CHANGES IN BODY TEMPERATURE AND OXYGEN CONSUMPTION IN RABBITS FOLLOWING THE ADMINISTRATION OF SODIUM AMYTAL

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Many investigations have demonstrated that the administration of barbiturates to animals causes a drop in body temperature [2-5,8,11] and considerable decrease in the basal metabolic rate [5-10]. However, to what extent the fall of body temperature effected by these narcotics is due to primary change in the basal metabolism or to primary disturbance in the thermoregulator mechanisms as a whole is not yet clear: in the latter case, the temperature drop could cause a secondary decrease in the metabolic level.

To solve these questions, we performed experiments comparing the changes which took place in the body temperature and oxygen consumption of rabbits, making our determinations at the shortest possible time intervals after the injection of sodium amytal.

METHOD

The body temperature of the animals was taken in the rectum, and the oxygen intake over ten minute periods was determined in a Renier and Reise type closed system as modified by P. N. Veselkin [1]. Sodium amytal was injected subcutaneously in doses of 40-200 mg/kg of a 5% aqueous solution.

RESULTS

Only slight fluctuations (up to 0.5 deg in 21 cases) of the body temperature, taken every hour for five to seven hours, were observed in 15 rabbits (28 experiments), while a space of 0.8 deg between the highest and lowest body temperature was only observed in seven experiments during the observation period.

After the subcutaneous injection of 40 mg/kg sodium amytal (12 experiments), the rabbits became sluggish and lay on their sides for 2-6 hr, but reacted vigorously when touched and, if pushed, crawled away, dragging their hind legs. In eight experiments, the body temperature dropped 0.4-5.4 deg after two to three hours. In two cases, there was practically no drop in temperature, while in the other two experiments, the body temperature rose 0.5 deg.

In nine rabbits, the oxygen consumption was determined hourly immediately after the temperature was taken. The experiments showed that the 40 mg/kg dose of sodium amytal reduced oxygen consumption 19-38% from the original level, the greatest decrease being observed after 1-2 (sometimes 3-4) hr. Oxygen consumption returned to the original level after 2-6 hr. In one experiment, no reduction of oxygen consumption occurred. On the whole the body temperature decreased more slowly than did the oxygen consumption, its maximum decrease often coinciding with the start of a relative increase in the metabolic level. In several cases, however, full restoration of the metabolic level was not observed until after equalization of the temperature curve.

In the individual experiments, we could observe no direct relationship between the changes in body temperature and metabolic level. Sometimes the body temperature even increased after the sodium amytal injection, although the oxygen consumption decreased.

Although the change in body temperature was comparatively uniform as to time and degree, the dynamics of the metabolic decrease could vary sharply (Fig. 1).

On the whole, the experiments in which 50, 100 and 200 mg/kg doses of the narcotic were administered

produced the same results.

The subcutaneous injection of 100 mg/kg sodium amytal (five experiments) caused deep sleep lasting about 5-6 hr (rabbits reacted weakly or not at all to a needle prick, although the corneal reflexes were retained) after an initial, brief period of excitation. The body temperature fell 3.6-7.8 deg after 4-6 hr, while oxygen consumption decreased 43-58% after only 1-4 hr. In three experiments, the original level of oxygen consumption was restored after 5-6 hr, but restoration of the original body temperature took 7-9 hr.

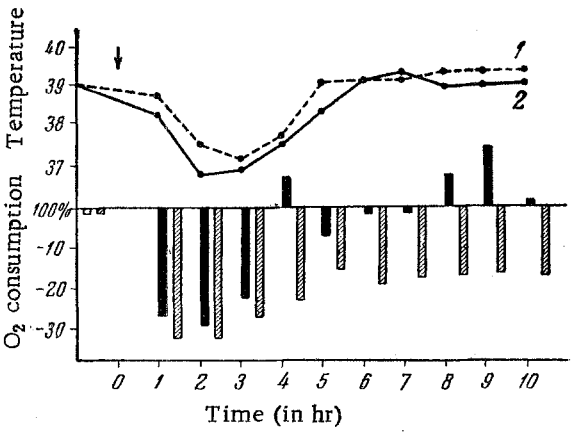

Fig. 1. Changes in body temperature and oxygen consumption in two rabbits after subcutaneous injection of sodium amytal in a dose of 40 mg/kg. Solid line and black columns give data for rabbit No. 1; dotted line and striped columns, for rabbit No. 2; arrow indicates sodium amytal injection.

No direct correlation between the changes in the general metabolic level and those in the body temperature was observed in these experiments either. Fig. 2 presents the results of two experiments by way of example.

Fig. 2 shows that the almost identical changes in oxygen consumption which occurred in the two rabbits following the administration of 100 mg/kg sodium amytal were attended by completely different changes in the temperature curves.

Six rabbits were given the narcotic in a dose of 200 mg/kg; three of these died within the first two hours after the injection, two rabbits died after two hours and one died after five hours. In these rabbits, the oxygen consumption (determined continuously except for the short intervals necessary for measuring the body temperature) fell considerably after about an hour and remained reduced until the animal's death. The temperature drop developed later in these experiments also. When the animals died, the level of oxygen consumption was still relatively high (43-50% of the original 10-15 min before death), and the body temperature was 33-36°.

After the administration of a uniform dose of sodium amytal, therefore, both the decrease in body temperature and the reduction of oxygen consumption varied greatly in different animals, evidently depending on the individual sensitivity of the animals to the barbiturate. When the dose of the narcotic was increased, however, both the hypothermia and the decrease in oxygen consumption were generally intensified – to a marked degree, according to the average data (Fig. 3).

The experiments also indicated that, in most of the experiments, the oxygen intake decreased before the body temperature, and that this precedence was retained during the restorative period. This gives reason to conclude that the fall of body temperature effected by sodium amytal to a certain extent results from a primary decrease in the metabolism. It is clear, however, that the degree to which thermogenesis diminished in most of our experiments could not itself cause such a sharp drop of body temperature if the heat losses were confined proportionately to this. The fact that no direct correlation was observed between the degree of decrease in body temperature and that in metabolism in any experiment also indicates that disturbance of the mechanism of thermoregulation must play an important part in the mechanism of the hypothermia development as well as the decrease in thermogenesis. But there are not sufficient grounds to consider the developing hypothermia the cause of the reduced metabolic rate either.

The data obtained brought up the question of just what, exactly, is the nature of barbiturates' effect on the thermoregulator centers. It was interesting in this connection to determine whether the ability to respond to the injection of pyrogenic agents by a rise of body temperature is retained by rabbits under the influence of barbiturates. In previous works [2,3], we demonstrated that the administration of a bacterial pyrogen to dogs during amytal hypothermia caused as sharp (and sometimes an even sharper) rise of body temperature as in the control experiments in which the dogs had not first received the narcotic. This reaction was particularly pronounced in dogs deprived of sight, smell and hearing; the reaction of such animals to pyrogens was also more acute under normal conditions. On the basis of these data, we concluded that the sensitivity of the thermoregulator center to a pyrogenic stimulus is higher in dogs under conditions of amytal sleep.

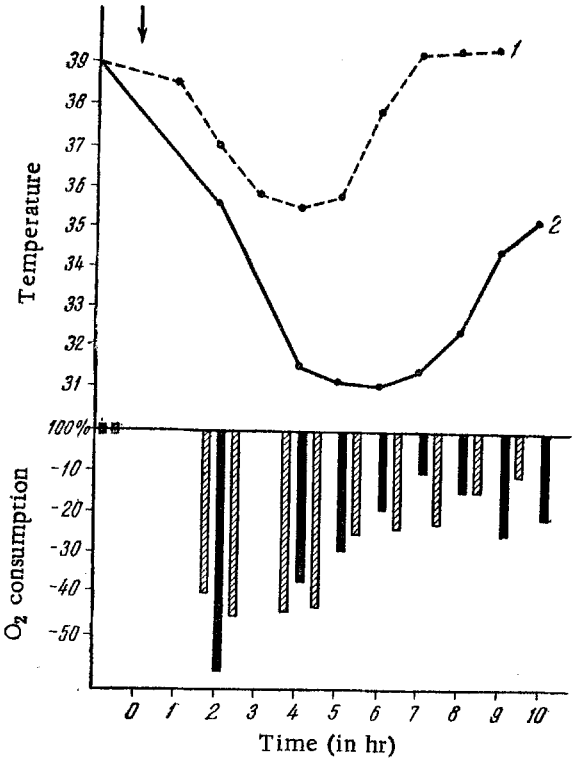

Fig. 2. Changes in body temperature and oxygen consumption in two rabbits after subcutaneous injection of 100 mg/kg sodium amytal. Symbols the same as in Fig. 1.

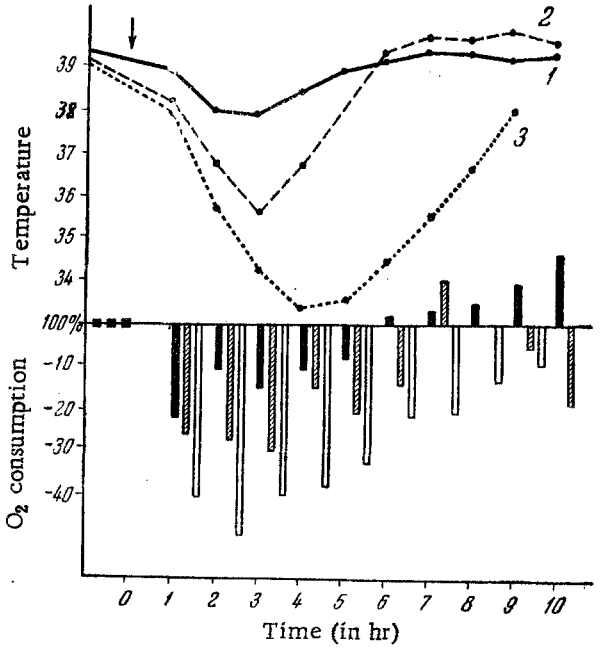

Fig. 3. Changes in body temperature and oxygen consumption after subcutaneous injection of sodium amytal in different doses (average data). Temperature curves: 1) 40 mg/kg; 2) 50-55 mg/kg; 3) 100 mg/kg; oxygen comsumption: black columns - 40 mg/kg; striped columns - 50-55 mg/kg; white columns - 100 mg/kg; ↓- sodium amytal injection.

To determine whether this conclusion held true for other types of animals also, we conducted 12 experiments in which a culture of B. mesentericus was injected (subcutaneously in a dose of 2 ml/kg) into rabbits which had received 40 mg/kg sodium amytal 2-3 min before the injection of the pyrogenic agent. After a period of variably pronounced, initial hypothermia, the body temperature increased considerably (an average of 1.1 deg) in all but one of these experiments, while in only 3 out of 12 control animals did the temperature rise much higher than the original level and then, much later in the experiment (see table).

Greatest Fall and Subsequent Rise of Body Temperature in Relation to Original Level in Rabbits after the Subcutaneous Injection of Sodium Amytal (40 mg/kg) and a Culture of B. mesentericus (2 ml/kg)

Change in body temperature after sodium amytal injection (control)			Change in body temperature after injection of sodium amytal and B. mesentericus culture		
Expt. No.	after 2-3 hr	after 5-10 hr	Expt. No	after 1-3 hr	after 5-9 hr
1	—	+0.5°[1]	13	—	+0.7° (5)[1]
2	—0.8° (3)	—	14	—	+1.1° (5)[1]
3	—5.4° (3)	—	15	—2.9° (2)	+0.9° (8)
4	—3.2° (3)	+0.2° (8)	16	—4.7° (3)	+0.1° (8)
5	—2.2° (2)	+0.4° (7)	17	—1.1° (3)	+1.5° (6)
6	—1.9° (3)	+0.3° (9)	18	—1.4° (2—3)	+1.3° (6)
7	—0.4° (2—3)	+0.3° (7)	19	—0.6° (2)	+0.7° (6)
8	—0.4° (2—3)	+0.2° (8)	20	—0.6° (2)	+1.4° (6)
9	—0.9° (3)	+0.1° (7)	21	—0.3° (1)	+2.0° (6)
10	—0.9° (2—3)	+0.6° (10)	22	—0.9° (2)	+1.5° (7)
11	—0.9° (2)	—	23	—0.5° (2)	+1.1° (5)
12	—	+0.5° (5)	24	—0.3° (1)	+1.2° (9)
Average	—1.4°	+0.3°		—1.1°	+1.1°

Note: Figures in parentheses show hour of maximum fall or rise of body temperature after the injections.

[1] Experiments discontinued after five hours.

Therefore, the sensitivity of thermoregulator centers to inadequate, "extraordinary" stimuli under conditions of amytal narcosis is also true in the case of rabbits. At the same time, the thermoregulator apparatus reacts much less strongly to the adequate stimuli developing in connection with the reduced thermogenesis and hypothermia, at least during the early stages of the barbiturate's effects. The fact that the temperature was restored in several experiments before the original metabolic level indicates that, at the later stages of the narcotic's effect, the thermoregulator apparatus begins to react to adequate stimuli as well, by equalizing the body temperature in spite of still reduced thermogenesis.

SUMMARY

In comparing the changes of body temperature and of oxygen intake in rabbits after sodium amytal injection no direct relationship was noted between the changes of the BMR level and body temperature (Fig. 1).

Sodium amytal given in a dose of 40 mg/kg reduces the oxygen intake by 19-38% with respect to the inital level. The highest reduction occurred in 1-2 (at times in 3-4) hours. With increase of the dose of this narcotic (100, 200 mg/kg) there are seen hypothermia and a drop of oxygen intake (Fig. 3).

Body temperature dropped in 4-6 hours by 3.6-7.8°C, whereas oxygen intake by 43-58% already in 1-4 hours.

Oxygen intake decreases in the majority of experiments earlier than body temperature. This leads to a conclusion that reduction of body temperature under the action of sodium amytal is to some extent the result of primary BMR reduction.

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All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. *Some or all of this periodical literature may well be available in English translation.* A complete list of the cover-to-cover English translations appears at the back of this issue.
