CONDITIONED-REFLEX CHANGES IN RESPIRATORY ARRHYTHMIA

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Many workers have shown that a conditioned reflex can be formed to involve the heart. Several investigations of conditioned reflexes formed on the heart using pharmacological stimuli have been made [2-6]. The object of the present investigation was to discover if conditioned-reflex changes could be produced in respiratory arrhythmia in dogs in response to injection of morphine. The choice of morphine as unconditioned stimulus was made because this substance raises the tone of the vagus nerve nuclei, as a result of which the respiratory arrhythmia is increased a short time after its injection [7].

EXPERIMENTAL METHOD

Experiments were carried out on two dogs weighing 12 and 15 kg, which received an injection of morphine daily in the same experimental situation. The doses of morphine given to one of the dogs (Gera) were 0.05 g, and those given to the other (Chernyi) were 0.2 g. During the experiment the ECG was recorded continuously in lead 2 by means of a cardiocyclograph [1]. The intensity of the respiratory arrhythmia was expressed by the coefficient of arrhythmia of cardiac activity [3], namely the ratio between the sum of the differences between each preceeding and succeeding cycle and the total duration of the cycles (not less than 75 cycles):

$$K_{DA} = \frac{\Sigma_{k=1}^{n} / T_k - T_{k+1}}{\left(\Sigma_{k=1}^{n} \frac{T_k + T_{k+1}}{2} \right)} \cdot 100,$$

where n is the number of cardiac contractions and T the duration of each cycle.

The higher this coefficient, the more marked the arrhythmia.

To test for the presence of a conditioned reflex, the dog was given an injection of physiological saline in the same conditions as those in which morphine was injected. The experiments were carried out after extinction of the dog's orienting reflex to the situation, for which purpose the dog was left for several hours in the room in which the experiment was to be carried out on many occasions before the systematic injections of morphine began.

EXPERIMENTAL RESULTS

Injection of morphine was accompanied by salivation and vomiting or by a desire to vomit. Besides these toxic manifestations, a change was observed in the rhythm of respiration, in the heart rate, and in the coefficient of respiratory arrhythmia. During the first minutes after the injection of morphine, an increase in the respiration and heart rates was observed. After 15-20 min, the respiration and heart rates both began to slow, and the maximal slowing took place after 30-40 min. After 1.0-1.5 h the respiration and heart rates were close to their original values again. Corresponding changes took place in the coefficient of respiratory arrhythmia. The initial coefficient of respiratory arrhythmia had a mean value of 23.9, the heart rate was 74/min, and the respiration rate 22/min. Forty

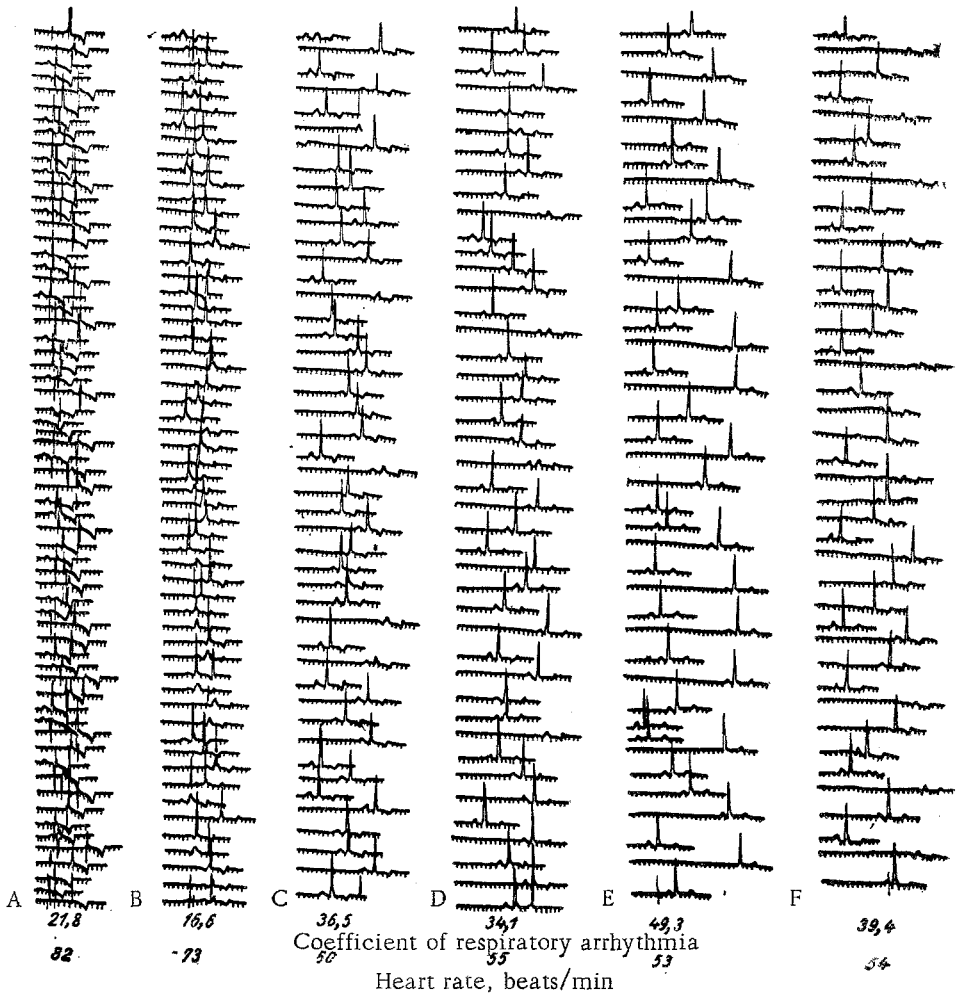

Fig. 1. Electrocardiographic changes before (A), and 15 min (B), 20 min (C), 30 min (D), 40 min (E), and 50 min (F) after injection of morphine.

minutes after injection of morphine the most marked changes were found in all the indices. For instance, the coefficient of respiratory arrhythmia rose considerably and attained a mean value of 40, while the heart rate was 51/min and the respiration rate 15/min. The electrocardiographic changes arising after administration of morphine are shown in Fig. 1.

After the 35th injection, instead of morphine physiological saline was injected. In these conditions the animal's reaction to injection of physiological saline corresponded qualitatively to its reaction to injection of morphine, but it was weaker.

A clearer conditioned-reflex reaction was obtained after 41 injections of morphine, when injection of physiological saline reproduced the unconditioned-reflex reaction perfectly clearly. The original coefficient of arrhythmia in this particular experiment was 13.8, the heart rate 82/min, and the respiration rate 22/min. The coefficient of respiratory arrhythmia reached 27.5 between 30 and 35 min after injection of physiological saline, while the heart rate slowed to 74/min and the respiration rate slowed to 18/min (Fig. 2).

The conditioned reflex was subsequently extinguished: during the first days a typical conditioned-reflex reproduction of the unconditioned-reflex reaction was observed, but after 12 days extinction began to take place.

In the experiments on the dog Chernyi, approximately the same results were obtained, although the conditioned-reflex changes taking place in the respiratory arrhythmia were less marked, and 55 combinations with the injection of large doses of morphine were required in order to establish the conditioned reflex.

Fig. 2. Electrocardiographic changes in response to injection of physiological saline after repeated injections of morphine. Legend the same as in Fig. 1.

SUMMARY

Chronic experiments were conducted on 2 dogs in a study of conditioned reflex activity on the respiratory arrhythmia following morphine administration. Morphine was injected subcutaneously daily for 30-35 days (0.05 g to one dog and 0.2 gm to the other). The ECG was recorded by means of a cardiocyclograph (lead 2 standard).

Fifteen to twenty min following morphine administration a marked slowing of the heart rate occurred with respiratory arrhythmia intensified more than twice.

Due to elaboration of the conditioned reflex following 30-35 morphine injections, injection of physiological saline in the same experimental conditions led to a similar slowing of the cardiac rhythm and intensification of the respiratory arrhythmia, as was the case with morphine administration. The data obtained testify to the possibility of producing conditioned reflex changes in the tone of the vagus nerve nuclei.

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