EFFECTS OF ACUTE HYPOCAPNIA AND HYPERCAPNIA ON NEUROMUSCULAR TRANSMISSION AND ON MONOSYNAPTIC SPINAL REFLEX IN WAKEFUL MAN

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SUMMARY

The effects of both acute hypocapnia and hypercapnia on neuromuscular transmission (NMT) and monosynaptic spinal reflex (MSR) in conscious subjects were studied by observing the averaged evoked electromyogram. The M-wave amplitude increased to 165 ± 25% (mean ± standard error) during acute hypocapnia with an end expiratory carbon dioxide concentration of 2.5 ± 0.2 vol.% and decreased to 73 ± 7% during acute hypercapnia with an expiratory concentration of 6.8 ± 0.1 vol.%, in comparison with the control value. The H-wave amplitude increased to 226 ± 82% during acute hypocapnia and decreased to 85 ± 9% during acute hypercapnia in comparison with the control value. These results indicate that both NMT and MSR in conscious man are facilitated by acute hypocapnia, and that NMT is inhibited by acute hypercapnia. However, the effect of acute hypercapnia on MSR could not be ascertained only by the observation of the H reflex in these conditions.

There have been a number of studies concerning the effects of alteration in carbon dioxide tension of blood on neuromuscular transmission (NMT) and on monosynaptic spinal reflex (MSR) in animals. Although there have been a few controversial reports (Gamstorp and Vinnars, 1961; King, Garrey and Bryan, 1932), it is generally agreed that hypocapnia facilitates both NMT and MSR, while hypercapnia inhibits these in animals (Brooks and Eccles, 1947; Esplin and Rosenstein, 1963; Frederickson and Schenk, 1959; Hughes, 1970; Katz, Ngai and Papper, 1963; Kirstein, 1951; Kitahata, Taub and Sato, 1969; Payne, 1958). Similar effects were also reported in anaesthetized man (Baraka, 1964; Freund, Martin and Hornbein, 1969; Katz and Wolf, 1964).

The present study was undertaken to determine the effects of acute hypocapnia and hypercapnia on NMT and MSR by observing the averaged evoked electromyogram (e.e.m.g.) in conscious man.

METHODS

Experiments were carried out in 13 volunteers (male medical students) ranging in age from 20 to 28 years. The informed consent was obtained from all subjects. The experimental set up is illustrated in figure 1.

The subjects were encouraged to relax as much as possible on the operating table in the supine position. The tibial nerve was stimulated electrically through two chlorided silver needle electrodes inserted subcutaneously at the popliteal fossa. To prevent sliding, the electrodes and their associated wire leads were fixed with adhesive tape 5 cm apart on the skin. Square pulses of 1.0 msec duration were delivered every two seconds from an electronic stimulator (Nihon-Kohden MSE-3R) through its isolation unit. Although it takes more than 1 min for full recovery of the H reflex, it was confirmed that the averaging of ten sequential responses elicited at every two sec gives more constant values in such acute hyper- or hypocapnic procedures. The stimulus intensity was adjusted so that it generated about half of the maximal H reflex which was preceded by the small direct motor response (M wave). Both M and H waves were obtained by two silver needle electrodes which were inserted into the calf muscle about 2 cm apart along the muscle fibres. The action potentials were amplified, displayed on an oscilloscope, and led to a digital computer (Nihon-Kohden ATAC 501-20) for averaging. Ten sequential responses were averaged for each data point (inset fig. 1).
EFFECTS OF ACUTE HYPOCAPNIA AND HYPERCAPNIA

Fig. 1. Schematic diagram of experimental apparatus and arrangements. The photograph (right upper part) is an average evoked e.m.g. recorded from the calf muscle in response to ten electrical stimuli applied to the tibial nerve. S = the stimulus artifact; M = the M wave; H = the H wave.

At the start of the inhalation of oxygen by mask, the H reflex showed a slight increase in amplitude seemingly because of anxiety. Within 10 min, however, the amplitude of the H reflex was restored to a relatively constant value. A control value of the M and H waves in a steady state during pure oxygen inhalation for 30 to 60 min was obtained for each subject.

Gases were introduced through a three-way stopcock and the tail tube of a 8-l. reservoir bag attached to an anaesthetic facepiece with an interposed non-rebreathing valve.

The facepiece was fitted and fixed snuggly with an anaesthetic headband to prevent any gas leakage during the study. By turning the three-way stop-cock, inhalation gases could be changed from 100% oxygen to a mixture of about 8% carbon dioxide in oxygen for the induction of acute hypercapnia without the knowledge of the subject.

Acute hypocapnia was induced by increasing tidal volume and respiratory rate with manual assistance of respiratory movement of the bag for 15 min.

The end expiratory carbon dioxide level under the mask was measured with an infrared analyser (Shimazu). The mean value was 4.2% (range 4.0–4.5%) under control conditions; 2.5% (range 2.2–3.2%) during hyperventilation by manual assistance, and 6.8% (range 6.4–7.1%) during carbon dioxide inhalation (figs. 2, 3).

The mean arterial pH and Pco₂ during spontaneous respiration at the control were 7.411 (range 7.366–7.460) and 39.0 mm Hg (range 35–43 mm Hg), respectively. Immediately before the end of assistance of respiration, the mean pH increased to 7.574 (range 7.480–7.680) and Pco₂ fell to 26.0 mm Hg (range 22–32 mm Hg). At the termination of carbon dioxide inhalation, mean pH was 7.260 (range 7.210–7.320) and mean Pco₂ 51.2 mm Hg (range 47.6–56.6 mm Hg).

Throughout the experimental procedures, minute volume was measured with a Wright respirometer. Both systolic and diastolic arterial pressures were monitored by a sphygmomanometer. Respiratory rate, pulse rate and e.e.g. were also monitored and recorded (fig. 1).

RESULTS

Effect of acute hypocapnia.

In 6 of 7 subjects, the M wave amplitude showed a significant increase in magnitude from 133 to 271% of the control value under hypocapnia. In the remaining subject, there was no change in the M wave amplitude. The H wave amplitude showed a significant amplitude increase from 110 to 700% of the control value under hyperventilation. The M and H wave amplitude returned to the control levels approximately 20 min following cessation of manual assistance of ventilation. The sequential changes in mean amplitudes of the M and H wave under acute hypocapnia are shown in figure 2.

Effect of acute hypercapnia.

In all subjects the M wave amplitude decreased from 94 to 56% of the control value. The H wave amplitude also decreased from 79 to 56% of the control value. The M and H wave amplitudes returned to control levels within 10 min of discontinuation of carbon dioxide inhalation. The sequential changes are shown in figure 3.

Effect of acute hypocapnia or hypercapnia on other parameters.

The transient increment or decrement of the mean respiratory rate (RR), minute volume (MV), blood pressure (BP), and pulse rate (PR), are shown in figure 4.

At 5 min after the start of the procedure of inducing acute hypocapnia, the mean respiratory rate increased to 180 ± 4% (mean ± standard error) of the control value. The mean minute volume also increased to 253 ± 5% of the control value. However, there were no statistically significant differences in either mean systolic or diastolic arterial
EXC.

M-WAVE

H-WAVE

H/M RATIO

cont. on 3 5 off 3 15

Fig. 2. The effect of acute hypocapnia on the M and H wave amplitude. Hyperventilation started at “on” and discontinued at “off”. Changes in the M wave amplitude (M-WAVE), the H wave amplitude (H-WAVE), and the ratio of H wave to M wave amplitude (H/M RATIO) are expressed as percentages of the control value, respectively. Each point represents the mean of seven subjects, and each bar represents the standard error of mean. EXP.CO2—the end expiratory CO2 level under the facepiece.

DISCUSSION

The increase in M wave amplitude that occurred with hypocapnia in this experiment is likely to be related to increase in NMT. This increase in NMT with hypocapnia has also been noted in animals (Katz, Ngai and Papper, 1963) and in man (Katz and Wolf, 1964). On the other hand, Hughes (1970) showed that hypocapnia did not affect supramaximal twitch response in cats. There is agreement that hypercapnia decreases NMT in animals (Hughes, 1970; Payne, 1958) and in man (Katz and Wolf, 1964).

Although the H wave amplitude reflects the activity of MSR (Hoffmann, 1918, Magladery, 1955), its amplitude could be modified by the activity of NMT. Therefore, to evaluate MSR, the simultaneous change in both the H and M wave amplitudes must be carefully taken into consideration. With constant stimulation the ratio of H to M waves could be accepted as an estimate of the activity of the motorneurone pool.

Under acute hypocapnia, both the H and M
With acute hypercapnia, both the H and M waves rapidly decreased their amplitude in the present study. However, the H/M ratio increased after 3 min of carbon dioxide inhalation. At the same time, most subjects began to complain of apprehension, euphoria, or hallucination concomitant with the appearance of a high frequency and low voltage e.e.g. pattern. MSR activity is well known to be influenced by the activities of higher levels of the central nervous system (Brooks, Koizumi and Siebens, 1956; Laitinen and Ohno, 1970; Sprague et al., 1948; Suda, Koizumi and Brooks, 1958). The increase of H/M ratio in our experiment could be caused by central facilitation of the MSR in the advanced stage of hypercapnia. Therefore, it is not possible to quantify the depressive effect of hypercapnia on MSR in terms of the decrease in the H reflex amplitude alone in conscious man.

Since both manual assistance to ventilation and carbon dioxide inhalation resulted in marked increase in minute volume, influences from the respiratory movement of the thorax on MSR must be considered. Kitahata, Taub and Sato (1969) confirmed in the cat, however, that the factor responsible for the alteration of MSR activity was the change in carbon dioxide concentration rather than the mechanical effects of hyperventilation or carbon dioxide inhalation. Although carbon dioxide inhalation slightly increased blood pressure and pulse rate in this study, Bradley, Schlapp and Spaccarell (1950) showed that spinal cord depression by carbon dioxide in the spinal cat was not a consequence of changes in arterial pressure.

In view of these studies, therefore, the change in MSR activity of conscious man during acute hypocapnia and hypercapnia must be the result of changes of carbon dioxide tension, even though the mechanism by which it acts upon synaptic transmission is not well understood.

REFERENCES


Les effets de l'hypocapnie et de l'hypercapnie aigues sur la transmission neuromusculaire et sur le reflexe spinal monosynaptique chez l'homme eveille

SOMMAIRE
Les effets de l'hypocapnie et de l'hypercapnie aigues sur la transmission neuromusculaire (NMT) et sur le reflexe spinal monosynaptique (MSR) chez des sujets conscients ont été étudiés en observant l'électromyogramme évocado moyen.

L'amplitude de l'onde H augmenta à 165 ± 25% (moyenne ± erreur standard) durant l'hypocapnie aigüe avec une concentration d'anhydride carbonique à la fin de l'expiration de 2,5 ± 0,2 vol.%, et tomba à 73 ± 7% durant l'hypercapnie aigüe avec une concentration d'anhydride carbonique à la fin de l'expiration de 6,8 ± 0,1 vol.%, comparativement aux valeurs de contrôle. L'amplitude de l'onde H augmenta à 226 ± 82% durant l'hypocapnie aigüe et diminua à 85 ± 9% durant l'hypercapnie aigüe, en comparaison à la valeur-contrôle. Ces résultats indiquent que le NMT aussi bien que le MSR chez le sujet conscient sont facilités par l'hypocapnie aigüe et que la NMT est freiné par l'hypercapnie aigüe. Mais l'effet de l'hypercapnie aigüe sur le MSR ne pouvait pas être vérifié uniquement par l'observation du reflexe H dans les conditions décrites.

Die Wirkung von akuter Hypo- und Hyperkapnie auf die neuromuskuläre Transmission und auf monosynaptische spinale Reflexe beim wachen Menschen

ZUSAMMENFASSUNG
Die Wirkung von akuter Hypo- und Hyperkapnie auf die neuromuskuläre Transmission (NMT) und auf monosynaptische spinale Reflexe (MSR) wurde beim wachen Probanden durch Beobachtung eines durchschnittlich ausgelösten Elektromyogramms untersucht. Die M-Wellenamplitude stieg auf 165 ± 25% (Mittel ± SD) während akuter Hypokapnie mit einer endexspiratorischen CO₂-Konzentration von 2,5 ± 0,2 vol.%, und sank auf 73 ± 7% während akuter Hyperkapnie mit einer endexspiratorischen CO₂-Konzentration von 6,8 ± 0,1 vol.%, im Vergleich zum Kontrollwert. Die H-Wellenamplitude stieg auf 226 ± 82% während akuter Hypokapnie und sank auf 85 ± 9% während akuter Hyperkapnie im Vergleich zum Kontrollwert. Diese Ergebnisse zeigen, daß sowohl die NMT als auch die Auslösung von MSR beim wachen Menschen durch akute Hypokapnie beschleunigt werden und daß die NMT durch akute Hyperkapnie unterdrückt wird. Jedoch konnte der Effekt akuter Hyperkapnie auf die MSR nicht allein durch die Beobachtung des H-Reflexes unter diesen Bedingungen gesichert werden.

EFFECTOS DE LA HIPOCAPNIA E HIPERCAPNIA AGUDA SOBRE LA TRANSMISION NEUROMUSCULAR Y SOBRE EL REFLEJO ESPINAL MONOSINAPTICO EN EL HOMBRE DESPIERTO

RESUMEN
Los efectos de la hipocapnia e hipercapnia aguda sobre la transmisión neuromuscular (NMT) y sobre el reflejo espinal monosináptico (MSR) en sujetos despiertos fueron estudiados mediante la observación del electromograma evocado promedio. La amplitud de la onda M aumentó a 165 ± 25% (media ± error standard) durante la hipocapnia aguda con una concentración espiratoria final de anhidrido carbónico de 2,5 ± 0,2 vol.%, y disminuyó hasta 73 ± 7% durante la hipercapnia aguda con una concentración espiratoria final de 6,8 ± 0,1 vol.% en comparación con el valor de control. La amplitud de la onda H aumentó a 226 ± 82% durante la hipocapnia aguda y disminuyó hasta 85 ± 9% durante la hipercapnia aguda en comparación con el valor de control. Estos resultados indican que en el hombre despierto la NMT y el MSR son facilitados por la hipocapnia aguda y que la NMT es inhibida por la hipercapnia aguda. Sin embargo, el efecto de la hipercapnia aguda sobre el MSR no podía ser determinado solamente mediante observación del reflejo H en estas condiciones.