CHANGES IN THE THRESHOLD OF THE MOTOR REACTION IN RESPONSE TO DIRECT STIMULATION OF THE CEREBRAL CORTEX AND IN THE REFLEX EXCITABILITY OF THE SPINAL CORD DURING ETHER ANESTHESIA WITH ARTIFICIAL HYPERVENTILATION

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Hyperventilation modifies the functional state of the central nervous system [3, 7, 14] so that the coordination of movement is disturbed [13], pain sensation is dulled [17], and the waves of electrical activity of the cerebral cortex are slowed [16]. However, the character of the changes in the excitability of the central nervous system occurring during hyperventilation has not been studied. The wide use of hyperventilation in modern anesthesiology [2, 4, 5] makes the investigation of this problem a matter of particular importance at the present time.

We have studied the changes in the threshold of the motor reaction during electrical stimulation of the motor area of the cerebral cortex and also the changes in the reflex excitability of the spinal cord during electrical stimulation of the peroneal nerve in animals anesthetized with ether and maintained on artificial hyperventilation.

EXPERIMENTAL METHOD

Experiments were carried out on 61 intact and 14 spinal dogs weighing 6.5-20 kg; 67 animals received a preliminary injection of morphine in a dose of 5-8 mg/kg and 8 animals a corresponding injection of a dose of 2 mg/kg. The cerebral cortex was stimulated in the upper part of the sigmoid gyrus with thin electrodes 5 mm apart. The changes in the reflex excitability were analyzed by the method described elsewhere [13], based on the study of the comparative effect of anesthesia and hyperventilation on intact and spinal animals. The threshold of reflex excitability of the spinal cord was determined during stimulation of the left peroneal nerve. The motor reaction was recorded as the contraction of the quadriceps femoris, the semitendinosus or the triceps cruris muscle.

The threshold of stimulation (TS) was measured by means of a sliding induction coil, connected through a step-down transformer (6 V) to the city supply system, and in some experiments by a current from a type SIF-3M stimulator.

The initial value of TS was determined in intact dogs 2 h, and in spinal dogs 3 h [10] after the preliminary operation, and the animal was then anesthetized. An ether-oxygen mixture in concentrations of 2, 3, and 6% was supplied through a tracheotomy tube by the closed and semiclosed methods, under the control of continuous thermogas analysis [12]. From $1\frac{1}{2}$ to 2 h after administration of the anesthetic began, its concentration in the inspired and expired mixture was almost equal and at the required level. This indicated dynamic equilibrium of the distribution of ether in the body, i.e., the development of the stage of maintenance of anesthesia [8, 9]. Hyperventilation began 2 h after the beginning of administration of ether and continued for 1 h. It was performed with a special spiropulsator [2], with a minute volume of pulmonary ventilation of 0.8-1.1 liter/kg, with a rate of artificial respiration of 24 per min. During hyperventilation the concentration of ether was maintained at the same level as at the preceding stage of anesthesia.

TABLE 1. Stability of the Threshold of the Motor Reaction in Response to Direct Stimulation of the Cerebral Cortex and of the Threshold of Reflex Excitability of the Spinal Cord of Unanesthetized Dogs when Fixed to the Vivisection Table

Date of expt.	Initial data			Fixation for 2 h			Fixation for 4 h		
	cortex	pyramidal tract	spinal cord	cortex	pyramidal tract	spinal cord	cortex	pyramidal tract	spinal cord
3/10	23,5	—	—	23	—	—	—	—	—
3/28	25	—	—	25	—	—	24,5	—	—
1/13	23	22	—	24	22	—	24	22	—
1/15	23	22	—	23	23	—	23	23	—
9/28	—	—	34	—	—	34	—	—	—
1/17	—	—	27	—	—	26	—	—	26
M	23,6	22	30,5	23,7	22,5	30	23,8	22,5	

Note. Magnitude of TS given in centimeters between the coils of the induction apparatus.

The TS was determined again 2 h after the beginning of inhalation of ether, again at the end of hyperventilation, 30 min after the cessation of hyperventilation, and, finally, 1 h after the cessation of anesthesia and elimination of ether from the body.

EXPERIMENTAL RESULTS

In 6 control experiments (without anesthesia and hyperventilation), when the dogs were fixed on the vivisection table for 2-4 h, the threshold of the motor reaction (in response to stimulation of the cerebral cortex) and the reflex excitability of the spinal cord remained unchanged (Table 1).

Inhalation of a 2% ether-oxygen mixture produced stage I anesthesia in the dogs. After inhalation of 3% ether the level of anesthesia corresponded to stage III_1, and after inhalation of 6% ether to stage III_3.

In 5 experiments in which the cortex was stimulated through electrodes inserted into its substance for a depth of 1.0-1.5 mm, a 3% ether mixture brought about an increase in the threshold of the motor reaction.

At the end of the 2nd hour of anesthesia the TS rose on the average by 2.7 cm ($P<0.001$). A similar pattern was seen in 8 experiments in which the motor cortex was stimulated through two pairs of electrodes: contact electrodes placed on the surface of the cortex, and buried electrodes inserted directly beneath the contact electrodes to a depth of 5-7 mm in the region of the pyramidal tract. For example, a 3% ether-oxygen mixture gave a regular increase in the TS in both cases, on the average by 3.2 cm ($P<0.01$) and by 3.4 cm ($P<0.001$). Artificial hyperventilation, carried out for 1 h against the background of administration of 3% ether, did not alter the threshold of the motor reaction in response to direct stimulation of the cortex and of the pyramidal tract. The value of the TS during hyperventilation remained the same as it was during anesthesia ($P> 0.5$).

During inhalation of 6% ether, despite the development of deep anesthesia (III_3), the motor reaction in response to stimulation of the cerebral cortex appeared in all the 11 experiments. In these circumstances the TS increased on the average by 2.2 cm ($P<0.001$). Hyperventilation, against the background of the action of 6% ether, caused no further changes in the TS. The mean value of TS at the end of the 2nd hour of anesthesia and during hyperventilation was 21.6 cm.

Identical changes in TS in the period of anesthesia and hyperventilation were also observed in experiments in which the cortex was stimulated by current from a stimulator (Table 2).

TABLE 2. Changes in Threshold of Motor Reaction during Direct Stimulation of the Cerebral Cortex and Pyramidal Tract in Dogs Under Anesthesia and Hyperventilation

Date of expt.	Initial data		Anesthesia for 2 h		Hyper-ventilation		After desaturation	
	cor-tex	pyramid-al tract	cor-tex	pyramid-al tract	cor-tex	pyramid-al tract	cor-tex	pyramid-al tract
1/20	20	20	60	70	40	40	40	40
1/8	20	33	50	90	50	90	20	40
1/21	10	10	50	60	100	100	100	100

Note. The threshold is expressed in volts.

When the reflex excitability of the spinal cord was studied during anesthesia in intact dogs, initially a 3% ether mixture was given, and in 2 of 6 experiments it lowered the excitability to zero. In the other four experiments the TS rose on the average by 9 cm. Accordingly, a lower concentration of ether was used (2%), and this gave a depth of anesthesia corresponding to stage I.

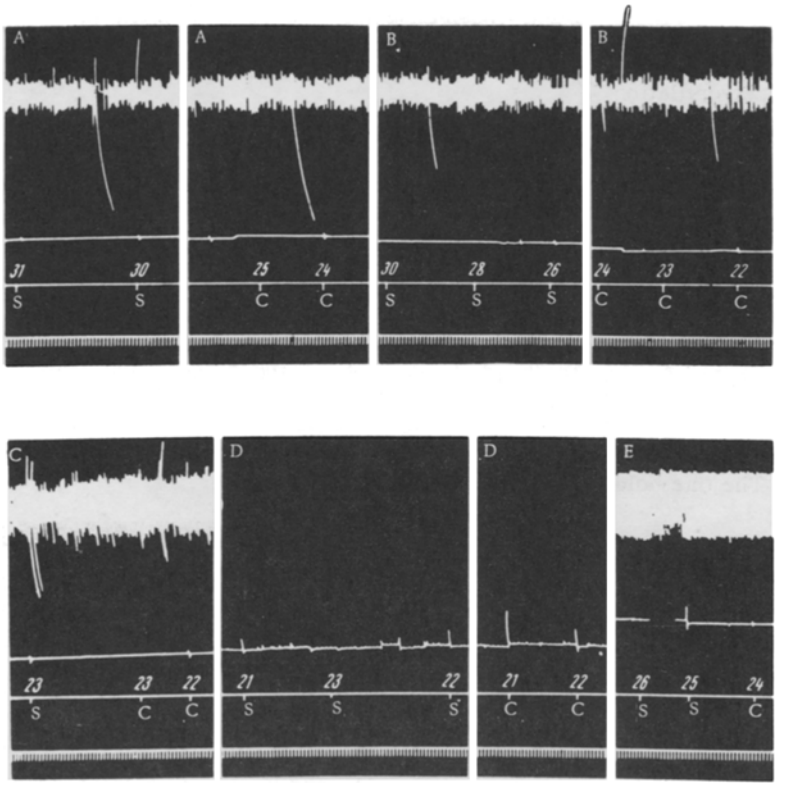
Under the influence of 2% ether the reflex excitability of the spinal cord fell in all 16 experiments. The value of TS rose on the average by 4.7cm from its initial level ($P < 0.001$). Hyperventilation produced a further fall in reflex excitability with an increase in TS on the average by 3.1 cm compared with its level under anesthesia and before application of artificial respiration with hyperventilation ($P < 0.001$), and by 7.8 cm compared with its level before anesthesia ($P < 0.001$). Thirty minutes after the cessation of hyperventilation, when the animals were breathing spontaneously, although the reflex excitability was increased by the ether-oxygen mixture,it did not reach the level recorded before hyperventilation ($P < 0.01$). The comparative influence of ether and hyperventilation on the threshold of the motor reaction in response to stimulation of the cerebral cortex and on the reflex excitability of the spinal cord in intact dogs in shown in the figure.

In 9 experiments in which hyperventilation was applied without anesthesia for a periof of 1 h,the direct excitability of the cortex of the intact dogs remained unchanged, while the reflex excitability of the spinal cord fell. In these circumstances the TS rose on the average by 5.5 cm. In the spinal animals hyperventilation without anesthesia produced the opposite effect. The reflex excitability increased in the spinal dogs, as demonstrated by the fall in the value of TS, on the average by 2.5 cm.

In spinal dogs anesthetized with ether (3%), hyperventilation was not accompanied by a lowering of reflex excitability in all the experiments, as was observed in the intact animals. A fall in excitability took place in only 2 of the 7 experiments, and total disappearance in only one. In the remaining 4 experiments the reflex excitability increased. At the same time the mean values of the TS did not differ significantly in anesthesia and hyperventilation, which demonstrated the absence of changes in the reflex excitability of the spinal cord during hyperventilation when applied to anesthetized spinal animals.

Hyperventilation during anesthesia caused the pulse rate to rise by 22-40 beats per minute and the arterial pressure to fall inconstantly, on the average by 12 mm. Investigation of the arterial blood gases by Van Slyke's method, performed in 12 experiments by M. D. Litvinenko, revealed a fall in the carbon dioxide concentration of the blood during hyperventilation by comparison with its level at the end of the 2nd hour of anesthesia, on the average from 29.5 to 17.72% ($P < 0.001$). The blood oxygen concentration had a mean value of 16.7% during anesthesia, and of 17.73% during hyperventilation ($P = 0.01$).

The changes in the excitability of the central nervous system during ether anesthesia with artificial hyperventilation were reversible in character. The degree of recovery (1 h after cessation of inhalation of ether) depended on the concentration of the anesthetic, producing different depths of anesthesia. The threshold of the motor reaction in response to direct stimulation of the cerebral cortex amounted to 94-100% of the initial level. The threshold of reflex excitability of the spinal cord in the intact animals likewise was almost completely restored, and it amounted, on the average, to 89% of the initial level, compared with 98% in the spinal dogs.



Changes in the threshold of the motor reaction in response to direct stimulation of the motor cortex and changes in the reflex excitability of the spinal cord during inhalation of 2% ether and artificial hyperventilation against this background. A) Before anesthesia; B) 1 h after inhalation of ether; C) 2 h after inhalation of ether; D) during hyperventilation; E) 1 h after cessation of inhalation of ether. On the kymogram the letter S denotes the reflex excitability of the spinal cord and C the threshold of the motor reaction to stimulation of the cortex. Significance of the curves (from top to bottom): pneumogram, tracing of contractions of semitendinosus muscle, marker of stimulation, time marker (4 sec). The numbers denote the distance in centimeters between the coils of the induction apparatus.

The facts described above show that during inhalation of 3% ether the reflex excitability of the spinal cord in intact dogs falls in stage III_1 of anesthesia, whereas the motor reaction to stimulation of the cerebral cortex is not completely lost even in deeper anesthesia produced by inhalation of 6% ether. This evidently depends on the higher sensitivity to anesthesia of the mechanism of afferent transmission of excitation than of the mechanism of transmission of influences from the cerebral cortex. The rapid exclusion of the reflexes of the spinal cord during anesthesia may also be attributable to influences from the higher levels of the central nervous system [6, 11, 13], including the reticular formation of the brain stem [8, 15, 16]. The deeper fall of the reflex excitability of the spinal cord during anesthesia in the intact dogs than in the spinal animals, observed in these experiments, confirms this suggestion. The difference in the degree of lowering of excitability during stimulation of the motor cortex and of the pyramidal tract under the influence of ether may be evidence of the preferential action of the anesthetic on the synapses connecting the pyramidal tract to the motor neurons of the spinal cord rather than on the cells of the cerebral cortex. The decrease in the reflex excitability of the spinal cord during hyperventilation against the background of the same concentration of ether in the inhaled mixture is dependent on the hypocapnia developing in these circumstances [1, 7, 18]. Hypocapnia evidently exerts its influence through the brain, for the separation of the spinal cord from the higher levels of the central nervous system largely lowers, and may actually abolish, the inhibitory effect of hyperventilation on the reflex excitability of the spinal cord.

SUMMARY

It was found in 75 experiments on dogs that ether in 2, 3, and 6% concentrations increases the motor reaction threshold in direct stimulation of the motor zone of the brain cortex and the pyramidal tract by 3.3-3.4 cm with regard to the initial values (stimulation threshold is expressed in centimeters between coils of an induction apparatus). The reflex excitability of the spinal cord in intact dogs is lost under the effect of a relatively small anesthetic concentration in the inhaled mixture (3%). The spinal excitability threshold increases under the influence of ether inhalation (3%) by 9 cm on the average. In spinal animals, the reflex excitability at the same degree of anesthesia decreased to a lesser extent. In hyperventilation, the motor reaction threshold does not change in direct stimulation of the brain cortex under conditions of anesthesia, and the threshold of the reflex excitability of the spinal cord increases by 7.8 cm on the average. In spinal dogs, hyperventilation concurrent with anesthesia fails to produce changes in the reflex excitability.

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