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RELATIVE RESISTANCE OF CENTRAL MECHANISMS DETERMINING THE DEPTH AND FREQUENCY OF RESPIRATION

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Hypercapnia in vagotomized cats can induce not only an increase in the depth of respiration, but also an increase in the frequency of inspiratory volleys. With deepening of anesthesia, the increase in depth of the inspiratory volleys continues, whereas the increase in the respiration rate disappears. These observations point to differences in the central mechanisms controlling the frequency and depth of respiration, of which the former is more susceptible to suprabulbar influences.

KEY WORDS: control of respiration; frequency and depth of respiration; hypercapnia; vagus nerve.

It is generally accepted that under normal conditions CO_2 increases the depth and frequency of respiration. However, the results of the action of hypercapnia in vagotomized animals are surprisingly contradictory. According to some workers [1, 5, 14] vagotomy prevents the increase in the respiration rate induced by hypercapnia, whereas according to others [2, 4, 11, 12] it has no such action.

Yet this is a very important problem. If vagotomy prevents the increase in respiration rate induced by CO_2, the respiration rate is determined by a vagal mechanism whereas the depth of respiration is determined by central mechanisms. If the increase in the respiration rate is not prevented, it follows that not only the depth, but also the rate of respiration are determined by central mechanisms.

During the analysis of this problem the writers' attention was drawn to the following circumstance. Some workers [7, 9, 11, 12] have found that after vagotomy hypercapnia induces an increase in the respiration rate in unanesthetized animals. Others [4], on the other hand, claim that after vagotomy an increase in the respiration rate takes place only in anesthetized animals and not in waking animals.

EXPERIMENTAL METHOD

Experiments were carried out on 18 cats anesthetized with pentobarbital (30-35 mg/kg) intraperitoneally. Subsequent doses of pentobarbital were injected intravenously (5-7 mg/kg). The vagus nerves were divided in

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TABLE 1. Respiration Rate of Anesthetized Cats

№ cat	Before vagotomy		After vagotomy	
	initially	CO_2	initially	CO_2
1	24	40	15	20
2	28	30	20	27
3	20	55	7	20
4	20	33	11	24
5	19	46	9	19
6	16	40	9	18
7	20	35	12	20
8	22	30	11	24
9	16	24	10	10
10	30	54	22	24
11	24	54	17	33
12	27	54	15	31
13	13	22	12	12
14	15	24	15	15
15	22	26	12	14
16	30	30	13	15
17	20	30	10	12
18	28	30	20	27
Mean	22,0±1,2	36,5±2,7	13,0±1,0	20,0±1,5
	$P<0,05$		$P<0,05$	

the neck. The gas mixture consisted of 7% CO_2 in air. The electromyogram (EMG) was recorded by means of electrodes sutured to the sternal part of the diaphragm.

EXPERIMENTAL RESULTS

Inhalation of the hypercapnic mixture induced an increase in the depth of respiration in all the animals: the inspiratory volleys increased sharply. By contrast with the depth, changes in the frequency of respiration showed considerable individual variation (Table 1). For instance, in experiment No. 16, there was no increase in the respiration rate, whereas in experiments Nos. 2, 18, and 15 the increase in the respiration rate was very slight, and in experiments Nos. 3, 11, and 12 it was very great. Statistical analysis of the experimental results showed that the increase in the respiration rate was significant. In man, hypercapnia also always increases the depth of respiration, whereas the respiration rate is subject to individual variation [3, 13].

Under normal conditions, before vagotomy, hypercapnia thus regularly acts on the mechanisms determining the depth of respiration, whereas it acts less regularly on the mechanisms determining the respiration rate. The same result also was observed after vagotomy. In the vagotomized animals inhalation of the hypercapnic mixture caused an even greater increase in the depth of respiration than in intact animals, whereas the changes in the respiration rate in these experiments also showed considerable individual variation (Table 1). For instance, in experiments Nos. 9, 13, and 14 there was no increase in the respiration rate, in experiment No. 15 the increase was slight, but in experiments Nos. 3, 4, 6, 8, 11, and 12 it was considerable. Statistical analysis of the experimental results also showed that the increase in the respiration rate during inhalation of the hypercapnic mixture by the vagotomized animals was significant. The results thus confirm that the action of CO_2 on vagotomized animals causes not only an increase in the depth, but also an increase in the frequency of respiration. Hence it follows that not only the increase in depth, but also the increase in rate of respiration can be determined by central mechanisms.

Additional pentobarbital solution was injected intravenously into animals in which hypercapnia after vagotomy caused an increase in the respiration rate. As the depth of anesthesia increased, the increase in the respiration rate caused by hypercapnia gradually diminished and eventually disappeared completely, whereas the increase in the depth of respiration persisted (Fig. 1). The mechanisms controlling the depth of respiration are thus more tolerant than the mechanisms controlling the frequency of respiration. The reason may be that the mechanisms controlling the frequency of respiration are more dependent upon suprabulbar structures. This hypothesis is supported by the fact that during individual development inhalation of CO_2 initially induces an increase only in the depth of respiration, and not until later does it increase the respiration rate also [6, 15]. The same effect is also observed during the action of CO_2 in adults: an increase in ventilation initially develops on account of an increase in the depth of respiration, and not until later on account of an increase in its rate.

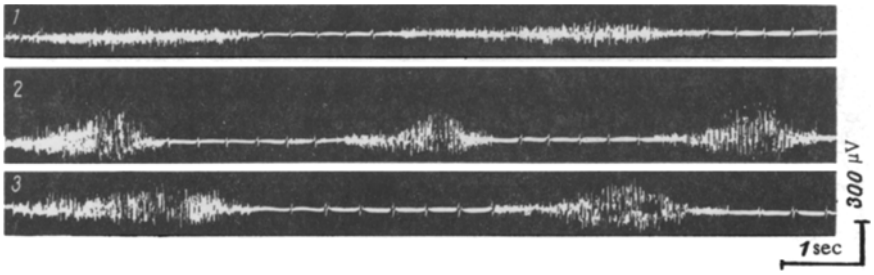

Fig. 1. 1) EMG of diaphragm of vagotomized cat; 2) inhalation of CO_2 causes increase in depth and frequency of inspiratory volleys; 3) with increase in depth of anesthesia CO_2 causes increase only in depth of inspiratory volleys and no increase in respiration rate.

The existence of two different mechanisms for the regulation of the depth and frequency of respiration explains why widely different combinations of depth and frequency of respiration are observed in disease, and why during attempts to find correlation between the depth and frequency of respiration, many contradictions frequently arise.

The possibility of independent regulation of the depth and frequency of respiration is extremely important also in the adaptation of respiration to the basic activity of the body. For instance, during rhythmic physical work the respiration rate comes under the control of the rhythm of the movements. During acyclic work, the pulmonary ventilation also increases on account of an increase in the respiration rate, for deep breathing would interfere with the performance of purposive movements. The widely held view that the ratio between the depth and rate of respiration is determined entirely by the level at which the minimal quantity of work [10] or force [8] is expended is evidently oversimplified.

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