EFFECT OF VAGOTOMY ON HYPERVENTILATION APNEA

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In order to study the role of afferentation from the lungs in the perception of respiratory failure experiments were carried out on cats to examine the effect of bilateral vagotomy on hyperventilation apnea. Vagotomy in cats was found to increase the threshold of sensitivity of the respiratory center to CO_2. The effect of vagotomy, however, was not due to the abolition of afferent impulses from the lungs, but to the hypocapnia arising in vagotomized animals as the result of an increase in their alveolar ventilation. An analysis of the literature confirms this hypothesis.

Guz et al. [6, 8, 15] have shown that blocking the vagus nerves in man prevents the perception of respiratory failure during voluntary apnea. This has accentuated interest in the problem of the effect of blocking the vagus nerves on sensitivity of the respiratory center to CO_2. However, the problem remains unsolved. Investigations have yielded conflicting results. Some workers have found that the ventilation response to CO_2 is increased after vagotomy, others that it is decreased [2, 7, 9, 11, 16, 17, 20].

Since the effect of CO_2 inhalation under normal conditions depends on the percentage of CO_2 in the inspired air, the phenomenon of hyperventilation apnea was used as a means of determining the threshold sensitivity of the respiratory center to CO_2.

EXPERIMENTAL METHOD

Five cats weighing 2.5-3.7 kg were anesthetized with pentobarbital (35-40 mg/kg, intraperitoneally). Tracheotomy was performed and the vagus nerves were divided in the neck. The blood pressure was recorded in the carotid artery by means of an electromanometer (Barovar). Activity of the diaphragm was recorded on an electromyograph (Disa Electronic). Ventilation of the lungs was measured by means of a water spirometer with two-way valve. Blood samples were taken periodically from the femoral artery through previously introduced cannulas, and the pH and p_aCO_2 were determined with the micro-Astrup apparatus. Hypoventilation was carried out for 2-3 min until spontaneous activity of the diaphragm had ceased. The mean of the values obtained in two pairs of this series before and after vagotomy was calculated for each experiment. The probability of the null hypothesis (P) was calculated by the method of comparing pairs (before and after vagotomy).

EXPERIMENTAL RESULTS AND DISCUSSION

It is clear from the results given in Table 1 that after vagotomy the respiration rate fell and the respiratory movements became considerably deeper. The minute ventilation was unchanged. Slight alkalosis developed. These observations show that vagotomy in cats causes an increase in the alveolar ventilation.

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TABLE 1. Effect of Vagotomy on Ventilation of the Lungs and CO_2 Tension in the Arterial Blood (M ± m)

Indices studied	Before vagotomy	After vagotomy	P
Minute ventilation (in ml)	460±14,0	460±15,7	>0,5
Respiration rate (per minute)	22±1,8	12±1,1	<0,01
pH of arterial blood during spontaneous breathing	7,276±0,003	7,332±0,007	<0,01
P_aCO_2 during spontaneous breathing (in mm Hg)	35,2±1,04	29,6±0,91	<0,01
pH of arterial blood at time of cessation of phasic impulses	7,418±0,011	7,452±0,001	<0,05
P_aCO_2 at time of cessation of phase impulses (in mm Hg)	26,2±0,61	19,9±0,56	<0,01
pH of arterial blood at time of first inspirations after apnea	7,314±0,009	7,330±0,009	<0,02
P_aCO_2 at time of first inspirations after apnea (in mm Hg)	37,1±1,00	30,4±0,43	<0,01
Duration of posthyperventilation apnea (in sec)	45±4,6	26±3,8	<0,01

The vagotomized cats were subjected to hyperventilation from 30 min to 1 h after the operation. Phasic volleys from the diaphragm ceased when p_aCO_2 was 19.9 mm Hg (26.2 mm Hg in the intact animals) and at pH 7.45 (at pH 7.42 in the intact animals). Meanwhile continuous tonic activity continued to be recorded in some experiments. The first volleys of phasic activity after apnea occurred when p_aCO_2 was 30.4 mm Hg and at pH 7.33.

As these results show vagotomy increased the sensitivity of the respiratory center to CO_2. The development of apnea necessitated hyperventilation of the animals to a lower CO_2 tension. In some experiments even at this level of the CO_2 tension only the phasic activity of the diaphragm disappeared and the tonic activity remained. The first inspirations after apnea in the vagotomized animals began at a lower CO_2 tension.

These results, indicating increased sensitivity of the respiratory center to CO_2 in the vagotomized animals, are in harmony with the widely held view that under normal conditions the Hering-Breuer inhibitory reflex not only limits the inspiratory activity of the respiratory center, but also has a tonic inhibitory effect on its sensitivity to CO_2 [19].

It is important, however, to note that vagotomy itself in cats lowers the CO_2 tension of the arterial blood. Against the background of hypocapnia the sensitivity of the respiratory center to CO_2 is increased [1, 12, 13]. The effect of vagotomy cannot therefore be due to blocking of the effect of the pulmonary afferentation on the respiratory center, but may be due to the changes in respiration produced by the vagotomy itself: an increase in alveolar ventilation, leading to hypocapnia.

Analysis of the literature confirmed this hypothesis. Those workers who investigated dogs and cats [2, 9, 11, 14, 16] found that vagotomy increases the sensitivity of the respiratory center to CO_2. This concurs with the fact that in dogs and cats vagotomy increases the alveolar ventilation and, consequently, produces hypocapnia.

In rabbits the Hering-Breuer inhibitory reflex is seen at its strongest [19], and in those animals vagotomy should apparently evoke the most marked increase in sensitivity of the respiratory center to CO_2. Yet in vagotomized rabbits, with a higher level of p_aCO_2, the ventilation responses to CO_2 are reduced [17, 20]. This corresponds to the fact that during hypercapnea the excitability of the respiratory center to CO_2 is reduced [4, 17].

Observations on man are particularly interesting. In man blocking the vagus nerves causes a decrease in the respiratory response to CO_2 [7]. This likewise cannot be explained by abolition of the Hering-Breuer inhibitory reflex, for in man this reflex plays no part in eupneic respiration. The mechanism of the effect of blocking the vagus nerves in man requires further investigation [3, 5, 10].

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