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EFFECT OF PHOSPHATIDYLCHOLINE ON BODY TEMPERATURE AND POSTERIOR HYPOTHALAMIC UNIT ACTIVITY IN ANIMALS

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The effect of synthetic preparations and biologicals on body temperature and on its regulation in various animals and man has now been studied on a sufficiently wide scale [1, 3]. The participation of many neurotransmitters, neurohormones, and other substances in central mechanisms of temperature regulation has been established [1, 7]. Information has recently been obtained that certain exogenous phospholipids can induce changes in metabolism of certain neurotransmitters [5, 9]. However, the effect of phospholipids, as the most important structural components of biological membranes, on the temperature regulating apparatus has not been studied. In particular, we have no information on the effect of liposomes, composed of phospholipids, when introduced into the body on its temperature and on neuronal activity in temperature-regulating centers.

The aim of this investigation was to study the effect of phosphatidylcholine (PCh) liposomes on body temperature and on unit activity in the posterior hypothalamus, which performs integrative functions in central mechanisms of temperature regulation.

METHODS

The effect of PCh on body temperature was studied in 36 albino rats weighing 160-180 g and in 16 rabbits weighing 2.5-3.2 kg, under thermoneutral conditions (20-24°C). The animals' body temperature was measured in the rectum (at a depth of 3 cm in rats and 6 cm in rabbits) by means of a TPÉM-1 electrothermometer. The effect of PCh on units activity in the posterior hypothalamus (coordinates $P_1L_1H_{13-15}$ according to Sawyer's atlas) was investigated in 8 rabbits anesthetized with urethane (1.5 g/kg, intraperitoneally). The method of extracellular recording of spontaneous unit activity and of its analysis was described previously [2]. Unit activity was studied during heating of the body of an animal previously cooled (to 36°C) in air. Heating was carried out in a special thermally insulated chamber by means of a current of heated (40-42°C) atmospheric air from an EK-3 electrocalorifier. The brain temperature (mesencephalic region) was measured continuously by a miniature thermistor (diameter 0.8 mm) and readings were recorded on a V7-21A Universal Measuring Instrument. PCh liposomes were made as follows. An alcoholic solution of PCh was evaporated to dryness *in vacuo* in a current of nitrogen at 30°C. The cooled suspension of PCh in distilled water (0.5 g to 100 ml) was sonicated on a UZDN-1 apparatus for 10 min (frequency 22 kHz, current 0.2 A).

Standard egg PCh, carbachol, and L-noradrenalin bitartrate monohydrate (Calbiochem, USA) were used in the experiments. Aqueous solutions of PCh and also liposomes were injected into the lateral ventricles: in the experiments on rats in a volume of 20 µl under

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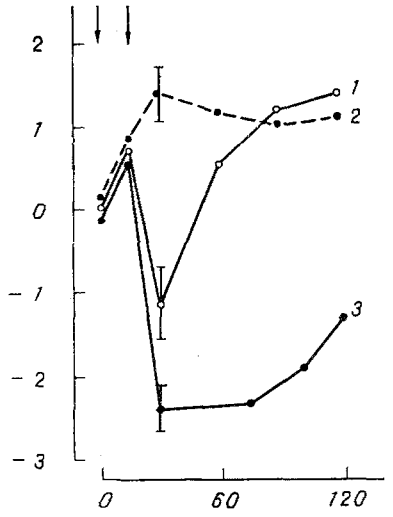

Fig. 1

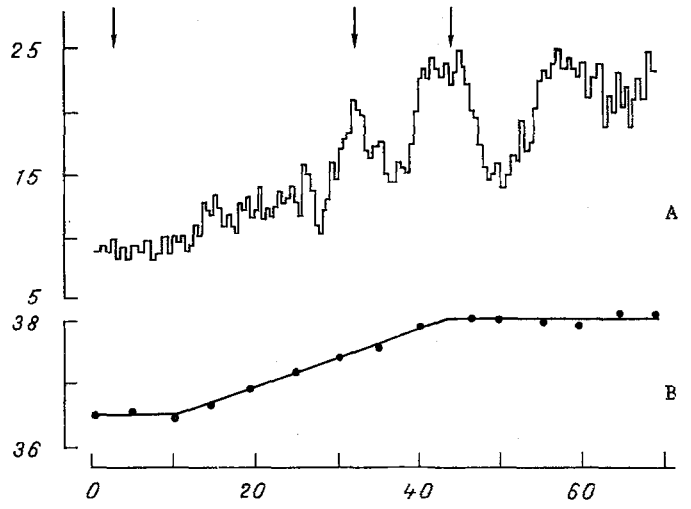

Fig. 2

Fig. 1. Effect of NA and carbachol on PCh-induced rise of body temperature in rats after injection of substances into lateral ventricles. Abscissa, time (in min); ordinate, changes in body temperature (in °C). 1) PCh + NA (n = 8); 2) control: PCh + H_2O :n = 12); 3) PCh + carbachol (n = 6). First arrow indicates time of injection of PCh (100 μg) into cerebral ventricles; second arrow indicates time of injection of NA (20 μg), carbachol (5 μg), or distilled water (20 μl) in control experiment, into lateral ventricles.

Fig. 2. Effect of PCh on unit activity of temperature-sensitive posterior hypothalamic neuron of a rabbit during heating of its body. Abscissa, time (in min). A) frequency histogram of unit activity (spikes/sec); B) brain temperature (in °C). Arrows indicate time of injection of PCh (250 μg) into cerebral ventricles.

local anesthesia (0.5% procaine subcutaneously), and in the experiments on rabbits in a volume of not more than 50 μl, through stereotaxically oriented cannulas. PCh also was injected intravenously.

RESULTS

Intravenous injection of PCh liposomes into rats in a dose of 50 mg/kg caused a very small rise of the animals' body temperature (by 0.70 ± 0.13°C, after 30 min; $P < 0.05$). Injection of PCh (100 μg per animal) into the rats' cerebral ventricles gave a greater hyperthermic effect. The body temperature rose from 37.00 ± 0.28° to 38.60 ± 0.10°C after 30 min. This hyperthermic response could be prevented, or the body temperature actually lowered below its initial value (Fig. 1) by subsequent (15 min after injection of PCh) injection of noradrenalin (NA, 20 μg) or carbachol (5 μg) into the cerebral ventricles. Experiments on rabbits showed that PCh (intravenously in a dose of 50 mg/kg) had different effects on the animals' body temperature. For instance, if the initial temperature was 38.50 ± 0.08°C, PCh did not change it. A fall of body temperature (by 0.40 ± 0.09°C after 20 min) under the influence of PCh was observed if the initial temperature was 39.40 ± 0.09°C.

The study of unit activity in the rabbits' posterior hypothalamus showed that during heating of the animals (when the brain temperature rose from 36.0 to 39.9°C), 30 of the 36 neurons did not change their discharge frequency (thermoinsensitive neurons) and 6 neurons increased their discharge frequency by not less than 1.6 Hz during a rise of their body temperature by 1.0°C (thermosensitive neurons). Of 30 thermoinsensitive neurons, 12 had an average discharge frequency of 7.80 ± 0.82 Hz and 18 neurons generated action potentials with an average frequency of 12.50 ± 0.79 Hz. Injection of PCh (250 μg) into the cerebral ventricles of the rabbits, when their brain temperature was 36.5-38.5°C, had no effect on spontaneous activity of 12 neurons, whose discharge frequency was 7.80 ± 0.82 Hz. However, all 18 neurons with a high discharge frequency (12.50 ± 0.79 Hz) lowered (by not less than 25%) their spontaneous activity under the influence of PCh (latent period of response 118.3 ± 26.9 sec, duration 361.20 ± 56.17 sec).

If the brain temperature was between 36.0 and 36.5°C, the thermosensitive neurons had an average discharge frequency of 8.80 ± 1.14 Hz. Injection of PCh (250 μg) into the cerebral ventricles under these conditions had no effect on their activity. If the brain temperature was 38.0-38.5°C these neurons increased their discharge frequency to 19.70 ± 0.88 Hz. Injection of PCh under those conditions caused the discharge frequency of all 6 neurons to fall (latent period 89.20 ± 20.34 sec; duration 410.00 ± 65.73 sec). One typical response of such a neuron is illustrated in Fig. 2. It must also be pointed out that two of the thermosensitive neurons studied in this experiment inhibited their discharge under the influence of NA, injected into the cerebral ventricles (20 μg). The discharge frequency fell regardless of the brain temperature when NA was injected.

Exogenous PCh (especially if injected into the cerebral ventricles) can thus raise the body temperature of rats. The effect of PCh on the body temperature of rabbits depends on the animals' initial body temperature. A change in the discharge frequency of some thermoinsensitive posterior hypothalamic neurons of rabbits under the influence of PCh, injected into the cerebral ventricles, depends on the initial discharge frequency of these neurons. PCh also inhibits the increase in discharge frequency of thermosensitive neurons of this part of the hypothalamus, caused by a rise of brain temperature during heating of the animals' body.

It can be tentatively suggested that one probable mechanism of the effect of PCh on body temperature and posterior hypothalamic unit activity of animals is a change in neurotransmitter metabolism in the brain under the influence of this phospholipid, described in the literature [5, 6, 9]. Similar changes in neurotransmitter metabolism in the thermoregulatory centers of the hypothalamus may lead to a change in functional activity of the central mechanisms of thermoregulation. We also know [4, 8] that PCh, like other phospholipids, becomes incorporated into cell membranes, where it can modulate their specific state and thus exert their influence on the function of those neurons that participate in thermoregulation.

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