CHANGES IN UNIT ACTIVITY OF THE RESPIRATORY CENTER IN ADRENALIN APNEA

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Unit activity in the region of the respiratory center in the medulla of anesthetized cats was recorded extracellularly with glass microelectrodes. After intracellular injection of an apnea-inducing dose of adrenalin, some inspiratory neurons continued to discharge regular volleys of spikes during apnea, increasing the duration of the volleys and the number of spikes in each volley. Other neurons stopped generating regular volleys and discharged uniformly and continuously throughout the period of apnea. Most inspiratory neutrons, however, ceased their activity completely during apnea. Among expiratory neurons, none were recorded which generated regular volleys of spikes during the period of adrenalin apnea. The activity of these expiratory neurons stopped at different times after injection of adrenalin.

Adrenalin has a powerful effect on respiration and can cause it to stop (adrenalin apnea) [2, 4]. It is usually accepted that apnea is the result of a reflex effect of adrenalin on activity of the respiratory center through changes in arterial pressure which act upon receptors of the cardio-aortic and carotid sinus zones [1-4]. In addition, the possibility of a direct action of adrenalin on the respiratory center cannot be ruled out.

Whatever the method of action of adrenalin on the respiratory center, analysis of changes in activity of the respiratory neurons during adrenalin apnea is a matter of considerable interest for elucidation of the functional organization of this center and the mechanism of spontaneous recovery of respiration after apnea. No information on this problem can be found in the accessible literature.

EXPERIMENTAL METHOD AND RESULTS

Experiments were carried out on cats anesthetized with nembutal (35-40 mg/kg). Unit activity in the bulbar respiratory center was recorded extracellularly with glass microelectrodes (1-3 μ; 2.5 M KCl). Temporary cessation of respiratory movements (adrenalin apnea) was produced by injection of 0.1 % adrenalin solution (in ampules for injection) in a dose of 0.3-1 ml per animal. The duration of volleys of spikes in various phases of respiration, the number of spikes, the mean frequency, duration of intervals between volleys, and the distribution of interspike intervals in the volley were analyzed.

Activity of 28 neurons, 15 inspiratory and 13 expiratory, was recorded. Adrenalin apnea usually occurred 10-15 sec after intravenous injection of adrenalin. The time of onset of apnea was preceeded by a gradual diminution in the depth and an increase in the duration of the respiratory movements. After injection of adrenalin, and before the onset of apnea, various groups of inspiratory and expiratory neurons increased the number of spikes per volley appreciably (inspiratory by 1.29 ± 0.39 times, expiratory by 1.21 ± 0.41 times), and also increased the duration of the volleys (inspiratory by 1.1 ± 0.26 times, expiratory by 1.26 ± 0.38 times) approximately to the same degree, so that the mean frequency of spikes in the volleys changed only negligibly (on the average by 1.03 ± 0.17 times for inspiratory neurons and by 0.96 ± 0.2 times for expiratory; in all cases

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TABLE 1. Changes in Activity of Inspiratory Neurons during Adrenalin Apnea

Expt. No.	No. of spikes per volley		Duration of volley (in sec)		Mean frequency of spikes of volley (spikes/sec)		Length of interval between volleys (in sec)	
	A	B	A	B	A	B	A	B
1	88	268	2,6	13,2	33,6	20,4	2,9	7,9
2	77	164	1,1	3,3	68,5	49,1	4,0	6,8
3	55	333	4,3	24,4	12,8	13,8	4,1	6,1
	—	69[1]	—	4,9[1]	—	19,0[1]	—	6,1[1]
	—	210	—	11,6	—	18,2	—	4,7
	—	53[1]	—	4,9[1]	—	15,0[1]	—	5,7[1]
	—	183	—	12,3	—	14,8	—	7,0
4	—	125	—	3,8	—	33,0	—	0,6
	—	57[1]	—	1,1[1]	—	50,5[1]	—	0,9[1]

*Values obtained after starting up artificial respiration in period of apnea

Fig. 1. Change in unit activity of respiratory center after injection of adrenalin. A) normal breathing; B) changes in unit activity after injection of adrenalin; C) restoration of original activity. Top tracing shows unit activity, bottom tracing respiratory movements (inspiration upward). Time marker 1 sec.

$P < 0.001$). Characteristically, the typical distribution of spikes in the volley shown by the different groups of neurons during normal breathing was undisturbed after injection of adrenalin.

During the period of adrenalin apnea, usually lasting 15-60 sec, the following qualitative changes took place in unit activity. Some inspiratory neurons continued to discharge regular volleys of spikes, although the duration of the volleys and the number of spikes per volley were increased. Other neurons ceased to generate regular volleys and discharged continuously and evenly throughout the period of apnea. Most inspiratory neurons, however, ceased their activity completely during apnea (Fig. 1).

In the period of adrenalin apnea, regular generation of volleys was not observed by any of the expiratory neurons. The activity of some groups of expiratory neurons ceased even before apnea developed. Regular volleys of another group of expiratory neurons ceased at the moment of onset of apnea. A group of expiratory neurons whose spikes continued during normal respiration throughout the phase of expiration, their frequency reaching a maximum in the middle or at the end of the volley, began to discharge continuously after the onset of apnea, the frequency of the spikes gradually decreasing until they ceased altogether.

All types of respiratory neurons, except a certain group of inspiratory neurons, thus either ceased to discharge completely or generated a continuous discharge of spikes during the period of adrenalin apnea.

It is characteristic of the inspiratory neurons mentioned above that during normal breathing the volley of spikes persists throughout the phase of inspiration. Usually, at the beginning of the volley the frequency of the spikes increases a little, after which it remains noticeably unchanged throughout the rest of inspiration. Only just before the volley ends does the frequency of the spikes decrease slightly (Fig. 2A). In the period of apnea, similar changes in spike frequency in the volleys were observed, i.e., the character

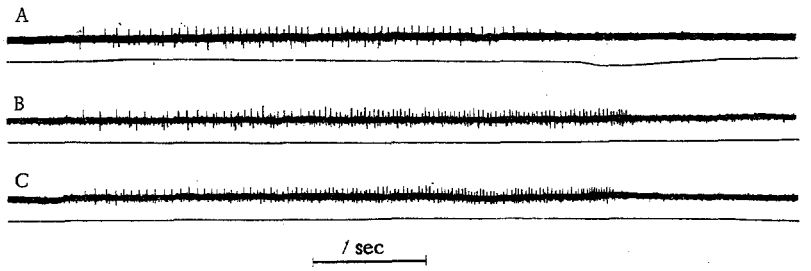

Fig. 2. Changes in activity of inspiratory neurons during adrenalin apnea. A) During normal respiration; B, C) during apnea (tracing is continuous 18 sec after injection of adrenalin). Top tracing shows unit activity, bottom tracing respiratory movements (inspiration upward). Winding speed 50 mm/sec.

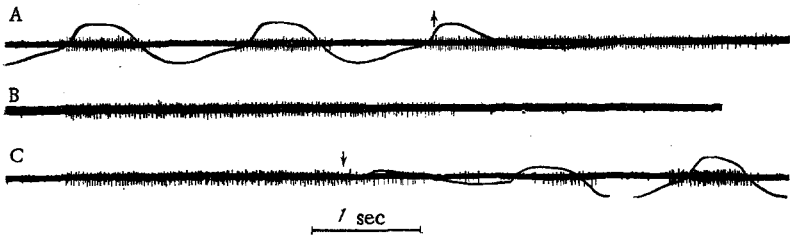

Fig. 3. Effect of artificial respiration on activity of inspiratory neurons during adrenalin apnea. A, B) (Continuous tracing): stopping artificial respiration; C) starting up artificial respiration (recording made 14 sec after end of A). Legend as in Fig. 1. Arrows indicate time of stopping and starting artificial respiration.

of the change in frequency of spikes in the volley was undisturbed (Fig. 2B), although spike activity of the neurons showed considerable quantitative changes (Table 1). It is clear from this table that during apnea the duration of the volleys, the number of spikes per volley, and the duration of the intervals between volleys were all increased several times. Because the changes in the number of spikes per volley and in the duration of volleys were in the same direction, the mean frequency of spikes per volley showed a smaller change. The duration of intervals between volleys of spikes also increased slightly. It is very important to note that the starting up of artificial respiration in the period of apnea (Table 1) did not immediately cause a decrease in the number of spikes per volley or in the duration of the volleys to bring them nearer to normal (Table 1; Fig. 3). Stopping the artificial respiration produced changes in the opposite direction.

In the case of reversible apnea with spontaneous recovery of the respiratory movements, the quantitative indices and the character of unit activity virtually returned to their initial levels (Fig. 1C).

Injection of adrenalin depressed activity of the so-called reticular neurons, which is not synchronized with the phases of the respiratory cycle. Often activity of the reticular neurons ceased even in cases when apnea did not develop. In cases when apnea developed, spike activity of the reticular neurons ceased before respiration was interrupted.

After the action of adrenalin had stopped, the initial form of unit activity was gradually resumed.

Verificatory experiments with denervation of the carotid sinus zone (unpublished data) showed that adrenalin apnea is the result of reflex inhibition of activity of the respiratory center from the carotid sinus zones associated with elevation of the blood pressure after injection of adrenalin.

The cessation of respiratory movements in adrenalin apnea is evidently explained by reflex inhibition of unit activity followed by disturbance of the relationships between inspiratory, expiratory, and reticular groups of neurons of the bulbar respiratory center. Reticular neurons with regular, continuous discharge of spikes cease their activity first, and this is followed by disturbance of function of some groups of expiratory neurons. The expiratory neurons ceased to generate regular volleys, and this in turn disturbs

the activity of the inspiratory population of respiratory neurons. With a decrease in the flow of afferent impulses from baroreceptors of the carotid sinus zone, normal activity of the respiratory neurons is restored and respiratory movements resumed. The facts described above suggest the existence of special mechanisms for maintaining the rhythmic activity of certain groups of neurons in the bulbar respiratory center in cases when volley activity of most types of neurons is disturbed or abolished.

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