EFFECT OF CHRONIC STIMULATION OF NEGATIVE AND POSITIVE EMOTIOGENIC HYPOTHALAMIC CENTERS ON PRODUCTION OF CARDIAC ARRHYTHMIAS

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Changes in cardiac activity arising during prolonged (up to 1 or 2 weeks) electrical stimulation of the ventromedial hypothalamic nuclei were investigated in chronic experiments on 46 rabbits. Disturbances of the cardiac rhythm, in the form of tachycardia, atrial flutter and fibrillation, ventricular extrasystoles, and paroxysmal ventricular techysystole developed mainly during the first days of stimulation and were stopped by administration of Inderal. In animals subjected to stimulation of the ventromedial nuclei for 1-2 weeks, functional "weakness" of the cardiac pacemakers was found, as shown by an increase in poststimulation depression of automatic activity of the pacemakers and the appearance of Luciani's periods. Disturbances of the cardiac rhythm arising in response to stimulation of the ventromedial nuclei are abolished by stimulation of the lateral hypothalamic area.

KEY WORDS: *Chromic stimulation of the hypothalamus; ventromedial nucleus; lateral hypothalamic area; cardiac pacemakers; cardiac arrhythmias.*

During brief electrical stimulation of various parts of the hypothalamus disturbances of cardiac activity may arise [1, 5, 7-14]. These disturbances are seen particularly clearly during stimulation of the negative emotiogenic centers of the hypothalamus, namely its ventromedial nuclei [2, 6]. The effect of stimulation of positive emotiogenic centers of the hypothalamus on cardiac activity has been inadequately studied. The only available observations show that stimulation of the lateral hypothalamus leads to delay in the development of aconitine arrhythmia [3].

Changes in cardiac activity were studied during prolonged electrical stimulation of the ventromedial hypothalamic nuclei and the lateral hypothalamic area.

EXPERIMENTAL METHOD

Experiments were carried out on 46 unanesthetized chinchilla rabbits weighing 2.5-3 kg. Nichrome bipolar electrodes, with an interpolar distance of 0.3-0.5 mm, were inserted stereotaxically into the ventromedial nucleus of the hypothalamus of all the animals. In 14 rabbits similar electrodes were inserted simultaneously into the lateral hypothalamic area. The location of the electrode was verified from behavioral responses to stimulation of the hypothalamic emotiogenic centers and also from examination of serial sections of the brain, fixed in formalin, after the experiment.

For 1-2 h daily over a period of 1-2 weeks the ventromedial hypothalamic nucleus or lateral hypothalamic area of the immobilized animals was stimulated (50 Hz, 0.5 msec, 100-400 μA). Before each stimulation session the interelectrode resistance was measured and the voltage increased so that the current remained constant.

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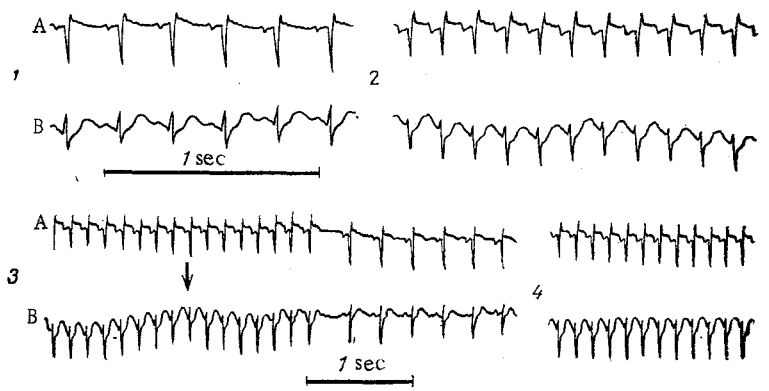

Fig. 1. Development of sinus tachycardia in rabbits after stimulation of ventromedial hypothalamic nucleus and its disappearance during stimulation of lateral hypothalamic area: 1) initial frequency of excitation 240/min; 2) sinus tachycardia 420 beats/min, arising after stimulation of ventromedial nucleus; 3) cessation of sinus tachycardia during stimulation of lateral hypothalamic area (arrow indicates beginning of stimulation); 4) restoration of sinus tachycardia on discontinuing stimulation of lateral hypothalamic area. ECG recorded in esophageal lead (A) and standard lead II (B).

Disturbances of cardiac activity during isolated or combined stimulation of negative and positive emotiogenic centers of the hypothalamus were recorded. The functional stability of the sino-atrial node and of the potential ventricular pacemakers of isolated rabbits' hearts, perfused by Langendorff's method, taken from animals at different stages of chronic stimulation of the ventromedial hypothalamic nuclei, was studied. Stability was assessed from the duration of the preautomatic pause arising after the end of the fast electrical stimulation (square pulses of above-threshold strength, 2 msec in duration, with a frequency of up to 600-800/min for stimulation of the sinoatrial node and up to 200-250/min for stimulation of the cardiac ventricles, over a period of 3 min). Potential ventricular pacemakers were investigated under conditions of complete atrioventricular block. In experiments on isolated heart the electrical activity of the atria and ventricles was recorded. In the chronic experiments the ECG was recorded in standard lead II and the esophageal lead. Electrical activity of the atria of some animals was recorded by means of bipolar intracardiac electrodes applied to the heart through the external jugular vein.

EXPERIMENTAL RESULTS

In 25 rabbits during the first minutes after the beginning of stimulation of the ventromedial hypothalamic nuclei the heart rate fell on the average by 23% (from 273 ± 7.7 to 210 ± 8.2; $P < 0.001$). Incomplete atrioventricular block developed in four of these animals. These changes were due to cholinergic influences, for they disappeared after injection of atropine (0.5-1 ml of a 0.1% solution). In 13 animals the heart rate rose during the first few minutes of hypothalamic stimulation on the average by 27% (from 271 ± 8.1 to 345 ± 8.3; $P < 0.02$).

Between 10 and 15 min after the beginning of stimulation nearly all animals developed well-marked tachycardia, up to 300-320 beats/min, which could be abolished by injection of Inderal (0.5-2 mg/kg). Persistent tachycardia up to 350-400 beats/min was observed in five of them. After the end of hypothalamic stimulation the tachycardia gradually disappeared although in some cases it reappeared on the day after a regular session of stimulation (Fig. 1). This dynamics of the heart rate usually remained the same during each successive session of stimulation over a period of several days. In 8 of the 46 rabbits stimulation of the ventromedial nucleus had no marked effect on the heart rate.

Prolonged (up to 2 weeks) stimulation of the negative emotiogenic centers of the hypothalamus also led to the appearance of various cardiac arrhythmias. In 26 of the 46 rabbits persistent bouts of atrial flutter and fibrillation developed (Fig. 2A). Five animals

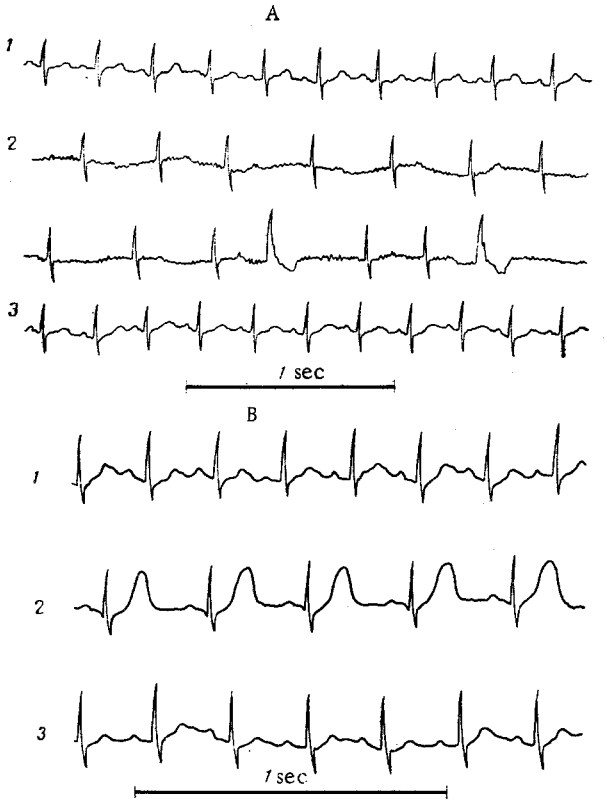

Fig. 2

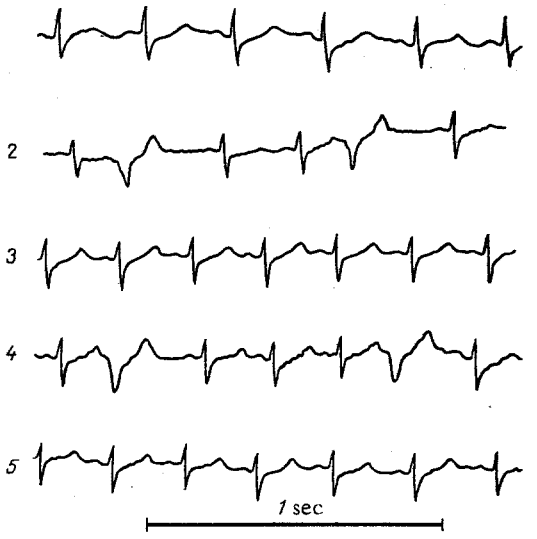

Fig. 3

Fig. 2. Development of atrial fibrillation (A) and giant T wave (B) during stimulation of ventromedial nucleus in rabbits and restoration of normal cardiac activity during combined stimulation of ventromedial nucleus and lateral hypothalamic area. ECG recorded in standard lead II before (1) and during stimulation of ventromedial nucleus (2) and during additional stimulation of lateral hypothalamic area (3).

Fig. 3. Development of venticular extrasystoles in a rabbit during stimulation of ventromedial nucleus and its disappearance during added stimulation of lateral hypothalamic area: 1) initial frequency of excitation; 2) appearance of left-ventricular extrasystoles during stimulation of ventromedial nucleus; 3) disappearance of extrasystoles during added stimulation of lateral hypothalamic area; 4) resumption of extrasystoles on discontinuation of stimulation of lateral hypothalamic area; 5) restoration of regular sinus rhythm after cessation of stimulation of ventromedial nucleus. ECG recorded in standard lead II.

developed a giant T wave (Fig. 2B). Paroxysmal ventricular tachysystole developed in 4 rabbits and ventricular extrasystoles in 12 rabbits (Fig. 3). All these disturbances appeared during stimulation of the ventromedial hypothalamic nuclei and they sometimes lasted for 15-20 min after stimulation had ended. Next day, before the regular session of stimulation, in some experiments single ventricular extrasystoles were observed.

Bouts of atrial flutter and fibrillation, ventricular extrasystoles, and paroxysmal tachysystole developed most frequently during the first days of hypothalamic stimulation. Toward the end of the first week they appeared less frequently. All these disturbances of cardiac rhythm were abolished by injection of the β-adrenoblocker Inderal (0.5-2 mg/kg). The α-adrenoblockers phentolamine and atropine did not abolish these disturbances.

Functional "weakness" of the cardiac pacemakers was discovered in the hearts of most animals subjected to stimulation of the ventromedial hypothalamic nuclei for 1-2 weeks. After application of high-frequency electrical stimuli (600-800/min for 3 min) to the sinoatrial node, its automatic activity was inhibited for a short time, but this was not observed in the hearts of the control group of rabbits. Other evidence of functional weakness of the potential pacemakers was given by a marked increase in poststimulation inhibition of

automatic activity of the ventricular pacemakers and the appearance of Luciani's periods, i.e., the periodic inhibition of atuomatic activity of the idioventricular pacemaker.

Prolonged stimulation of the positive emotiogenic centers on the hypothalamus (lateral hypothalamic area) in the same animals did not cause the appearance of a disturbance of cardiac rhythm. On the contrary, the sudden tachycardia, atrial fibrillation and flutter, the giant T wave, and the ventricular extrasystoles or paroxysmal ventricular tachysystole arising under the influence of stimulation of the ventromedial nuclei disappeared when the lateral hypothalamic area was stimulated at the same time (Figs. 1, 2, and 3). Under these circumstances the paroxysmal tachycardia, fibrillation, and ventricular extrasystoles ceased rapidly during the first few seconds or minutes of stimulation. Normalization of the T wave took place gradually over a period of 10-15 min after the beginning of stimulation. The mechanisms of cessation of the disturbances of cardiac activity during stimulation of the lateral hypothalamus require further investigation.

The cardiac arrhythmias which developed disappeared after injection of Inderal. This suggests that they are produced by adrenergic mechanisms, the state of which is changed during stress [4].

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