Effects of food deprivation on daily changes in body temperature and behavioral thermoregulation in rats

YODA, Tamae, Larry I. Crawshaw, Kyoko Yosida, Liu Su, Takayoshi Hosono, Osamu Shido, Sotaro Sakurada, Yutaka Fukuda, and Kazuyuki Kanosue. Effects of food deprivation on daily changes in body temperature and behavioral thermoregulation in rats. Am. J. Physiol. Regulatory Integrative Comp. Physiol. 278: R134–R139, 2000.—Homeothermic animals regulate body temperature ($T_b$) by using both autonomic and behavioral mechanisms. In the latter process, animals seek out cooler or warmer places when they are exposed to excessively hot or cold environments. Thermoregulation is affected by the state of energy reserves in the body. In the present study, we examine the effects of 4-day food deprivation on circadian changes in $T_b$ and on cold-escape and heat-escape behaviors in rats. Continuous measurement of $T_b$ during food deprivation indicated that the peak $T_b$ amplitude was not different from baseline values, but the trough amplitude continuously decreased after the onset of food deprivation. Cold-escape behavior was facilitated by food deprivation, whereas heat-escape behavior was unchanged. After the termination of food deprivation, the lowered $T_b$ returned to normal on the first day. However, cold-escape behavior was still facilitated on the third day after food reintroduction. Autonomic and behavioral thermoregulatory effects are modulated in the face of food shortage so as to maintain optimal performance during the active period, whereas increasing energy conservation occurs during the quiescent phase.

METHODS

Animal preparation. A total of 24 adult male pathogen-free crj-Wistar rats (300–400 g, Charles River Japan, Osaka, Jap an) were used in this study. They were reared with free access to food and water at 22°C and a 12:12-h lighting schedule (on 0700–1900). The experiment was approved by the Animal Care Committee of Osaka University Medical School. Under ketamine-hydrochloride anesthesia (250 mg/kg ip) each rat was implanted with a biotelemetry device (Physiotel, DataScience, St. Paul, MN) in the peritoneal cavity to measure deep body temperature and activity. Experiments started at least 1 wk after surgery.

Experimental apparatus and procedure. In the first series of experiments, circadian changes in body temperature were measured. Eight rats were used in this experiment. They were maintained in separate cages (45× 25× 20 cm) at a room temperature of 22°C and a 12:12-h on-off lighting schedule (on 0700–1900). A telemetry receiver board (CTR86, DataScience) was placed under each cage. The outputs of the receivers were fed into a computer (LabPro, DataScience) and sampled every 1 min. Body weight of the rats was measured every day at 1600. After a 10-day baseline period of free access to food and water, rats were deprived of food for 4 days (96 h). Food deprivation started at 1600. Water was available ad libitum throughout the entire experiment. Measurements of body temperature and activity were continued for 10 days after the end of food deprivation.
In the second series of experiments, the effects of food deprivation on behavioral thermoregulation were analyzed. Sixteen rats were used in these experiments. The system for testing behavioral thermoregulation (Chen et al., Ref. 4) consisted of a chamber (60 × 50 × 50 cm) with an inlet and an outlet that received air from two supply units (CAU-210, TABAI ESPEC, Osaka, Japan). One of them supplied cold air (0–30°C, 3 m³/min) and, the other, hot air (20–45°C, 3 m³/min). The air circulation from two supply units in the chamber was switched by computer-controlled valves (Macintosh 7200/80 with an interface Mac ADIOS II, GW Instruments). The rat was placed in a plastic box (50 × 10 × 30 cm) within the chamber. The top of the box was covered with metallic mesh, and the side of the box was perforated so that air flow over the animal was facilitated. The location of the rat within the box was monitored by light-emitting diodes 2 cm above the floor of the box, placed at 10-cm intervals along the longer side of the box, and directed toward photoelectric cells on the opposite side. The position of the rat was thus located within one of five 10 × 10-cm square areas. Air with the “load temperature” blew into the chamber except when the animal entered a predetermined reward zone, at which time the air was replaced with the “reward temperature” for 30 s. To receive a subsequent reinforcement the animal had to leave the reward zone and reenter it. Because of the length of the chamber, two telemetry receiver boards (CTR86, DataScience) were required. They were placed under the plastic box, and their outputs were fed into the computer together with the output of a thermocouple that measured air temperature at the outlet of the chamber. During experiments, air temperature, body temperature, and the position of the animal were recorded at 1-s intervals.

The sixteen rats were divided into three groups, six for the heat-escape experiment, six for the cold-escape experiment, and four for the no-reinforcement experiment. All testing was randomized. The temperature of the reward air was 3°C. For each rat, a 3-h experiment was run three times at 2-day intervals in the normally fed condition. Then, the rat was deprived of food for 4 days (96 h). The food deprivation started at 1600 on the day after the third experiment. The behavioral thermoregulation measurements were made twice during food deprivation (on the 1st and 3rd days) and three more times after refeeding (on the 1st, 3rd, and 7th days).

In the cold-escape experiment, the experimental paradigm was the same as the heat-escape experiment. In this case, load temperature was first to 72 or 13°C, and the reward temperature was 40°C. Rats learned the cold-escape paradigm quickly only if they had already experienced the heat-escape paradigm (4). For this reason, each rat was initially run twice in the heat-escape experiment with a 40°C load temperature. Then, the rat was run in the cold-escape experiment eight times in total: three times before food deprivation, two times during food deprivation, and three times after refeeding.

In addition, a no-reinforcement experiment was performed to evaluate whether the food-deprivation-induced increase in thermoregulatory demands. In this experiment, the air temperatures of the two supply units were set to the same temperature. Therefore, although the valves turned on when a rat entered the reward zone and turned off 30 s later, the temperature in the chamber did not change. Each rat was tested with this protocol three times at an air temperature of 25°C. Then the rat was tested on the first and third days of food deprivation with an air temperature of 3°C.

Data analysis. The data were analyzed using a two-way ANOVA for repeated measurements. The least-significant difference for the comparison of means between the groups was calculated. Values are expressed as means ± SE. P < 0.05 was considered significant.

RESULTS

Daily rhythm of body temperature. Figure 1 shows average daily cycles of body temperature and activity in eight rats before, during, and after 4 days of food deprivation. Body temperature was high in the dark (active) phase and low in the light (inactive) phase. This
rhythm remained prominent even during food deprivation. During food deprivation, body temperature in the dark phase was not different from that in the initial fed condition. Body temperature in the light phase, however, dropped to progressively lower levels on each subsequent day of food deprivation. As a result, the amplitude of daily change in body temperature became progressively greater as food deprivation continued. The body temperature in the light phase returned to a normal level on the first day of refeeding. Activities of rats in both the active and inactive phases tended to increase during food deprivation. However, these values are not significantly different from the corresponding control values on the day before the food deprivation.

Figure 2 indicates the change in body weight of the same rats depicted in Fig. 1. The day before the food deprivation, body weight was 372.2 ± 6.0 g and it dropped to 308.9 ± 5.8 g after 4 days of food deprivation.

Behavioral thermoregulation. Cold-escape behavior in the light phase was remarkably facilitated by food deprivation. Figure 3 shows cold-escape behavior of a rat before and during food deprivation. A transient sharp increase in air temperature indicates that the rat entered the reward zone and obtained warm reward air. In the control session, 1 day before food deprivation (Fig. 3A), the rat moved around in the box soon after it was placed in the experimental box. As a result, the air temperature in the chamber changed frequently, but after 20 min the rat became quiet and rarely obtained reinforcement. The rat moved vigorously once again after the load temperature was changed from 3 to 13°C. This behavior lasted only 10 min, and the rat remained quiet through the rest of the experiment. On the other hand, on the third day of food deprivation (Fig. 3B), the rat moved in and out of the reward zone frequently and regularly so it obtained a large number of reinforcements at load temperatures of both 3 and 13°C. Average number of reinforcements, body temperature, and air temperature are presented in Fig. 4. As illustrated in Fig. 3, rats moved vigorously for a while after they were put into the chamber or after the load temperature was changed. The subsequent reinforcements likely represent exploring behavior in response to changes in environmental condition and not thermoregulatory behavior. For this reason, the data presented in Fig. 4 are taken from the last 60-min period at each load temperature, that is, from the 30th to 90th min and from the 120th to 180th min in each session. At both load temperatures (3 and 13°C), the number of rewards on the first day of food deprivation was not significantly different from control values (Fig. 4A). On the third day of food deprivation, however, the number of reinforcements was significantly greater than control values at load temperatures of both 3 and 13°C. In the example of Fig. 3, body temperature on the control day was maintained at ~37°C, whereas it dropped to 35°C on the third day of food deprivation. Although the average body temperature during food deprivation also tended to be
lower on the third day, it was not significant (Fig. 4C). The effect of food deprivation on the cold escape behavior decayed rather gradually after refeeding began (Fig. 4A and B). The number of rewards and ambient temperature were still significantly higher than controls on the third day of recovery at the load temperature of 3°C.

In contrast to the cold-escape behavior, food deprivation did not influence the heat-escape behavior. In the control fed condition, the rats obtained reinforcements more frequently than they did in the cold-escape experiment. The behavior of the rats was characterized by periodically moving in and out of the reward zone (Fig. 5A). This behavior was not modified by 3 days of food deprivation (Fig. 5B). Neither average number of reinforcements, body temperature, nor air temperature differed between control and food deprived conditions (Fig. 6).

In the control no-reinforcement experiment at 25°C, the rats moved around in the experimental box only after initial placement, as observed in the cold-escape and heat-escape experiments. The movements of the rats were little facilitated even during food deprivation and placement in the cold environment of 3°C. The average number of entrances into the reward zone in the last 60-min period was 8.3 ± 3.0 on the control day and 15 ± 2.9 on the third day of food deprivation. These values are not significantly different from each other. The value during food deprivation at air temperature of 3°C is significantly smaller than that of the cold-escape experiment on the third day of food deprivation.

DISCUSSION

The main finding of this study is that body temperature of food-deprived rats becomes progressively lower on the consecutive days in the inactive (light) phase of the daily cycle, whereas it remains at normal levels in...
the active (dark) phase. A similar effect was observed in birds. A decrease in body temperature in food-deprived pigeons (*Columba livia*), a diurnal species, is especially prominent in the dark phase (1, 6, 13, 15). Allowing the body temperature to fall in the inactive phase while maintaining a relatively normal body temperature in the active phase, seems to be a common strategy for dealing with acute food shortage in both birds and mammals.

Under the experimental conditions of this study, the overall activity of animals in the inactive phase during food deprivation was not significantly different from that of energy-replete animals. The lowered body temperature, therefore, is not likely to be the result of a reduction in activity. In food-deprived birds, a lower body temperature in the inactive phase was accompanied by lower metabolic heat production (6, 14). Lowered metabolic heat production at a neutral ambient temperature was also reported for food-deprived rats (9, 18). Low metabolic rates have also been reported in fasting newborn rats (2), as well as in pigs or humans with severe undernutrition (3, 10). Therefore, although not measured in the present study, it is likely that decreased metabolic heat production was a major contributor to the decreased body temperature observed in food-deprived rats during the light phase.

During the inactive phase, cold-escape behavior is sporadic in fed rats, but becomes more regular and continuous as food deprivation proceeds. This finding was also reported in birds (12) and mammals (7, 19). In the present study we used a novel experimental system to analyze thermoregulatory behavior (4). With this system, an increase in the number of reinforcements can safely be seen as elicited from thermoregulatory demands rather than from nonspecific increases in activity. In the current study, two factors support this interpretation. First, in the no-reinforcement experiment during food deprivation and at 3°C, the rats did not move as vigorously as in the cold-escape experiment. Second, in the cold-escape experiment, food-deprived rats moved in and out of the reward zone very regularly (Fig. 3B) in a pattern that was clearly different from the general exploratory movements that occurred in a random fashion when the rats were first placed in the plastic box (Fig. 3A).

Our interpretation of the function of the thermoregulatory adjustments seen during food deprivation is similar to that cited by previous authors (12, 13). Maintenance of a low metabolic rate is paramount. This can be accomplished both by maintaining a lowered body temperature when it does not compromise critical functions and by assiduously avoiding thermal microenvironments that would require an increased metabolic rate to maintain the (now lower) regulated temperature. In the current set of experiments, this strategy was evidenced both by a lowered body temperature and by a facilitation of cold-escape behavior in the inactive period. In the active phase, the observed maintenance of a high body temperature would facilitate the seeking of food resources.

In the 24-h experiments, body temperature dropped to as low as 36°C on the third day of food deprivation (Fig. 1). However, body temperature in the behavioral experiments both for cold-escape and heat-escape protocols was ~37°C for the same degree (3 days) of food deprivation (Figs. 4 and 6). This higher body temperature might reflect the ability of the rats to control ambient temperature. Indeed, in the heat-escape experiments, the average ambient temperature was quite high, ranging from 30 to 35°C. But in the cold-escape experiments, ambient temperature for the food-deprived rats was only ~16°C at 3°C load temperature and 21°C at 13°C load temperature. In the behavioral experiments, rats have to move often to get the thermal reinforcements. This precludes the quiescence and sleep that normally occur during this (light) period. Because sleep is associated with a lower body temperature (8, 11), the higher body temperatures seen in the behavioral experiments might simply reflect the fact that the animals were not sleeping.

We initially predicted that the effect of food deprivation on heat-escape behavior would be the opposite of...
that on cold-escape behavior; that is, heat-escape behavior would be suppressed. In fact, heat-escape behavior at load temperatures of both 35 and 40°C was not influenced by 3 days of food deprivation. For well-fed rats, heat-escape behavior clearly has a higher priority than cold-escape behavior, likely because rats are equipped with only weak autonomic defense mechanisms against heat compared with those against cold. In the present experimental condition, rats performed the heat-escape behavior at fairly high rates. It is possible, therefore, that food deprivation might have had a suppressive effect on this behavior, but it was not strong enough to influence the heat-escape behavior. This is probably not the case, however, because the number of cold-escape reinforcements obtained on the third day of food deprivation was about twice as high as the number of heat-escape reinforcements. Additionally, the number of reinforcements was consistently lower for the 35°C load temperature than for the 40°C load temperature, although the differences were not significant. Yet at the 35°C load temperature there was no effect of food deprivation. The differential effect of food deprivation on cold-escape and heat-escape behaviors does suggest that they are not just two sides of the same phenomenon; one can be affected independently of the other.

The lowered body temperature in the inactive phase of the 24-h experiments returned to normal on the first day of refeeding (Fig. 1). In contrast, the effect of food deprivation on the cold-escape behavior lasted longer after the termination of food deprivation (Fig. 4, A and B). This may indicate that different factors are responsible for the modulation of different effector activities, although the present experiment gives no data concerning what they are. Leptin could be involved, because restricted food supply produces a drop in body temperature in the inactive phase in mice and leptin administration abolishes the drop (5). Other possible mediators could involve signals from mechano- and/or chemoreceptors of the intestine, because these inputs were shown to be involved with the decreases in body temperature and resting basal metabolism that occur during food deprivation (18).

Perspectives

An especially interesting aspect of this study was how behavioral thermoregulation in the active phase was modified by food deprivation. Cold-escape operant behavior was strongly facilitated by food deprivation, whereas heat-escape behavior was unaffected. One useful question would involve an investigation of the effects of food deprivation in a thermal gradient. In this apparatus, the animal would be able to choose a particular temperature and remain there. They could also become quiescent and sleep at a particular temperature. Twenty-four-hour studies of resting metabolic rate and body temperature would also be interesting. Our current investigations are focused on how other autonomic responses such as skin vasomotion are modified by food deprivation.

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