Hypothalamic Temperature Records of a Monkey.* (27948)

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In the literature on temperature regulation there is a noticeable lack of data on long term continuous records of hypothalamic temperature. Forster and Ferguson(1) have taken such records on cats over periods as long as 5 hours. Now, with the development of more efficient methods for restraining animals, continuous, untended experiments are possible for even longer periods. The present study used such a method to study the hypothalamic temperature of a monkey on a 24-hour basis.

Method. The subject was a male rhesus monkey weighing approximately 7 kg at the beginning of the work and restrained in a monkey chair with yokes about his waist and neck. His legs were free but the arms were blocked so that he could not touch his head or feed himself. Hypothalamic temperature was sensed by a thermister planted in a 22-gauge hypodermic needle chronically implanted in the anterior hypothalamus at the following Horsley-Clark coordinates: AP –17 mm anterior to the earbars, lateral 1½ mm to the right of the sagittal sinus, and 7.5 mm above the interaural plane. A combination Yellow Springs telethermometer and Grass Model 5 Polygraph provided continuous temperature recordings with an accuracy of ± 0.1°C. The thermisters were calibrated in a constant temperature water bath; heat loss along the needle appeared to be negligible. Unfortunately, with the use of the monkey chair a chronic recording of rectal temperature was not practical. Time was recorded by the 24-hour clock system.

There were 2 observation periods on this animal. This was necessitated when the leads to the first thermister, implanted Jan. 16, 1962, broke after several weeks of recording. At that point the animal was removed from the chair and placed in his regular cage in the animal room. Two months later (April 13, 1962) another thermister was implanted at the same coordinates and the second series of observations were conducted.

Period 1. (January): Data were collected with the animal in our main laboratory with no attempt to isolate him from the noise or the personnel of the laboratory. Ambient temperature was 24°C. All feeding was accomplished by the experimenter's presenting Purina Monkey Chow pellets by hand. Feeding periods of approximately 3 hours' duration began at 13 hours daily, during which time the animal was given 8 to 10 pellets at a time until he rejected them. Water was available *ad libitum* throughout the day. During this time data were collected and plotted by the hour for 24 hours. In addition, minute records were kept of several feeding sessions.

Period 2. (April): Following several days of recording with the second needle the animal was taken from the general laboratory setting and placed in a constant temperature room maintained at 24°C (isolated). A constant noise background was supplied by a circulating fan. Lights were controlled automatically and came on at 6 hours and off at 18 hours. Under these conditions the room was entered by the experimenter at 13 hours to initiate feeding procedures similar to the former with the exception that they were arbitrarily terminated at 1430 hours. This period was the only time during which the animal was exposed to the experimenter. Daily food intake under isolated and non-isolated conditions was approximately 130 g.

Results and discussion. The upper portion of Fig. 1 shows the variation in hypothalamic temperature of the restrained monkey over a continuous period of approximately 3 days. In this, the non-isolation instance (period 1), the diurnal variations closely follow the activities of the laboratory. The lower portion of Fig. 1 shows similar data taken in the iso-

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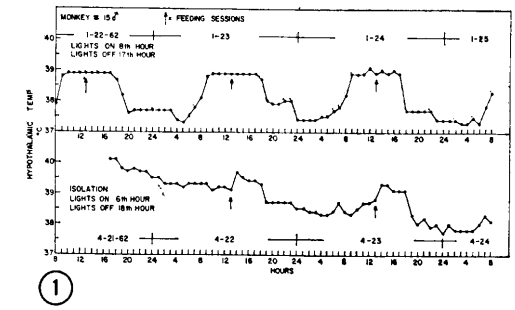

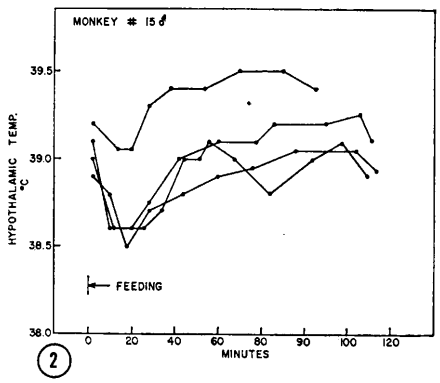

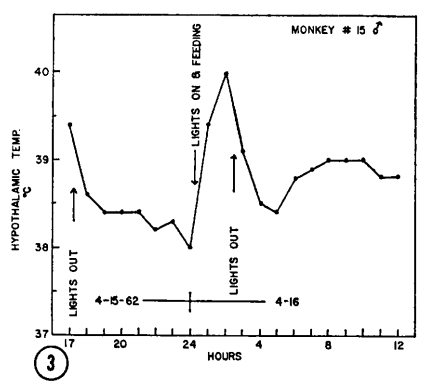

FIG. 1. Continuous records of hypothalamic temperature. Top portion of figure recorded under non-isolated conditions during period 1. Bottom portion recorded in isolation during period 2.

FIG. 2. Hypothalamic temperature during feeding sessions recorded under period 1 conditions (non-isolated).

FIG. 3. Changes in hypothalamic temperature of the monkey when fed just after midnight during period 1.

lation chamber (period 2). When first placed in the chamber there was a rise of approximately 1°C in hypothalamic temperature. However, over the period of 3 days there was a gradual decline of hypothalamic temperature with elimination of much of the amplitude of diurnal variation seen in the non-isolated condition. In this instance a rise in temperature during the feeding sessions was quite noticeable. This phenomenon was complicated by the presence of the experimenter in addition to ingestion of food.

Fig. 2 shows a breakdown of 4 representative feeding sessions recorded under non-isolated (period 1) conditions. In each case, at initiation of feeding, there was a drop in hypothalamic temperature with a return to approximately pre-feeding levels. The top line of this graph represents the first feeding session taken after implantation of the needle. The animal was still in the recovery phase after the operation (approximately 3 hours post-operative) and had a slight fever. Even so, the shape of this curve is quite similar to those of the others. This phenomenon, the drop in hypothalamic temperature at initiation of feeding, was seen also in the isolated condition. R. Abrams (personal communication) has observed a prompt rise in hypothalamic temperature following feeding sessions in the unanesthetized rat.

Fig. 3 shows temperature changes associated with a feeding session during the night hours under conditions of non-isolation (period 1). After lights out at 17 hours there was the usual drop in hypothalamic temperature until 24 hours. At approximately ½ hour after midnight, the room was entered, lights turned on, and a feeding session begun. The feeding session was terminated and the lights turned out at 0230 hours. Following entry into the room and feeding there was a rise in the animal's hypothalamic temperature to a point slightly above his normal daily levels and the usual fall when the lights were turned off.

These data indicate an intimate relationship between environmental contingencies and hypothalamic temperatures and suggest that in a monkey the diurnal variations of temperature may be the indirect result of such contingencies. This is the long held theory that the diurnal cycle of body temperature is due to the activity cycle. An extensive discussion of this and other facets of temperature regulation are presented by Hardy(2).

The initial fall of hypothalamic tempera-

ture at onset of feeding is unexplainable at present. At first it was believed to be related to the fact that the animal consumed most of his daily water intake during the feeding session, since the water was at room temperature, some 15°C below body temperature. This explanation was checked by feeding and withholding water; under such conditions the fall was still observed though somewhat attenuated. However, a similar fall with a subsequent rise in hypothalamic temperature was also observed when the animal's arms were held and he struggled. In fact, any sudden increase in the animal's activity level was usually accompanied by the initial fall and then a rise in temperature. These transients of hypothalamic temperature may be better explained in the future by observations of blood flow to the area. As McCook *et al.*(3) have suggested, the temperature of the hypothalamus should be determined not only by its rate of heat production, but also by the blood flow through it. It appears that caution is needed when making inferences about thermoregulation solely from hypothalamic temperature.

Summary. Continuous recordings of hypothalamic temperature were made on a rhesus monkey placed in a restraining chair. Under non-isolated conditions distinct diurnal variations in temperature were observed. The extent of these cycles appeared to be attenuated when the animal was isolated. In addition, feeding sessions under isolated conditions were accompanied by larger increases in temperature than during non-isolated conditions.

1. Forster, R. E., II, Ferguson, T. B., *Am. J. Physiol.*, 1952, v169, 255.

2. Hardy, J. D., *Physiol. Rev.*, 1961, v41, 521.

3. McCook, R. D., Peiss, C. N., Randall, W. C., PROC. SOC. EXP. BIOL. AND MED., 1962, v109, 518.

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Inhibitory Effects of Hadacidin on KB Cell Cultures.* (27949)

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A new growth-inhibitory substance active against human derived tumors was described by Gitterman *et al.* in *Penicillium frequentans* Westling broths(1). The structure and properties of the active principle, N-formyl hydroxyaminoacetic acid, which was designated hadacidin, were determined by Kaczka *et al.* (2). Shigeura and Gordon(3) demonstrated that hadacidin suppressed biosynthesis of adenylic acid *de novo* by competition with aspartate in the adenylosuccinate synthetase reaction.

The present study concerns inhibitory effects of hadacidin on KB cell cultures and suggests that sites of action of the inhibitor may be found in other areas as well as in purine metabolism.

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Materials and methods. In the procedure for appraising the effects of test compounds, 1 ml of whole medium containing 10,000 KB cells was pipetted into 16 × 125 mm tubes placed in a slanted position in racks. The cells were established (plated) by incubation for 24 hours at 37°C in a humidified atmosphere of 8% carbon dioxide-92% air. The medium was removed and the tubes rinsed twice with Earle's solution. The cells in duplicate tubes then were overlaid with 1 ml of growth medium containing graded amounts of test compounds. Incubation was continued for 4-5 days until maximal growth was attained in untreated tubes.

Cell protein was measured by the method of Oyama and Eagle(4). The media were collected and glucose content was determined by the procedure of Park and Johnson(5). Lactic acid was determined according to the