COMPARATIVE CHARACTERISTICS OF COLD AND FEBRILE TREMOR

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In experiments on anesthetized and unanesthetized cats it was concluded on the basis of the identity of distribution of cold and febrile tremor in muscle groups, its electromyographic picture, and the equal sensitivity to neurotropic agents that during cooling of the body and during a febrile reaction the same mechanism of central regulation of contractile thermogenesis is activated.

KEY WORDS: temperature regulation; fever; tremor; neurotropic agents.

The chief source of the increase in heat production when the body is exposed to cold and during a febrile reaction is muscle tremor [1, 2, 4, 6]. The evident analogy between the function of cold (CT) and febrile (FT) tremor suggests that in both cases the same mechanism of central control of contractile thermogenesis is activated.

This paper describes the results of a comparative analysis of CT and FT as reflected in various electromyographic indices.

EXPERIMENTAL METHOD

Experiments were carried out on anesthetized (chloralose and urethane, 50 and 500 mg/kg respectively) and unanesthetized cats with oxyphenonium premedication (2.5 mg/kg) in all experiments. The experiments were carried out in a chamber with an ambient temperature of 20-21.5°C. The anesthetized cats were fixed in a stereotaxic apparatus and also by means of two pins passed through the heads of the femora. The ventral part of the trunk rested on a thermostatically controlled heater, the temperature of which was maintained at between 20 and 21°C in the experiments with pyrogenal or at between 14 and 16°C for evoking CT. The unanesthetized cats were kept in a special chamber restricting their freedom of movement. In these experiments external cooling was carried out by lowering the temperature in the chamber to 14-16°C. The electromyogram (EMG) was recorded by means of wire electrodes [3], which in the chronic experiments (on unanesthetized cats) were sutured to the muscles 8-10 days before the first experiment. The EMG was recorded on a "Medicor" electromyograph. Parallel with the EMG, the brain temperature in the region of hypothalamus and the subcutaneous temperature of the dorsum of the foot of the anesthetized cats were recorded by means of thermocouples on an N-3020 automatic writer. Only the rectal temperature of the unanesthetized cats was recorded. To produce a febrile reaction pyrogenal was injected intravenously into the anesthetized animals and intramuscularly into the unanesthetized animals in a dose of 50 mean pyrogenic doses/kg. The neurotropic drugs were injected intravenously into the anesthetized and intraperitoneally into the unanesthetized animals.

EXPERIMENTAL RESULTS

Under the experimental conditions indicated above the brain temperature of the anesthetized cats either remained constant (about 37-38°C) or fell slowly on average by 0.03 ± 0.01°C/min. The subcutaneous temperature under these circumstances was between 32 and 34.5°C, and it usually fell at the rate of 0.04 ± 0.01°C/min. Only EMG activity of the diaphragm was recorded at this time in the animals.

Lowering the temperature of the electric heater led after 1-5 min to an increase in the rate of fall of the subcutaneous temperature (0.29 ± 0.05°C/min), and when the critical level was reached (26.57 ± 0.58°C) CT appeared.

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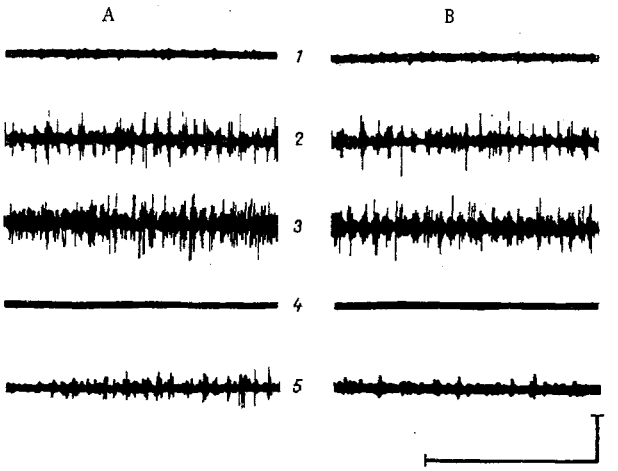

Fig. 1. EMG of sartorius muscle during cold and febrile tremor in unanesthetized cat. 1) Initial; 2) after exposure to cold (A) and pyrogenal (B); 3) regular tremor; 4) 10 min after injection of Seduxen; 5) 45 min after injection of Seduxen. Calibration: 0.5 sec, 500 μV. Experiments performed on same cat at intervals of 2 days.

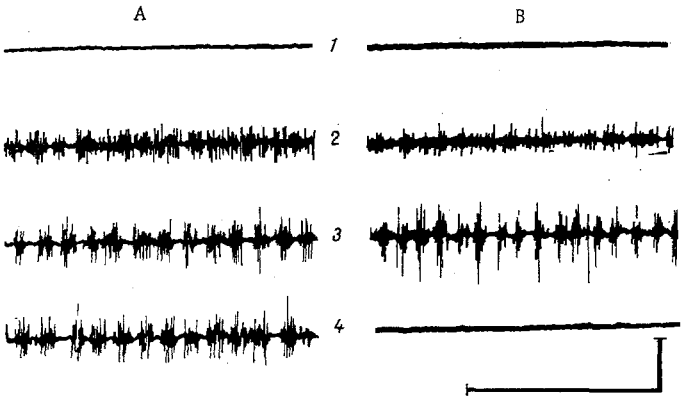

Fig. 2. EMG of sartorius muscle during cold and febrile tremor in anesthetized cats. 1) Initial; 2) temperature-regulatory tone after exposure to cold (A) and pyrogenal (B); 3) regular tremor; 4) 30 min after injection of sodium salicylate. Calibration: 0.5 sec, 500 μV.

Injection of pyrogenal (in another series of experiments) led after 15-30 min to acceleration of the fall of subcutaneous temperature (0.34 ± 0.02°C/min) in the anesthetized cats also, and this was followed by the development of FT. However, the critical level of the fall of subcutaneous temperature for the appearance of FT was considerably higher (30.88 ± 0.53°C) than in the experiments with cold. The appearance of CT in the anesthetized cats stabilized the brain temperature, which had been falling until then. In most experiments on the anesthetized animals FT did not cause the brain temperature to rise. Only in nine of 36 experiments did the onset of FT cause the brain temperature to rise at the rate of 0.01-0.02°C/min. As a rule FT in the unanesthetized animals increased the rectal temperature at the rate of 0.03-0.04°C/min, whereas CT in the unanesthetized animals only maintained the temperature at a constant level.

The experiments showed that both during cooling and during the febrile reaction, in both anesthetized and unanesthetized animals, tremor developed in the trunk muscles (rhomboid, latissimus dorsi, pectoralis major and minor, serratus anterior and posterior, intercostals, abdominal muscles) and the limb flexors (biceps brachii, sartorius, semitendinosus, tibialis anterior) but without involvement of the diaphragm and the extensors (triceps brachii, semimembranosus, gastrocnemius) in the process.

The pattern of the interference EMG in the anesthetized and unanesthetized cats during both CT and FT was characterized by grouping of the discharges of the neuromotor units with a mean frequency of about

20 sec^{-1} typical of tremor (Figs. 1 and 2). However, this mean frequency was unstable and could vary from 10 to 33 sec^{-1}. The volley type of EMG activity characteristic of tremor in the anesthetized animals (Fig. 2) was observed against the background of weak temperature-regulatory tone, which often disappeared completely with the development of regular tremor. In the unanesthetized animals (Fig. 1) tremor was recorded usually against the background of relatively well-marked temperature-regulatory tone and it was interrupted from time to time when the animal was restless.

Neurotropic hypothermic drugs in equal minimal doses (oxytremorine 0.05 mg/kg, phentolamine 2.5 mg/kg, Seduxen – diazepam – and chlorpromazine 0.5 mg/kg) inhibited both CT and FT. Conversely, scopolamine (0.5 mg/kg) and propranolol (5 mg/kg), which inhibit certain analogs of parkinsonian tremor [7, 9, 10], did not affect the course of CT and FT. Only sodium salicylate (200 mg/kg) acted as selective blocker of FT in both anesthetized and unanesthetized cats (Fig. 2).

Clearly CT and FT in anesthetized and unanesthetized cats have the same distribution in muscle groups, a characteristic and identical EMG pattern of rhythm grouping, and identical changes in response to injection of the neurotropic agents tested. The selective inhibitory effect of sodium salicylate on FT can be explained by the fact that neurotropic hypothermic drugs inhibit the neuronal system of control of CT and FT directly, whereas antipyretics inhibit the synthesis of prostaglandin E_1, the hypothetical mediator of pyrogenic activation of temperature-sensitive neurons in the hypothalamus [5, 8].

The results thus indicate that during external cooling and during the development of a febrile reaction the same mechanism of regulation of contractile thermogenesis is activated.

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