FUNCTIONAL CHANGES OF THE FROG RESPIRATORY CENTER AFTER ELIMINATION OF AFFERENT PULMONARY IMPULSES

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Several reports [2, 5, 9 - 16] compel the assumption that the periodic kinds of impulses flowing from the pulmonary receptors to the inspiratory center are mediated through the expiratory center which when its action is weak maintains the initial excitation in the inspiratory center and suppresses it when it is strong.

We here report the results of experiments in which we applied focal stimulation with a microelectrode, and made a direct measurement of the physiological parameters in the nerve cells of the inspiratory and expiratory centers and in the motor region of the respiratory center of the frog. The measurements were made during normal pulmonary respiration, while impulses from the lungs were eliminated. We also described the results of experiments in which single direct electrical stimuli were applied to the inspiratory center during various phases of the respiratory cycle. The experiments were made also for the purpose of determining the actual condition underlying the mechanism of integration by the respiratory center of the initial innate excitation in the inspiratory center and the regulating afferent influences from the pulmonary receptors.

METHOD

The animals chosen for the experiments were frogs, because in them we expect to find a simple primitive structural scheme of the vertebrate respiratory center. We used frogs which showed well-marked pulmonary respiration (Rana esculenta and R. ridibunda). In some of the experiments the frog was fixed to a board, and the central nervous system was left intact; there was an aperture opposite the mouth, and the animal was placed belly downwards. Myographic records were made of the respiratory movements of the base of the oral cavity in normal animals and in those with exposed lungs; in the first place the lungs were moistened with physiological saline (normal) and then with 2% novocaine solution. Control experiments showed that the actual exposure of the lungs itself does not cause any changes in the initial pulmonary respiration. A novocaine injection into the lymph sacs is also without effect on normal respiration. In other experiments, focal stimulation was applied to the inspiratory and expiratory centers and to the motor region by means of a nichrome electrode surrounded for the whole of its length with glass, except for the tip, which had a diameter of 30 μ. Its position was checked before the beginning of the experiment by observing the local contraction of the corresponding respiratory muscles in response to threshold stimulation, and after the experiment its position was confirmed histologically. A detailed description of the position of these regions, and of the methods of recording the responses has been made previously [3]. In the third set of experiments, additional stimulation was applied by a microelectrode placed in the inspiratory center, and records were made of the movements of the respiratory muscles of the base of the oral cavity in response to additional stimulation. The stimulation was made by applying threshold condenser discharges of 17 msec duration. The threshold was determined during the pause after expiration.

RESULTS

The investigations described showed that elimination of pulmonary impulses did not lead to disturbance of respiration until the 15th minute, and after 30 minutes typical Cheyne-Stokes breathing occurred. If in addition, the proprioceptors of the respiratory muscles of the base of the oral cavity are eliminated by moistening with 1% novocaine solution, then pulmonary respiration ceased for the first hour of observation. However, the ensuing oscillatory respiration continued and increased in amplitude. M. G. Antonova [1] observed the occurrence of Cheyne-Stokes breathing in frogs after only the pulmonary respiratory proprioceptors had been eliminated. It must therefore be supposed that oscillatory respiration in the frog results from the elimination of a widespread receptor region, when the only impulses which continue to arrive are those from the bifurcation of the aorta, whose influence on the respiratory center is decisive, as B. D. Kravchinskii showed [6].

The experiments in which the functional characteristics were analyzed showed that elimination of pulmonary impulses causes well-marked changes in the physiological parameters of both the inspiratory and the expiratory centers. For example, in an experiment performed on February 24, 1960, before elimination of the pulmonary impulses, the rheobase in the region of the inspiratory center was 8 v, the chronaxie was 0.323 msec, and the constant of accommodation (λ) 135 msec. The topography of the region is shown in Fig. 1. Half an hour after elimination of the impulses, the rheobase was 11 v, i.e. it had increased 1.3 times. The chronaxie had increased to 1.7 msec, i. e. almost six times, and the constant of accommodation (λ) had increased to 350 msec, i. e. three times. The other experiments showed the same tendency to a change of the physiological parameters of the inspiratory center due to elimination of the pulmonary receptors, and a table showing these results was drawn up.

TABLE 1. Physiological Parameters in the Region of the Nerve Cells of the Inspiratory and Expiratory Centers, Before and After Elimination of the Pulmonary Receptors

Inspiratory center[1]			Expiratory center[2]		
rheobase (in v)	chronaxie (in msec)	constant of accommodation λ (in msec)	rheobase (in v)	chronaxie (in msec)	constant of accommodation λ (in msec)
Before elimination					
7.3	0.186	61.8	10.1	0.209	105.7
After elimination					
17	1.277	225	15.7	0.999	113.9

[1] Mean results of 21 experiments.

[2] Mean results of 20 experiments.

Thus, by eliminating pulmonary impulses, excitability of the inspiratory center was reduced, the time for the development of a single excited condition prolonged, and accommodation greatly slowed down, which, as is known, indicates an enhanced power to maintain prolonged discharges.

Measurement of the parameters in the region of the expiratory center (as shown in Fig. 2) in an experiment performed on March 16, 1960 shows that before elimination of the pulmonary receptors, the rheobase was 13 v, the constant of accommodation λ 116 msec, and the chronaxie 0.259 msec. Half an hour after elimination of the receptors, the rheobase rose to 20 v, i. e. 1.75 times. The constant of accommodation λ was then equal to 120 msec, i.e. it had not changed. However, the chronaxie had increased almost ten times, because it now had a value of 2.22 msec. The same sort of changes were observed in the other experiments, whose results are given in the table. Therefore, when the flow of pulmonary impulses to both the expiratory and the inspiratory centers is eliminated, there is a fall in excitability and in functional lability, but the rate of the accommodative process remains almost normal.

The results obtained with elimination of impulses from the pulmonary receptors differ from those which we obtained previously [3]. Then, the parameters changed only in the inspiratory center, while the process of accommodation increased strongly, and at the same time there was a fall in excitability and functional lability. Pulmonary respiration ceased entirely, and so did oscillatory respiration, if there was any. When impulses from the pulmonary receptors were eliminated, although excitability and functional lability in both centers were reduced, the ability to maintain prolonged discharges was increased, particularly in the inspiratory center, where according to our findings and to the suggestions of other authors, the initial innate excitation process is initiated. Consequently, excitation of these two centers is still possible if the stimuli are made more intense or more prolonged. But because our previous experiments have shown that the initial innate excitation is developed in the inspiratory center through the action of maintained stimulation from the bifurcation of the aorta, it is clear that when impulses from the pulmonary receptors are blocked, the respiratory movements become relatively weak. Therefore, in order to attain a critical level, excitation of the inspiratory center from the receptors at the aortal bifurcation must act for longer. This requirement may be the reason for a disturbance of the natural breathing. Experiments in which measurements were made of the physiological parameters of the region of the motor respiratory center of the frog showed that elimination of the pulmonary receptors did not change the initial condition of the motor region.

The results which we obtained indicate that pulmonary impulses, just like impulses from the aorta, are very important for the maintenance of a high functional level during normal respiratory activity. This circumstance constitutes a proof of the proposal made by A. A. Ukhtomskii [8] that afferent impulses to the center increased its lability.

In other experiments, supplementary local stimuli from an anode or cathode were applied to the inspiratory center at various phases of a single respiratory cycle; they were first applied in the middle of the pause between inspiration, and stimuli were chosen which would evoke a supplementary inspiration ("extra inspiration"). Next, the same stimulation was applied during other phases of the cycle. It was found that the inspiration occurred earlier if cathodal stimulation was applied the moment before the natural intake of breath was due. If it occurred at a time when inspiration had already started, then the amplitude was increased (Fig. 3). If however it fell at a time when intake of breath had already occurred, then there was a break in the curve, and it was lower than normal, and took less time. This break-off was observed also when the stimulation was applied during the moment of maximum normal inspiration. If it was applied soon after expiration had started, no additional cathodal inspiration was produced. Later (and the effect was the more marked the nearer the expiration was to its maximum), extra responses to the supplementary stimuli appeared, which gradually increased. Additional stimuli to the ipsilateral center with an anode always caused suppression of respiratory movements at all phases of the respiratory cycle.

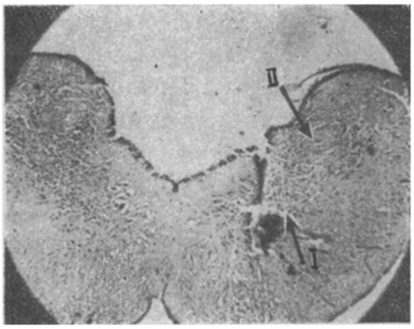

Fig. 1. Region of the inspiratory center Transverse section of the medulla oblongata of the frog at the level of emergence of the cranial nerves IX and X. I) Position of the end of the stimulating microelectrode; II) position of the tractus solitarius. Micrograph. Magnification ocular 15 X, objective 9 X 0.2. Taken with a 6 X 9 photographic attachment. Stained in hematoxylin.

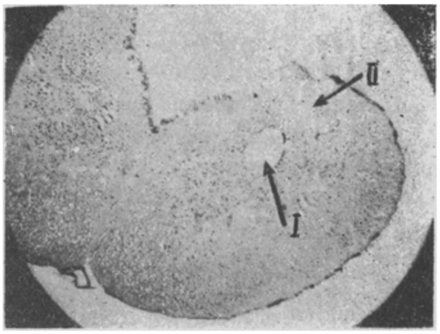

Fig. 2. Region of the expiratory center. Transverse section of the medulla of the frog at the level of the second spinal dorsal root. Explanation and photographic details as in Fig. 1.

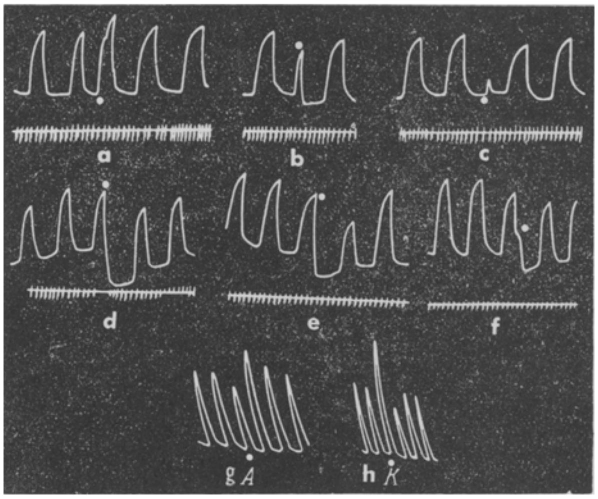

Fig. 3. Parts of a pneumogram recording the effects of local cathodal stimulation of the inspiratory center: a, b, c, d, e, f) recording of the respiration of a cat; g, h) recording respiration of a frog. Points over the record indicate the time of stimulation of the ipsilateral center. A) Action of anode; K) action of cathode.

Thus, the effect of additional cathodal stimulation of the ipsilateral center is determined by the degree of current spontaneous background excitation of the inspiratory center. If it was weak, the cathode reinforced it (when applied immediately before the beginning of an inspiration–Fig. 3, a) and if it was strong it depressed it (if applied, for example, during a breath which had already been initiated–Fig. 3, b and d). Consequently, only cathodal influences on the inspiratory center produce the alternative effects of reinforcement or suppression of the natural background activity of this center. The effect is analogous in its external manifestation to the two-fold action of the afferent impulses from the pulmonary receptors during normal respiration. If further experiments demonstrate directly the catelectronic nature of the action of pulmonary impulses, it will then be possible to reach a final conclusion as to whether the periodic suppression on the start of a natural excitation of the inspiratory center is caused by the periodic catelectronic action of impulses from pulmonary receptors. The two-fold nature of the action of these impulses might then be explained as the result of the integration of the degree of the current initial excitation of the inspiratory center and the extent of the growth of the catelectronic action of pulmonary impulses generated through the expansion of the lungs.

SUMMARY

Elimination of the afferent impulses from the frog pulmonary receptors caused respiratory disturbances of the Cheyne-Stokes type. The use of a microelectrode to measure the physiological parameters demonstrated that there was an increase of the rheobase and of the chronaxie of cells of both the inspiratory and expiratory centers. However, in the expiratory center the rate of accommodation remained at the initial level of about 130 - 300 msec, or was retarded even more in the inspiratory. This result suggested an increased capacity of the inspiratory center to maintain prolonged discharges under these conditions if the stimuli become relatively stronger. If by means of the microelectrode catelectronic threshold local stimulations are applied to the inspiratory center, opposite effects might be produced at different periods of the same respiratory cycle. There might be reinforcement at the initial stage, and depression at the time of maximal inspiration. The only effect of anodal stimulation was to depress inspiration. The results are considered in terms of the light they throw on the mechanism of the integration of afferent impulses, and on the normal inherent excitatory rhythm.

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