effects of the sensorimotor cortex on respiration, the stimulation of the sensorimotor cortex was carried out after microinjection of GABA or specific $GABA_A$ receptor blocker bicuculline in NST. It should be noted that these neurotropic agents possessed intrinsic respiratory activity: GABA injections inhibited AC activity, while bicuculline stimulated it. Similar regularities were also observed by other authors [3,8]. The combination of electrical stimulation of the most active areas of the sensorimotor cortex with activation of GABAergic system in NST produced more pronounced inhibition of RC compared to electrical stimulation alone (Fig. 2). The interburst intervals

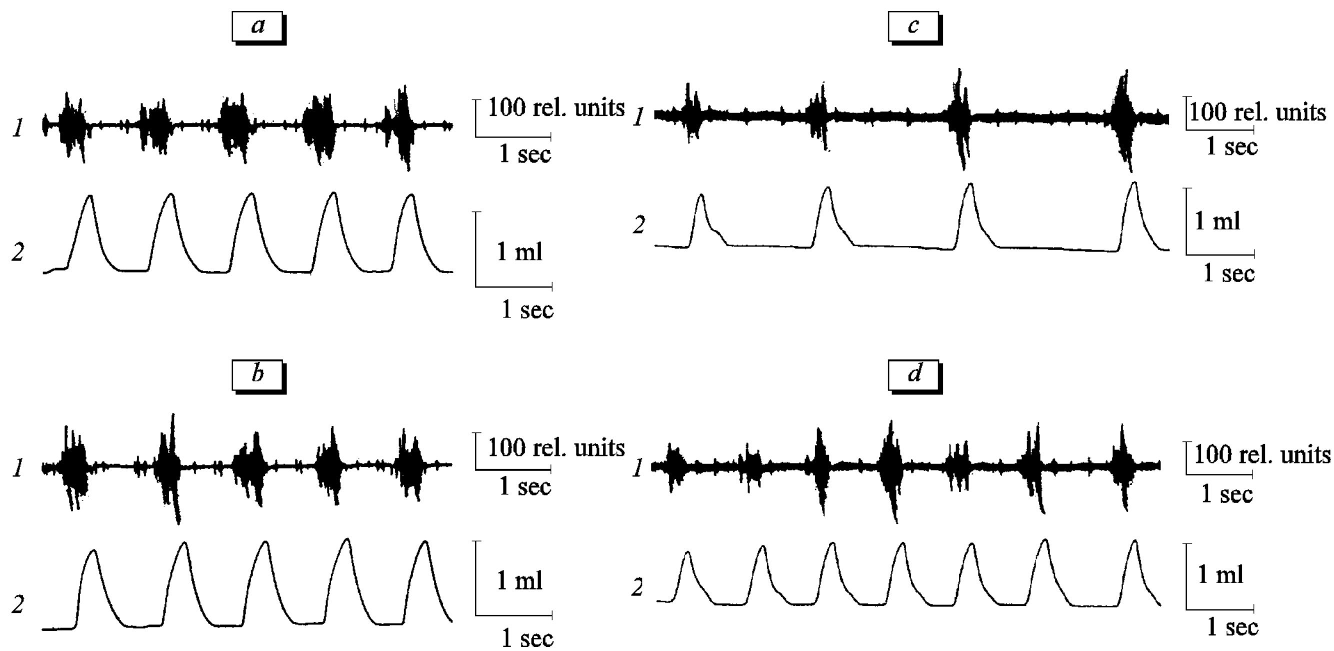
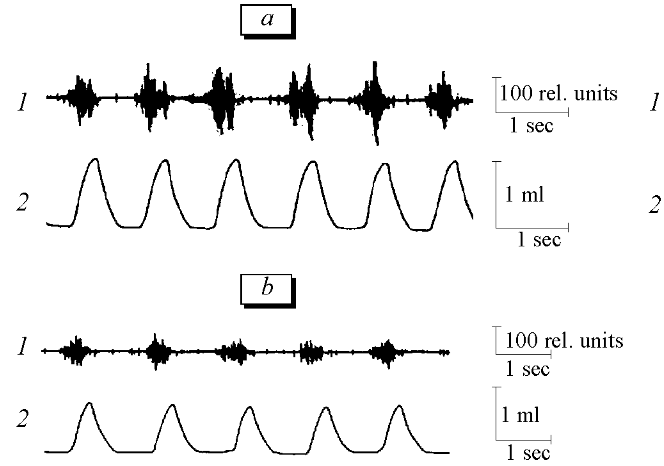


Fig. 1. Bioelectrical activity of diaphragm (*1*) and respiration pattern (*2*) before (*a, b*) and during electrical stimulation (150 μA, 50 Hz, 0.5 sec; *c, d*) of the rostral (*a, c*) and caudal (*b, d*) areas of the sensorimotor cortex.



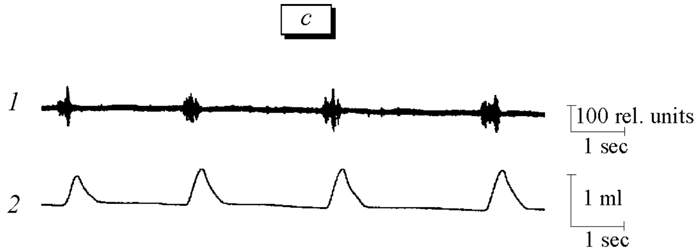


Fig. 2. Bioelectrical activity of diaphragm (*1*) and respiration pattern (*2*): *a*) initial, *b*) microinjection of GABA (10^{-3} M) in the nucleus of solitary tract, *c*) microinjection of GABA+electrical stimulation (150 μA, 50 Hz, 0.5 sec) of the rostral sensorimotor cortical area.

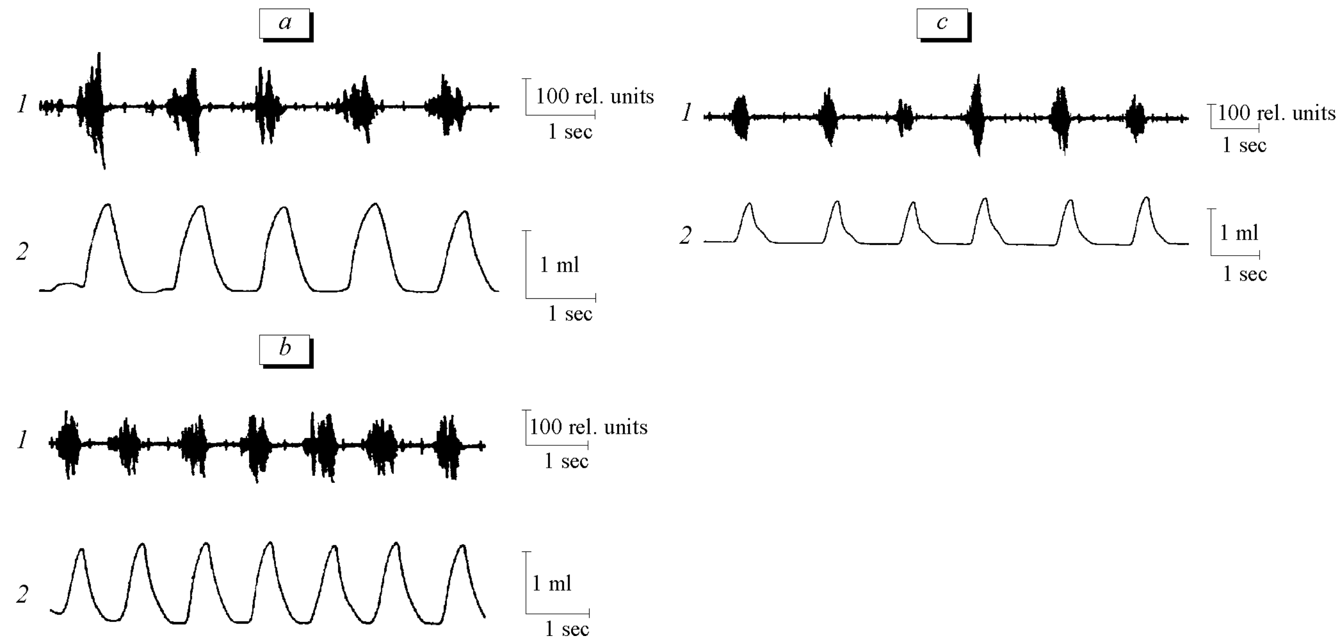


Fig. 3. Bioelectrical activity of diaphragm (*1*) and respiration pattern (*2*): *a*) initial, *b*) microinjection of bicuculline (10^{-3} M) in the nucleus of the solitary tract, *c*) electrical stimulation (150 μA, 50 Hz, 0.5 sec) of the rostral sensorimotor cortex+bicuculline (10^{-3} M).

increased by 42.8% ($p<0.01$), the frequency and minute volume of respiration decreased by 38.3 and 42.7% ($p<0.01$ and $p<0.05$), respectively (Fig. 2). The blockade of GABA receptors in NST attenuated the inhibitory effect of the sensorimotor cortex on respiration: the interburst intervals on diaphragm EMG increased by 23.6% ($p<0.05$), frequency and minute respiration volume decreased by 18.4 and 24.7% ($p<0.05$ and $p<0.01$), respectively (Fig. 3).

These findings suggest that rostral areas of the sensorimotor cortex are more closely connected with RC structures and modulate primarily the rhythmogenic function of RC. These respiratory effects can be realized via GABAergic system of NST.

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