EFFECT OF SEROTONIN ON TEMPERATURE REGULATION IN HIBERNATING SUSLIKS IN A STATE OF NORMOTHERMIA AND ON AWAKENING FROM DEEP HYPOTHERMIA

V. D. Sitnikov, N. N. Kudryavtseva,
M. A. Yakimenko, and N. K. Popova

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Hibernating animals, being heterothermic, spend a large part of the annual cycle in deep hypothermia, but in the winter period their body temperature is maintained at the normothermic level by mechanisms similar to those in homoiothermic animals [10]. It has been shown that serotonin plays an essential role in the mechanisms of hibernation [2, 7]. Serotonin or its precursor in biological synthesis, 5-hydroxytryptophan, if injected into animals during hibernation delays their awakening to a marked degree. Their body temperature, depending on the dose of the substances injected, is stabilized at a certain intermediate level, which can be maintained for several hours [7]. Meanwhile temperature-regulating contractile activity of the muscles is inhibited [3, 9]. Serotonin also lowers body temperature in active susliks in summer, as it also does in rats [13], which are true homoiothermic animals. However, it is not clear by what physiological mechanisms serotonin influences thermogenesis or whether they are the same in active animals emerging from deep hypothermia.

The aim of this investigation was to study the effect of serotonin on body temperature, total oxygen consumption, and contractile activity of the muscles in hibernating susliks in a state of normothermia and during awakening from hibernation.

EXPERIMENTAL METHOD

Experiments were carried out on 31 male red-cheeked susliks (*Citellus erythrogenys major*) weighing 210-280 g, caught in Novosibirsk Region. To study the effect of serotonin on normothermic animals, the experiments of series I were conducted in summer. Another batch of animals was transferred in September to a special room in which the temperature was 2-3°C, where the susliks fell into hibernation. Next spring the experiments of series II were carried out on susliks awakening from hibernation. Animals still in a state of hibernation were transferred to a room in which the temperature was 22-24°C, which induced them to awaken. Serotonin creatinine-sulfate (from Reanal, Hungary) in a dose of 10 mg/kg was injected intraperitoneally into both series of experimental animals, and the control animals received physiological saline. After preliminary fixation of transducers, the susliks were then placed in a gas exchange chamber. Their body temperature was measured by a thermocouple transducer introduced into their rectum to a depth of 6 cm. Contractile activity of the muscles was measured in the cervical interscapular region by the method described previously [1]. The oxygen consumption was measured by an open method, using a galvanic oxygen analyzer [4]. Signals from all the thermocouples and the oxygen analyzer were recorded on an EPP-09 multichannel automatic writer. The parameters recorded were averaged for every 5 min of the experiment. The data were analyzed by standard biometric methods [5].

EXPERIMENTAL RESULTS

Moving the susliks in a state of hibernation from an environment with a temperature of 2-3°C into a room at normal temperature led to rewarming and awakening of the animals. Their body temperature reached 37°C on average after 2 h. This process was accompanied by a considerable increase in the rate of oxygen consumption and an increase in electrical activity of the muscles (Fig 1). The maximal rate of oxygen consumption, noted after 75 min of reheating,

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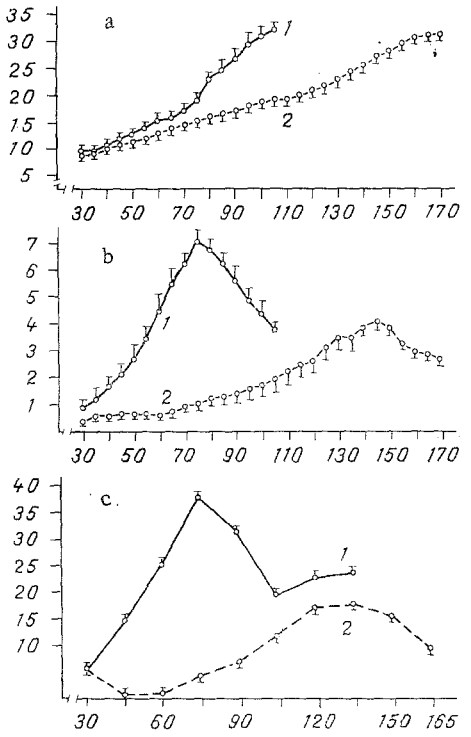

Fig. 1. Effect of serotonin on body temperature, oxygen consumption, and muscle contractility in suslik emerging from hibernation. 1) Control (injection of physiological saline), 2) injection of serotonin. Abscissa, time (in min); ordinate: a) temperature (in °C), b) oxygen consumption (in ml/100 g/min), c) contractile activity of muscles (in μV).

corresponded to the greatest value of muscle electrical activity. The coefficient of correlation between oxygen consumption and muscle electrical activity was 0.97 ($P < 0.05$).

Injection of serotonin into the animals significantly retarded their reheating: The mean rate of rise of body temperature in the control animals was 16 ± 0.6°C/h, whereas in animals receiving serotonin it was 6.4 ± 0.8°C/h. Delay of reheating was accompanied by a reduced rate of oxygen consumption and reduced muscle electrical activity. The maximal rate of oxygen consumption during reheating was reduced by 1.7 times under the influence of serotonin. However, the coefficient of correlation between oxygen consumption and muscle electrical activity remained very high, at 0.95 ($P < 0.05$).

Injection of serotonin into susliks in a state of normothermia lowered their body temperature by 2-2.5°C (Fig. 2). Body temperature continued to fall for 45-50 min. During this same period the rate of oxygen consumption decreased. The greatest fall in oxygen consumption was observed 15-20 min after injection of serotonin. However, the electrical activity of the muscles showed no significant change under these circumstances.

Starting with the 45th-50th minute after injection of serotonin the animals' body temperature stabilized at below the initial level, and later it showed a tendency to rise. During this period the rate of oxygen consumption increased to the same level as in the control. Meanwhile an increase in muscle electrical activity was observed. After injection of serotonin correlation between the rate of oxygen consumption and muscle electrical activity ceased to be significant, whereas in the control susliks correlation was fairly strong ($r = 0.79$, $P < 0.05$). The increase in muscle electrical activity in response to lowering of body temperature, beginning after 50 min, was evidently due to termination of the action of serotonin, for by this time the oxygen consumption had returned to its original level. It has been shown that 90% of the injected dose of serotonin is metabolized within 35-40 min [11].

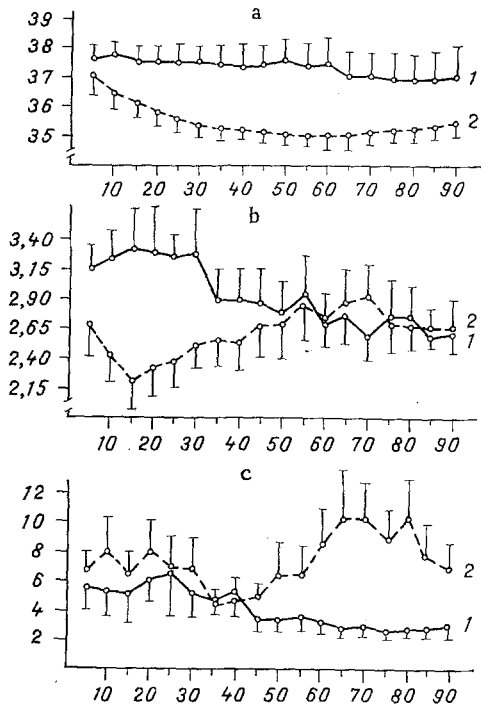

Fig. 2. Effect of serotonin on body temperature (a), on oxygen consumption (b), and on contractile activity of muscles (c) in normothermic susliks. Legend as to Fig. 1.

Thus both in a state of normothermia and on awakening from deep hypothermia serotonin has a similar action on susliks, for it lowers oxygen consumption and body temperature, or blocks any further rise of these parameters on awakening. However, it must be emphasized that depression of the total oxygen consumption in susliks emerging from a state of deep hypothermia is more marked than in animals in a state of normothermia. Additionally, during the rewarming process, a marked inhibitory effect on contractile activity of the muscles was observed previously [3, 8].

The results are evidence that the main, if not the only, role in the mechanisms of rewarming of susliks emerging from hypothermia is played by contractile thermogenesis of the skeletal musculature. A decisive argument in support of this statement is given by the strong correlation between the intensity of contractile activity of the muscles and the total rate of oxygen consumption during awakening from hibernation. This conclusion is in agreement with previous data [9] and is confirmed by experiments in which serotonin, which blocks rewarming by reducing the rate of oxygen consumption and the contractile activity of the skeletal musculature, into awakening suslks. However, correlation between these parameters still remained very high as before ($r = 0.95$).

Fairly strong correlation between oxygen consumption and contractile activity of the muscles also was found in normothermic susliks ($r = 0.79$). However, after injection of serotonin this correlation was disturbed and the coefficient of correlation came close to zero, for serotonin, while lowering body temperature and oxygen consumption, had no effect on muscle contractility in the first 45-50 min. The contractile activity of the muscles then increased, whereas body temperature and oxygen consumption stabilized and increased a little.

In susliks in a state of normothermia in an ambient temperature of 22-24°C contractile activity of the skeletal muscles, incidentally, is postural-tonic and locomotor in character, and the thermoregulatory function of the muscles is to all intents and purposes absent. The experiments showed that under these conditions serotonin has no effect whatever on the level of muscle electrical activity. The fall in the total oxygen consumption under the influence of serotonin must therefore be attributed, not to a decrease in contractile activity of the muscles, but to depression of nonmuscular sources of thermogenesis.

It is a noteworthy fact that the lowered body temperature of susliks after injection of serotonin does not activate contractile thermogenesis. This lowering of the body temperature in normothermic intact animals must inevitably lead to marked activation of all types of thermogenesis. It can be postulated that activity of serotoninergic structures determines the setting point of thermoregulation in hibernating animals, whereas injection of serotonin or an increase in its brain concentration, which is observed in animals falling into hibernation [2, 12], shifts the setting point toward the region of lower body temperatures, thus enabling the hibernating animal to lower its body temperature without any compensatory activation of the mechanisms of thermogenesis.

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