THE RESPIRATORY REACTION TO REFLEX OF HUMORAL STIMULATION IN VARIOUS STAGES OF GENERAL ANESTHESIA

(UDC 612.284-06 : 615.781)

M. E. Marshak and T. A. Maeva

Laboratory of the Physiology and Pathology of Respiration and Circulation,
Institute of Normal and Pathological Physiology (Director, Active Member AMN SSSR,
V. V. Parin) AMN SSSR, Moscow
(Presented by Active Member AMN SSSR V. V. Parin)
Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 59, No. 3,
pp. 40-44, March, 1965
Original article submitted September 17, 1963

The problem of the effect of anesthesia on the reactivity of the respiratory center has become extremely important [2, 4]. On the basis of the fact that under deep anesthesia the respiratory reaction to CO_2 disappears but in response to reflex stimulation remains the same as under moderate anesthesia, the conclusion was made that there were independent central receptors structures: for CO_2 ("chemocenter") and for reflex effects ("reflex center").

However, in the literature there is evidence contradicting the indications which attest that under deep anesthesia the respiratory reaction to reflex stimulation does not remain unchanged but decreases [5, 6].

The important theoretical significance of this problem and the contradictory nature of the conclusions of different authors gave us grounds to investigate the effect of different stages of anesthesia on the respiratory reaction with neural and humoral stimulations of the respiratory center.

METHODS

The experiments were carried out on 29 cats with the use of nembutal of chloralose. We recorded pulmonary ventilation and the electromyograms of the diaphragm (inspiratory) and internal intercostal (expiratory) muscles.

The tracheotomized animal breathed through inspiratory and expiratory valves, the latter being connected with a gas meter having a low resistance. The electromyogram was recorded on the "Diza" electromyograph. In some experiments we used bipolar needle electrodes which were inserted into the diaphragm under the skin, and in other experiments we exposed the cupulae of the diaphragm and used fishhook electrodes; such electrodes were securely fixed in the diaphragm and did not shifts during intensification of respiration.

The order of experimentation was as follows. After recording pulmonary ventilation and the electromyograms while breathing ordinary air, the cat was switched over to breathing a gaseous mixture containing 7-9% O_2. Then after 15 min of breathing air the animal was again switched for 3 min to breathing a gaseous mixture with 7% CO_2.

After several minutes of breathing air we injected an additional quantity of anesthetic and after 10-15 min again recorded pulmonary ventilation and the electromyograms while breathing air and the gaseous mixtures with 7-9% O_2 and 7% CO_2. Such investigations were repeated 3 to 6 times during the experiment (by the end of the experiment the quantity of injected anesthetic was $1\frac{1}{2}$-2 times greater than the normal dose needed for the animal to fall asleep).

With this set-up of the experiment we could compare the data on pulmonary ventilation and the electrical activity of the respiratory muscles during respiration of air, 7-9% O_2, and 7% CO_2 at different stages of anesthesia.

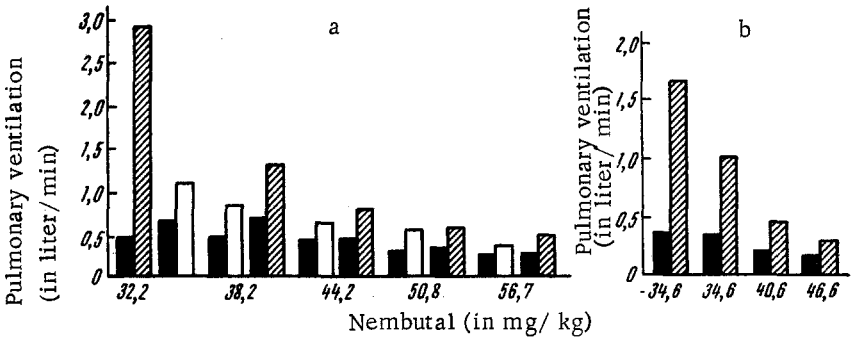

Fig. 1. Effect of different stages of anesthesia on pulmonary ventilation during respiration of air (black columns), gaseous mixture with 7% CO_2 (hatched columns), and gaseous mixture with 7% O_2 (white columns) with intact (a) and denervated (b) carotid and aortal zones.

RESULTS

Figure 1 shows data on the effect of different stages of anesthesia on pulmonary ventilation during respiration of air and in hypercapnia and hypoxia. In this experiment light anesthesia ensued with an intravenous injection of a nembutal solution at a rate of 34 mg/kg.

Then we gradually injected additional nembutal so that at the end of the experiment the quantity of anesthetic injected reached 68.1 mg/kg, i.e., was doubled.

As we see in Fig. 1a, pulmonary ventilation during respiration of atmospheric air decreased with deepening of anesthesia. An appreciable decrease in pulmonary ventilation occurred after injection of 50.3 mg/kg of nembutal. With moderate anesthesia pulmonary ventilation was 433 ml/min and after the total quantity of injected nembutal reached 56.7 mg/kg the pulmonary ventilation was only 250 ml/min. It is especially important to note that even with very deep anesthesia not only the reaction to hypoxia, but also to CO_2 was retained. (The character of the reaction to CO_2 was the same regardless of whether the mixture of CO_2 with air or with O_2 was given; in the latter case the decrease in pulmonary ventilation, as anesthesia deepened, was somewhat more evident that with respiration of a mixture of CO_2 and air.)

It is known that CO_2 has not only a central but also a reflex effect on the respiratory center through the chemoreceptors of the carotid and aortal zones. To elicit whether the respiratory reaction to CO_2 under deep anesthesia is accomplished only as a result of reflex effects, we set up experiments with denervation of the carotid and aortal zones. As we see in Fig. 1b, the respiratory reaction to CO_2 under deep anesthesia is retained even after excluding the reflex effect of CO_2 on the respiratory center. This indicates that under deep anesthesia the increase of pulmonary ventilation is caused by the direct effect of the increased content of CO_2 in the arterial blood on the respiratory center.

Figure 2 shows the electromyograms of the diaphragm and internal intercostal muscles in natural respiration of air, 7% CO_2, and 7% O_2 during deep anesthesia. The increase in the electrical activity of the inspiratory muscles and the quickening of respiration in hypoxia and hypercapnia is clearly evident.

The electrical activity of the expiratory muscle diminished.

The decrease in the electrical activity of the expiratory muscle in hypercapnia and hypoxia should be considered as a manifestation of our previously noted successive reciprocity in the coordination of the inspiratory and expiratory activity of the respiratory center upon an increase of CO_2 tension or decrease of O_2 tension in the arterial blood [1].

Figure 3 shows the results of an experiment with artificial respiration (the frequency of artificial respiration was the same as in natural breathing). The respiratory reaction to hypercapnia and hypoxia was investigated in very deep anesthesia: the animal was injected with 142 mg of nembutal; it had fallen asleep after injecting 92 mg of nembutal.

With artificial respiration of air (see Fig. 3) the electrical activity of the three inspiratory muscles in deep anesthesia was very weakly expressed. Respiration of 7% O_2, just as of 7% CO_2, was accompanied by a distinct enhancement of the electrical activity of the inspiratory muscles.

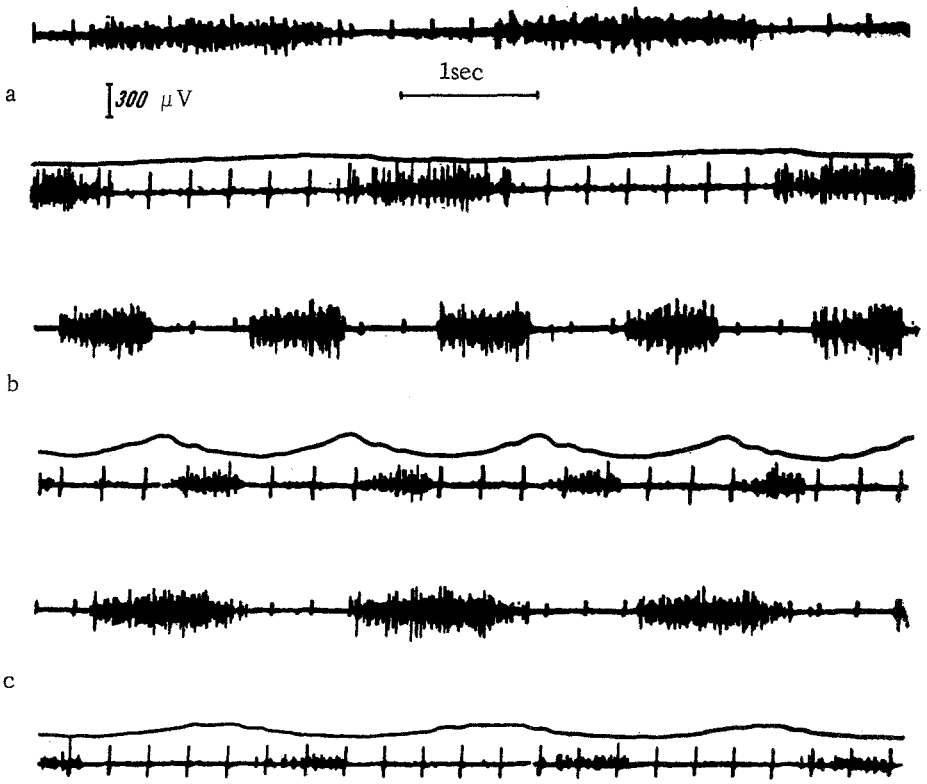

Fig. 2. Electrical activity of the respiratory muscles under deep anesthesia (natural respiration). Significance of the curves: (top to bottom) electromyogram of diaphragm, pneumogram, electromyogram of intercostal muscle. a) Respiration of atmospheric air; b) respiration of gaseous mixture with 7% CO_2; c) respiration of gaseous mixture with 7% O_2.

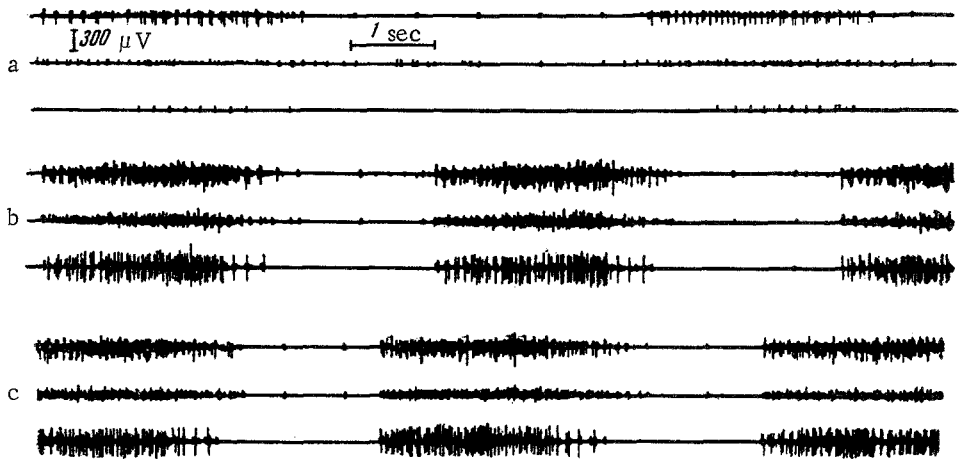

Fig. 3. Electrical activity of the respiratory muscles in deep anesthesia (artificial respiration). Significance of the curves: (top to bottom) electromyograms of the diaphragm, left external intercostal and right intercostal muscles. a) Respiration of atmospheric air; b) respiration of 7% CO_2; c) respiration of 7% O_2.

Thus our investigations demonstrated that in deep anesthesia against a background of lowered pulmonary ventilation, unidirectional respiratory reactions to reflex and humoral stimulations are observed: both hypoxia and hypercapnia evoke an increase of pulmonary ventilation and an enhancement of the electrical activity of the inspiratory muscles.

We tried to elucidate where the cause lay for the difference between the data in the literature [2, 4] and ours. This is apparently explained by the fact that the cited authors when determining the respiratory reaction to hypoxia and hypercapnia in deep anesthesia did not adequately take into account that with respiration of atmospheric air, deep anesthesia causes considerable changes of pulmonary ventilation and of the electrical activity of the respiratory muscles.

Actually (see Fig. 1a) on respiration of a gaseous mixture with 7% CO_2 during deep anesthesia pulmonary ventilation was 468 ml/min. This value was practically equal to the pulmonary ventilation of the same animal breathing atmospheric air during moderate anesthesia. Hence, it would seem, we can conclude that in deep anesthesia the respiratory reaction to CO_2 is absent. But if we take into account that deep anesthesia causes a decrease of pulmonary ventilation during respiration of atmospheric air, then it becomes clear that this conclusion is not valid. In the cited example (see Fig. 1) pulmonary ventilation dropped from 433 ml/min in moderate anesthesia to 250 ml/min in deep anesthesia. If we take into consideration that inspiration of 7% CO_2 in deep anesthesia caused an increase of pulmonary ventilation from 250 ml/min to 468 ml/min, then it becomes evident that in deep anesthesia the respiratory reaction was retained.

As confirmation of the presence in the reticular formation, of various receptor structures for humoral agents and reflex stimulations, Astrom [2] cites the results of the work of Comroe [3], who investigated the respiratory reaction during electrical and chemical stimulation of various points in the area of the respiratory center in the medulla oblongata, and also gave and account of Comroe's data that in 14 cases electrical stimulation was attended by a change of respiration and there was no respiratory reaction to the chemical stimulation. But for some reason Astrom did not take into account Comroe's indications that in 60 cases the respiratory reaction did occur both with electrical and chemical stimulation of the same point. The results of these investigations contradict the conclusions of Astrom, Euler, and Soderberg.

The results of our investigations do not agree with the data of Astrom, Euler, and Soderberg. Therefore we do not find sufficient grounds for the conclusion that afferent impulses and chemical agents excite different receptor structures of the reticular formation of the medulla oblongata.

LITERATURE CITED

1. M. E. Marshak, Vestn. AMN SSSR, 8, 16, 1962.
2. A. Astrom, Acta physiol. scand., 1952, Vol. 27, Suppl. 98.
3. J. H. Comroe Jr., Am. J. Physiol., 1943, Vol. 139, p. 490.
4. C. Euler and U. Soderberg, J. Physiol. (London), 1952, Vol. 118, p. 555.
5. E. Fromter, Z. Biol., 1961, Bd. 112, S. 331.
6. T. Gordh, Acta chir. scand., 1945, Vol. 92, Suppl. 102.