CHANGES IN THE OXYGEN TENSION OF THE BRAIN AND SKELETAL MUSCLE IN HYPER- AND HYPOCAPNIA

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It has been shown [6] that in hypoxia or hyperoxia the tissue oxygen tension is controlled chiefly by alterations of the tension in the arterial blood. We may also suppose that in hypoxia the oxygen tension changes in the tissue depends also to some extent on those of the blood supplying the tissue, and possibly on the course of the oxidative processes in them.

Here we have undertaken an investigation into the influence of hypoxia and hyperoxia on the oxygen tension of tissues. Although these factors have little influence on arterial blood oxygen saturation, they nevertheless produce marked changes in the blood supply to the tissues [2, 10, 12, 13, 16, 17, 18, 21, 23], and influence the rate of the oxidative processes in the body. Hypercapnia reduces the metabolic rate, while hypocapnia increases it [1, 3, 4, 5, 7, 8]. We must also take into account any possible influence of hyper- and hypocapnia on the affinity of hemoglobin for oxygen.

METHOD

Acute experiments were carried out on cats under urethane anesthesia, and changes of the oxygen tension in cerebral tissue and skeletal muscle were recorded polarigraphically [11, 14]; the method has been described in detail previously [6]. We made simultaneous records of the respiration (pneumogram) and the arterial pressure (mercury manometer), and in some of the experiments we recorded the relative changes in the degree of arterial blood oxygen saturation (by means of a photoelement) and the rate of blood flow in the femoral artery and in the meninges (using a thermoelectric method).

RESULTS

The experiments showed that hypercapnia induced by respiration of a gaseous mixture containing 7% of carbon dioxide usually caused different oxygen tension changes in the different tissues: in the brain it was increased, while in the skeletal muscle, in most cases, it was reduced (Fig. 1a).

In analyzing the results of the influence of hypercapnia, in addition to the changes in the blood supply to the tissue we must also take into account the effect on metabolism and on the dissociation curve of oxyhemoglobin, but there is no reason to suppose that there will be any difference in the action of hypercapnia on the last two quantities as between different tissues. Nevertheless, changes of the oxygen tension in the brain and skeletal muscle in hypercapnia are usually in opposite directions, and run parallel to the changes in the blood supply to these tissues (in hypercapnia the blood supply to the brain is increased, while that to the muscles is reduced – Fig. 1 b and c). We may therefore suppose that in hypercapnia changes in tissue oxygen tension are principally due to an alteration of the blood supply. It is however possible that during hypocapnia and in the subsequent recovery period oxygen tension changes in the tissues may be influenced by other factors, and the final result will be the result of a number of influences. Our observations indicate indirectly that this is in fact the case.

We must note that in hypercapnia, the direction of the changes of oxygen tension in the brain are more constant than in skeletal muscle. The explanation may be that in cerebral tissues all the factors mentioned above must act in the same direction to increase oxygen tension: in addition to an increased blood supply there is a shift in the

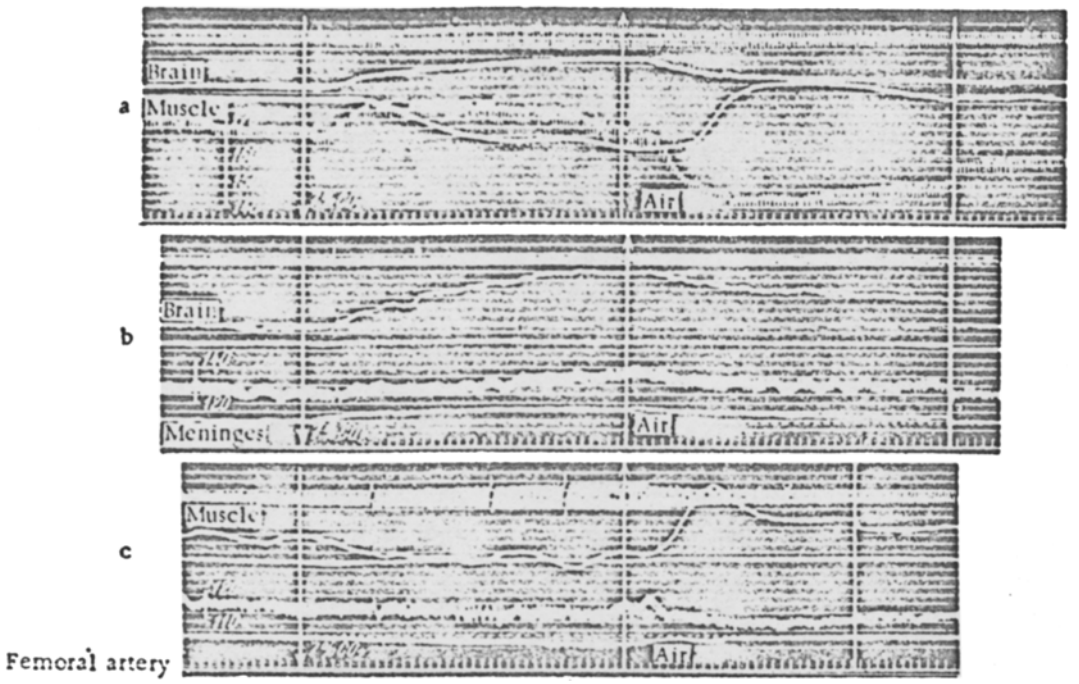

Fig. 1. Oxygen tension changes in the tissues in hypercapnia (11) . Curves, from above downwards: for a) respiration, cerebral oxygen tension, muscular oxygen tension, arterial pressure, time of marker (5 seconds); for b) respiration, cerebral oxygen tension, arterial blood oxygen saturation, arterial pressure, volume of blood per minute flowing through meninges, time marker (5 seconds); for c) respiration, oxygen tension in the skeletal muscle, arterial blood oxygen saturation, arterial pressure, volume per minute of flow in femoral artery, time marker (5 seconds). Here and in the subsequent diagrams, a dotted line indicates the initial levels.

dissociation of oxyhemoglobin to the right, which facilitates the transference of oxygen from the blood into the tissue. According to published reports, in hypercapnia the rate of oxidative processes in the brain either shows no change or is reduced, and if there is a reduced demand for oxygen it would be expected that the oxygen tension in the cerebral tissue would increase.

In hypercapnia, in muscle, besides factors leading towards an increase of oxygen tension (reduction of oxygen demand, change of the dissociation curve), there is another factor acting in the opposite direction, namely a constriction of the blood vessels. In most cases hypercapnia caused a fall of muscle oxygen tension, i.e. the effects of the changed blood supply prevailed over other influences. However, in some experiments with hypercapnia, instead of a reduction there was an increase of muscular oxygen tension, or else there was a reduction at the start of the experiment followed after repeated hypercapnia by an increased oxygen tension; under these conditions, there was no parallelism between the changes in the blood supply to the muscle, which was reduced, and the course of the oxygen tension changes. The probable explanation of the greater variability of the direction of the oxygen tension changes in muscle as compared with the brain is probably that the influences of the different factors in muscle act in different directions.

Hypocapnia, induced by artificial hyperventilation, also causes changes in various directions of the oxygen tension in the different tissues, but the changes are the opposite of those observed in hypercapnia: in the brain oxygen tension is reduced, while in the skeletal muscle it is usually raised (Fig. 2a). The reduction of the oxygen tension in muscle and in brain at the end of a period of hyperventilation is due to apnea which develops as a result of the hypocapnia. These changes of the tissue oxygen tension are caused mainly by differences in the blood supply to the different tissues: in the brain the hypocapnia causes a reduction of the blood supply, whereas in the muscle it is increased (Fig. 2b and c).

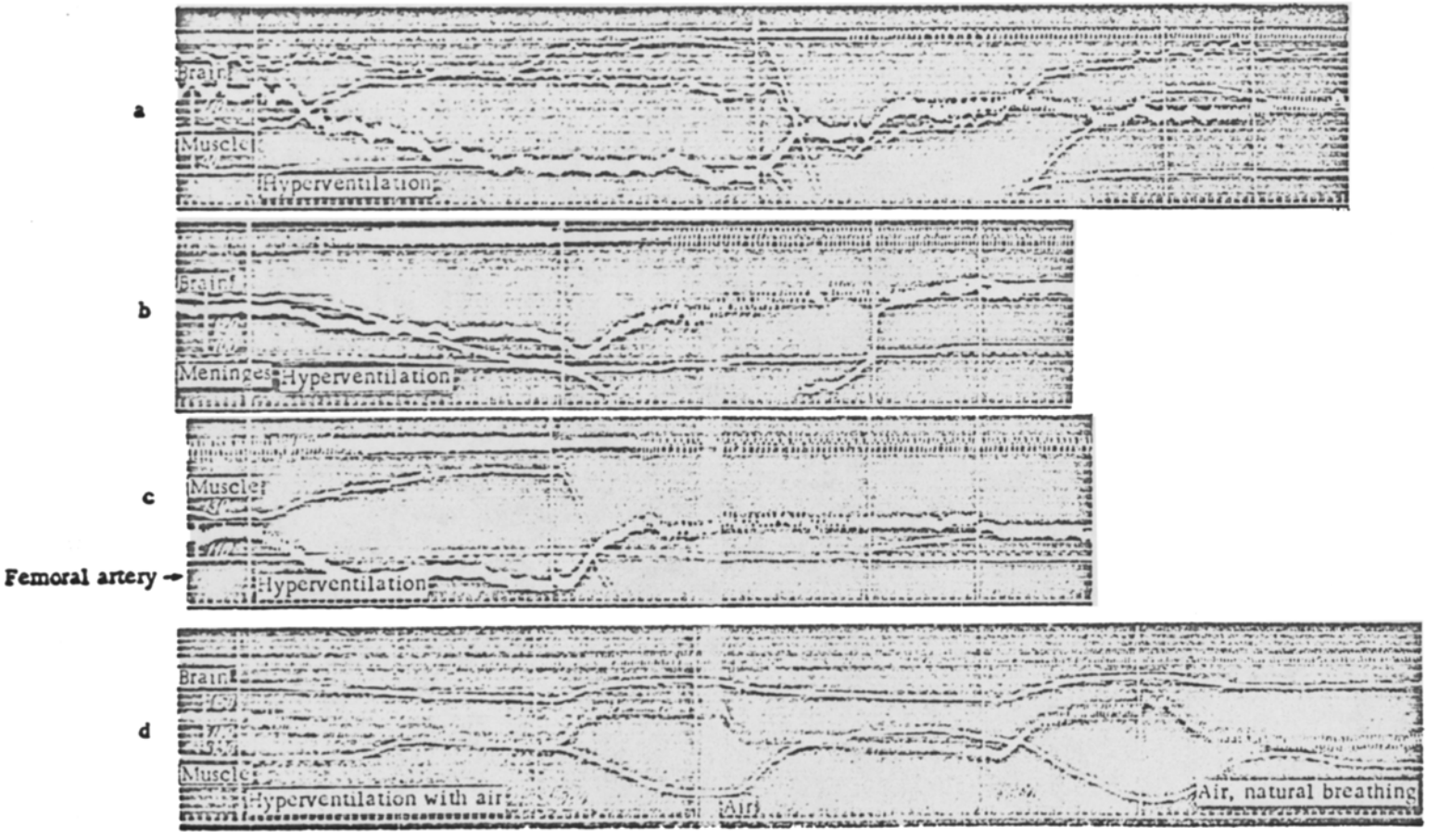

Fig. 2. Changes of cerebral and skeletal muscle oxygen tension in hypocapnia(↓↑)induced by hyperventilation (a, b, c), and the effect of the addition of 7% carbon dioxide (D). Curves, from above downwards: for a) respiration, cerebral oxygen tension, arterial pressure, muscular oxygen tension, arterial blood oxygen saturation, time marker (5 seconds); for b) respiration, cerebral oxygen tension, arterial pressure, volume flow in the cerebral meninges, time marker (5 seconds); for c) respiration, muscular oxygen tension, arterial pressure, volume flow in femoral artery, time marker (5 seconds); for d) respiration, cerebral oxygen tension, arterial pressure, muscular oxygen tension, time marker (5 seconds).

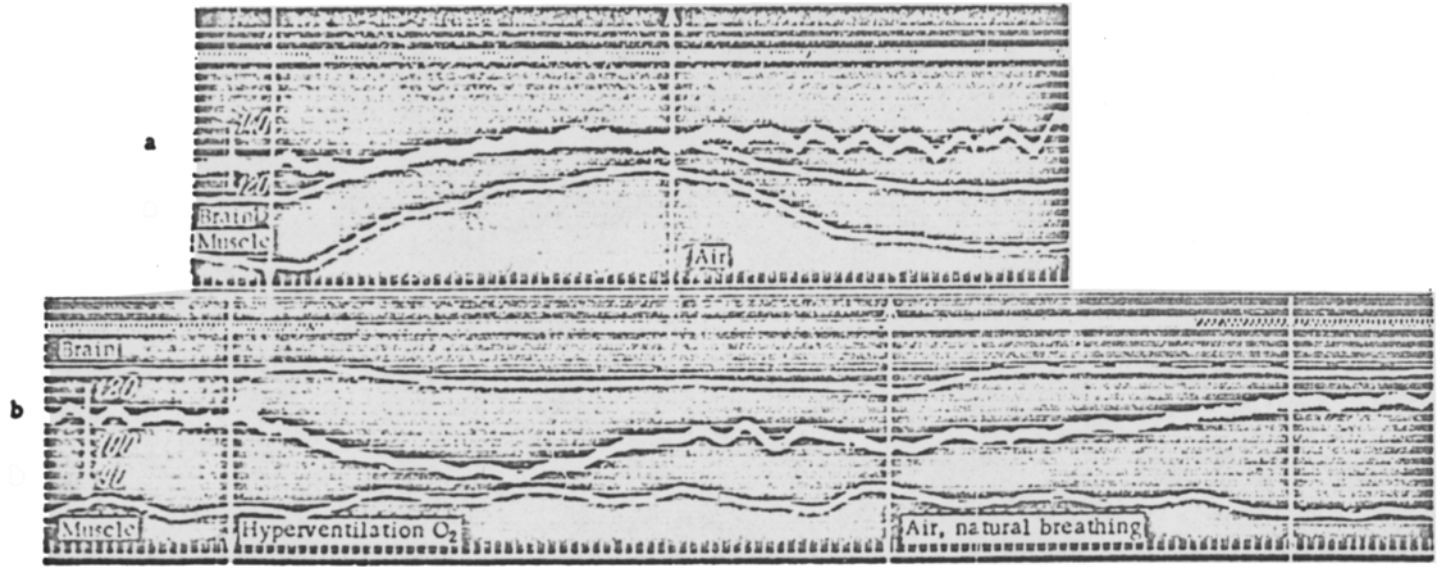

Fig. 3. Influence of breathing oxygen (↓↑) on the oxygen tensions in the brain and in the skeletal muscle during normal respiration (a) and artificial hyperventilation (↓↑) (b). Curves, from above downwards: for a) respiration, arterial pressure, cerebral oxygen tension, muscular oxygen tension, time marker (5 seconds); for b) respiration, cerebral oxygen tension, arterial pressure, muscular oxygen tension, time marker (5 seconds).

Again with hyperventilation, but with the addition of 5-7% carbon dioxide to the inspired air, the reduced cerebral oxygen tension is raised until it reaches or exceeds the original level, but the muscular oxygen tension is reduced until it equals or falls below the initial value (Fig. 2d). The conclusion is that it is the hypocapnia which determines the oxygen tension changes in the tissues which develop in response to hyperventilation.

Just as in hypercapnia, so also in hypocapnia the direction of the oxygen tension changes in the brain are much more constant than in the skeletal muscle. The explanation is that as in hypercapnia the actions of all factors which may influence the cerebral oxygen tension are in the same direction, and in this case towards a reduction of the tension. These factors include, in addition to a constriction of the cerebral vessels, a reduced dissociation of oxyhemoglobin, and a reduced general blood pressure, as was usually observed during hyperventilation.

In several reports [19, 20] in which it was shown that cerebral tissue hypoxia developed in hyperventilation (as indicated by the accumulation of lactic acid), the main reason was thought to be an impaired oxyhemoglobin dissociation. We cannot agree: although this factor should play some part in the reduction of cerebral oxygen tension in hypoxia, it is not the fundamental cause. The following fact is evidence: in hyperventilation with oxygen, just as with air, there is a marked fall of cerebral oxygen tension, i.e. the entry of pure oxygen into the lungs and the simultaneous hypocapnia does not prevent the development of cerebral tissue hypoxia (Fig. 3) [22]. When oxygen is inspired, its tension in the blood increases so much that the demand of the tissue for oxygen can be largely satisfied by the amount of oxygen present in the plasma; therefore in this case, some reduction in the dissociation of oxygen from its combination with hemoglobin can scarcely have any great influence in bringing about the reduction of cerebral oxygen tension in hypocapnia. The main reason for this change is the constriction of the cerebral vessels which develops in hypocapnia.

The critical significance of the changes in the blood supply to the tissue in determining the oxygen tension changes in hypocapnia is indicated also by the increased oxygen tension which is observed in most cases in the muscles under these conditions. Despite the simultaneous operation of factors leading to a reduction of oxygen tension (shift of the dissociation curve of oxyhemoglobin to the left and increased oxygen demand), the prevailing influence is the dilation of the blood vessles in the muscle which occurs in hypocapnia.

The constancy of the concentration of carbon dioxide in the blood bathing the tissue is of great importance for the normal functioning of the brain. There is evidence that the brain and heart have different sensitivities to this high concentration of carbon dioxide: a carbon dioxide tension which induces only mild changes in the electrocardiogram is sufficient completely to suppress the electroencephalogram [15].

The maintenance of a constant concentration of carbon dioxide in the blood bathing the cerebral tissue is brought about by changes in the cerebral blood supply: hypercapnia causes dilatation of the cerebral vessels and an increased blood supply which enables the excess carbon dioxide to be carried away. On the other hand, hypocapnia causes the cerebral vessels to constrict, and reduces the blood supply, so that the excess carbon dioxide can not be removed. Consequently, despite the considerable carbon dioxide tension changes in the arterial blood reaching the brain, corresponding changes in the venous blood leaving the brain are much less well shown [13]. However, in hypocapnia, too extensive a removal of carbon dioxide is brought about by the useful cerebral tissue hypoxia which develops through the constriction of the cerebral vessels.

In hypercapnia, the increased blood supply to the brain which makes it possible for the excess carbon dioxide to be removed takes place at the expense of the blood supply to the skeletal muscle, and possibly to other organs less sensitive to excess carbon dioxide and oxygen lack.

SUMMARY

Acute experiments were performed on cats under urethane anesthesia. A polarigraphic method was used to study the change of oxygen tension in the brain and skeletal muscle during hyper- and hypocapnia. Hypercapnia induced different oxygen tension changes in the different tissues: in the brain it was increased, and in skeletal muscle diminished. Hypocapnia caused by artificial hyperventilation caused the reverse changes: cerebral oxygen tension was reduced (whether hyperventilation was with air or oxygen), while that of the muscle was increased.

It is suggested that the changes in the oxygen tension occurring in the tissue during hyper- and hypocapnia were mainly due to variations in the tissue blood supply.

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