CARBON DIOXIDE SENSITIVITY OF THE RESPIRATORY CENTER IN CHRONIC HYPERCAPNIA

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The effect of carbon dioxide in exciting the respiratory center in subjects with chronic hypercapnia is of great interest in connection with the problem of to what extent the nervous center can adapt to the continuous influence of an adequate stimulus.

Scott [5] first investigated two subjects with chronic hypercapnia resulting from pulmonary emphysema; he determined the effect on pulmonary ventilation of breathing air containing an increased amount of CO_2. He found only a small increase in ventilation. A study of alveolar and pulmonary ventilation [4], when concentrations of 1, 3, and 5 % CO_2 were breathed by healthy subjects and by patients with pulmonary emphysema having an abnormal blood CO_2, showed that, normally, inhaling 5 % CO_2 increased ventilation by an average of 187 %, while in patients with a marked hypercapnia the increase was only 58 %. The authors throught that this small increase was due both to the increased alkali reserve and to a reduced sensitivity of the respiratory center to carbon dioxide.

The great difference in sensitivity of the respiratory center between healthy subjects and those with pulmonary emphysema was observed by Tenney [6], who thought that in addition to changes in the physicochemical constitution of the blood and to the mechanical interference with respiration, there is also some adaptation of the respiratory center to the action of carbon dioxide which develops in patients as a result of prolonged hypercapnia.

Two considerations have been advanced to explain this phenomenon.

The first inhalation of a gaseous mixture containing a certain concentration of CO_2 has a smaller excitatory effect on the respiratory center because of the change in the constitution of the blood (increased alkali reserve). However, this can scarcely be the reason for the reduced response from the respiratory center, because under the influence of the inspired CO_2, the partial pressure of the gas in the blood ought to increase to its previous level independent of any changes in the alkaline reserve, and its stimulant effect on the respiratory center should not be changed.

The second consideration is that under the influence of a prolonged hypercapnia, the sensitivity of the respiratory center to CO_2 is diminished. Shik, Kulik, and Shneiderovich [2] observed that the degree of chronic hypercapnia was inversely related to the increased ventilation in response to CO_2. Assuming that in prolonged hypercapnia the sensitivity of the respiratory center to CO_2 is reduced, they attempted to demonstrate this fact on animals which were kept for a considerable time in an atmosphere containing from 6-8 % carbon dioxide. However, when the sensitivity of the respiratory center of these animals to carbon dioxide was tested, it was found that it was not reduced and that the increased ventilation caused by the addition of CO_2 was no greater than it was before the subject had been exposed to it for a long time. The authors therefore concluded that the failure of patients to respond adequately by increased pulmonary ventilation to added CO_2 does not result from prolonged hypercapnia.

Therefore the problem of whether there is a change in excitability of the respiratory center to carbon dioxide (i.e., the question of whether there is or is not an adaptation) in patients with chronic hypercapnia still remains unsolved.

The present work represents an attempt to determine whether chronic hypercapnia does reduce the sensitivity of the respiratory center to CO_2.

METHOD

We used the method of electromyography of the respiratory muscles and made simultaneous recordings of the depth and frequency of respiration, as described previously [1]. For four minutes, the patient breathed into a Krogh spirometer from which the carbon dioxide absorbent had been removed; as a result the carbon dioxide gradually increased, finally reaching a level of 5-6 %. A study was made of 28 subjects suffering from pulmonary emphysema with chronic hypercapnia.

RESULTS

Analysis of the alveolar air and determination of the oxyhemoglobin in some of the patients showed that there was a marked hypoxemia and hypercapnia.

We used a concentration of CO_2 for the inspired air which in healthy human subjects caused an increased of pulmonary ventilation of 2-3 times or more, the increase being chiefly through increased depth of respiration.

In emphysematous patients, under these conditions the pulmonary ventilation increased considerably less, a result which agreed with published reports (Fig. 1). This effect was particularly marked for the depth of respiration. In the subjects investigated, the initial depth varied between 400 and 750 ml. After breathing CO_2, the depth increased to 600-1500 ml. An increase of two or more times compared with the normal value was found only in ten subjects; in 18, the increase was very much less, and in most of the patients the increase was not greater than 200-300 ml. The same thing was true of the total pulmonary ventilation, although in this case the difference between the healthy subjects and patients was less marked, because the increased ventilation in the patients occurred mainly through increase in the respiratory rate.

From the electromyograms and spirograms it was found that in spite of a small increase in the depth of respiration under the influence of carbon dioxide, the potentials in the respiratory muscles, which were abnormally large in the sick group even at rest, were further greatly increased when CO_2 was given, and reached a level considerably higher than that of the same muscles in healthy human subjects under the same conditions (Fig. 2). Therefore inspiring air enriched with carbon dioxide in hypercapniaic patients caused a considerable increase in excitation of the respiratory center, and it is impossible otherwise to explain the increased electrical activity of the respiratory muscles.

In all previous investigations, pulmonary ventilation has been taken as the index of activity of the respiratory center. However, under these conditions, when pulmonary ventilation is limited for other reasons, or because of pathological processes, the normal correspondence between the degree of excitation in the respiratory muscles and pulmonary ventilation is not maintained. In these cases

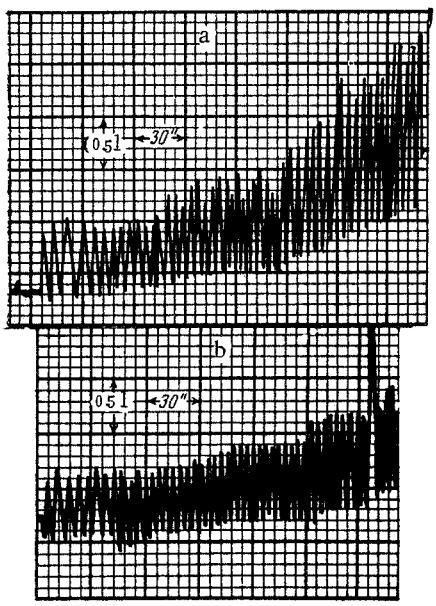

Fig. 1. Change in the pulmonary ventilation (spirograph curves) on breathing into a closed system in which the carbon dioxide concentration gradually increased. a) In a healthy subject; b) in a patient with pulmonary emphysema.

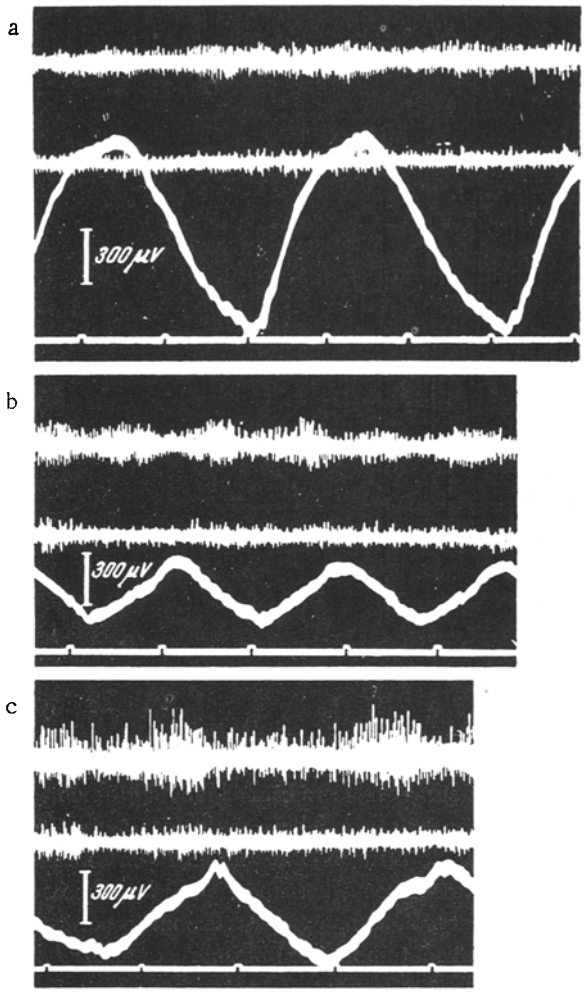

Fig. 2. Action potentials of the respiratory musculature. a) In a healthy human subject when breathing air containing 5 % CO_2; b) in a subject with pulmonary emphysema (second order respiratory insufficiency) when breathing normally; c) in the same subject, when breathing air containing 5 % CO_2. Curves from above, downwards : electromyogram of intercostal muscles; electromyogram of the external oblique muscle of the abdomen ; pneumogram; time marker (1 sec).

the electromyogram may give information about the flow of nervous impulses to the respiratory muscles, and from this information the condition of the respiratory center may be inferred.

The lack of correlation between the work of the respiratory muscles and the pulmonary ventilation rate in patients with pulmonary emphysema has previously been pointed out [3]. It was found that in them, the oxygen consumed by the respiratory muscles in breathing against the increased resistance rose considerably in response to quite small changes in the ventilation rate.

From our results it can be seen that the apparent reduction or absence of a respiratory response to carbon dioxide in cases of chronic hypercapnia is not due to loss of sensitivity of the respiratory center, as Cournand [4] and his co-workers supposed. When the carbon dioxide content of the inspired air is increased, the respiratory center is excited and causes a considerable increase in the flow of impulses to the respiratory muscles, causing an increased electrical activity in them. However, the increased muscular activity does not result in any great increase in the depth of respiration, because in a patient with pulmonary emphysema many factors impede ventilation; these include changes in the respiratory apparatus itself which causes the respiratory muscles to be ineffectual. In four out of the 18 patients in whom the added CO_2 caused only a small increase in ventilation, the electrical activity of the respiratory muscles also showed little change. In certain cases it may be that in addition to the reason given above, there is also a reduced nervous response to carbon dioxide.

Therefore, in chronic hypercapnia failure of respiration to respond to CO_2 is due mainly to pulmonary changes and not to adaptation of the respiratory center or of the chemoreceptors.

SUMMARY

By recording both the pulmonary ventilation and electrical activity of the respiratory muscles, the excitability of the respiratory center to carbon dioxide was investigated in patients with chronic hypercapnia due to emphysema of the lungs.

It was found that the electrical activity of the muscles responded sharply to CO_2, showing that the reduced respiratory response to CO_2 in chronic hypercapnia is due chiefly to pulmonary changes and not to adaptation of the respiratory center.

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