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Effects of Short-Term Food Deprivation on Sweating and Shivering Thresholds

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Starvation is known to lower the threshold core temperature for thermogenesis and then body core temperature in animals. However, little attention has been paid to the effects of food deprivation on heat loss mechanisms, especially in humans. We therefore determined the threshold temperatures for sweating and also shivering in humans after a 24-hour starvation. The subjects rested on a chair at an ambient temperature of 26°C and relative humidity of 45%. Their rectal temperature (T_{re}) and skin temperatures at 7 body sites were continuously measured. Then, they were warmed or cooled by bathing both legs in warm (42°C) or cold water (15°C), respectively. T_{re} and skin temperatures at the onsets for thermally-induced sweating and shivering were determined, and threshold mean body temperatures (T_b) for them were calculated. The 24-hour food deprivation significantly lowered the threshold T_b for shivering, but did not affect the sweating threshold T_b. The results suggest that, in humans, the interthreshold zone is widened by food deprivation solely due to a decrease in the threshold for the activation of thermogenesis.

Key words: starvation, heat loss, heat production, thermoregulation, leptin

INTRODUCTION

In the face of reduced food availability, various physiological functions of animals alter to cope with the negative energy balance (1). One of the events occurring in starved mammals and birds is hypothermia (2-5). A lower core temperature (T_{cor}) is thought to be advantageous for conserving energy by reducing metabolic heat production simply due to the Q_{10} effect. T_{cor} of homeotherms, including humans, is regulated within a range between threshold temperatures for heat loss and heat production by the thermoregulatory center. Thus, both heat loss and heat production thresholds should be examined to evaluate the mechanism of starvation-induced hypothermia. In birds and mammals, starvation has been shown to lower threshold T_{cor} for heat production (6-8), which may allow T_{cor} to stay at low levels especially in a cool environment (9). However, little is known how heat loss mechanisms are affected by food deprivation, especially in humans. In the present study, therefore, we determined threshold T_{cor}s for sweating and shivering of humans to assess alterations in thermoregulatory function due to food deprivation.

MATERIALS AND METHODS

This study was approved by the Ethical Committee for Human Experimentation of School of Medicine, Shimane University.

Subjects

Three male (mean age, height and body mass are 20.7 y, 170.3 cm and 64.4 kg, respectively) and 3 female (mean age, height and body mass are 20.3 y, 155.3 cm and 49.8 kg, respectively) subjects volunteered for the present experiments, giving written informed consent. Prior to participating, they were well familiarized with the test procedures and with the equipment to be affixed to their bodies.

For a week before the start of measurements, the subjects' clock times for waking up and going to bed were controlled by the subjects. During this period, all subjects were forbidden from participating in any strenuous exercise or exposure to extremely high or

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low ambient temperatures (T_a) to avoid adaptive changes in thermoeffector thresholds. In addition, the subjects were not allowed to have any food or beverage that contained large amounts of caffeine, alcohol or capsaicin for at least 3 days before the measurements. Water (without calorie) intake was not limited during the experiment.

Procedures

The subjects were instructed to arrive at the laboratory by 1300 h. They stayed quietly in an ordinary room of which T_a was 20-24°C for 30 min. Then, the subjects changed their clothes, i.e., the male subjects wore only shorts and the female subjects wore tank-top underwear and shorts, and entered a temperature-controlled room at a T_a of 26.0 ± 0.5°C and a relative humidity of 45 ± 5%. After all devices for measurements were fitted on the subjects, they rested on a chair in an upright position. After at least 30 min rest, the subjects immersed both legs in a water-bath (depth 28 cm; LTP-112, Tabai Espec, Osaka, Japan) in which the water temperature was controlled at 42.0 ± 0.1°C to induce sweating. When thermal sweating was clearly observed, the warm water immersion was terminated and the wet areas of the subjects were carefully wiped by dry towels. Then, a blood sample (about 10 ml) was taken from the vein at the left cubital region. At least 30 min after the blood sampling, the subjects immersed both legs in a water tank (depth 35 cm) in which the water temperature was controlled at 15.0 ± 0.1°C to induce shivering. Since the cold water immersion alone was not sufficient to lower T_{cor}, the subjects gradually took 350-700 ml of cooled isotonic drink until shivering occurred.

The tests were made twice for each subject in fed (control, CN) and starved (ST) conditions. In the CN, the subjects were allowed to eat meals regularly. On the day of measurements, they had breakfast (commercial balanced food, 1260-1680 kJ) between 0700 and 0800 h and lunch (4830-5250 kJ) between 1200 and 1230 h. The calorie intakes were set so that the amounts were similar to those in the normal daily lives of each subject. In the ST, the subjects skipped supper on the day before measurements, and breakfast and lunch on the day of the tests. For 3 subjects (2 males and 1 female), the CN tests were performed prior to the tests in the ST, while for the rest of subjects, the control measurements were made at least two weeks after the ST tests. For the female subjects, the menstrual cycle was adjusted in the two measurements.

Measurements

Rectal temperature (T_{re}), as an indicator of T_{cor}, in each subject was measured with a thermistor probe introduced 15 cm into the rectum. Skin temperatures were recorded at 7 body sites (forehead, trunk, forearm, hand, thigh, calf and foot) by skin thermistors held in place with surgical tape. The accuracy of the thermistors (SZL-64, Techno Seven, Yokohama) was estimated to be within ± 0.05°C. The temperature data were sampled every min with a data logger (K730, Techno Seven, Yokohama, Japan) through a scanning unit (X115, Technol Seven, Yokohama, Japan). Heart rate (HR) was estimated by the count of R-wave in one min on an ECG and the data were stored with a portable memory (VM4-064, VINE Co., Tokyo, Japan). In addition, T_a and water temperatures in water baths were monitored with thermistors throughout the test procedures.

Sweating rates (m_{sw}) at the forearm were measured by the ventilation method (10) with 1.0 cm^2 capsules (SKD-2000, Sukinos, Nagoya, Japan). The capsules were fixed to the skin of the left forearm with adhesive tape, and ventilated with air at a constant flow of 200 ml/min. The relative humidities of the inlet and outlet air were measured by capacitance hygrometers, and water contents and then m_{sw} were calculated with exclusive software (SKS-2000, Sukinos, Nagoya, Japan). In addition, m_{sw} were continuously recorded with a potentiometer (U-228, Pantos, Kyoto, Japan) to determine the onset of sweating precisely. The place where the sweating capsule was attached was marked so that m_{sw} were always measured at the same skin area in each test.

Blood was collected into 4 different types of tubes, one containing NaF for glucose assay, one EDTA-2Na for leptin assay, one EDTA-2K for blood cell count, and the other empty. After hematocrit (Ht) was measured, the tubes were centrifuged at 4°C, 1500 rpm. All the assays were performed by Japan Clinical Laboratories, Inc, Kyoto. Briefly, plasma osmolality (Osm) was determined by freezing point depression. Red blood cell (RBC) number was counted by laser flowcytometry method and plasma

levels of Na, K, Cl and glucose were measured by an ion selective electrode method. Total protein (TP) and albumin concentrations were measured by the biuret and bromocresol green methods, respectively, and triglyceride (TG) and free fatty acid (FFA) were measured by the enzyme method. Plasma concentrations of leptin were determined by radioimmunoassay. The blood sample for leptin assay was not obtained in one female subject.

Data analyses and statistics

Mean skin (T_{sk}) and mean body (T_b) temperatures were computed as follows: $T_{sk} = 0.07T_1 + 0.35T_2 + 0.14T_3 + 0.05T_4 + 0.19T_5 + 0.13T_6 + 0.07T_7$, $T_b = 0.7\ T_{re} + 0.3\ T_{sk}$, where $T_{1\text{-}7}$ are temperatures of the forehead, trunk, arm, hand, thigh, calf and foot, respectively (11).

The initial values of the parameters measured were obtained as averages for the 10 min period just prior to the start of body warming. The results are presented as means ± SEs. Statistical differences of values between two conditions were assessed by paired Student *t*-test. A significant level was considered to be $p < 0.05$.

RESULTS

Table 1 summarizes the mean initial values of T_{re}, T_{sk}, T_b and HR just before the start of leg warm-water immersion. The T_{re}. T_b and T_{sk} in the ST were slightly but obviously lower than those in the CN. The HR of the ST did not differ from that of the CN.

The onset of thermal sweating was determined by a prompt increase of m_{sw} in each measurement (Fig. 1). The time at the onset of thermal sweating after commencing the leg water immersion and the T_{re} or T_b corresponding to the sweating onset were defined as a sweating latency and threshold T_{re} or T_b for sweating, respectively. The initiation of shivering was reported by subjects and the T_{re} or T_b at the onset of shivering was defined as a threshold T_{re} or T_b for shivering. The sweating latency in the CN was 9.3 ± 0.5 sec and that in the ST was 10.5 ± 1.3 sec (no significant difference). The threshold T_b for sweating and shivering in both the CN and ST are shown in Fig. 2. The threshold T_b for sweating in the ST did not differ from that in the CN. However, the one-day

Table 1. Body temperatures and heart rates at rest

	CN	ST
T_{re}, °C	37.15 ± 0.12	37.05 ± 0.10
T_{sk}, °C	33.40 ± 0.08	33.23 ± 0.13
T_b, °C	36.03 ± 0.08	35.91 ± 0.09
HR, beats/min	72 ± 4	70 ± 3

Values are means ± SEs. CN, control condition; ST, fasting condition; T_{re}, rectal temperature; T_{sk}, mean skin temperature; T_b, mean body temperature; HR, heart rate.

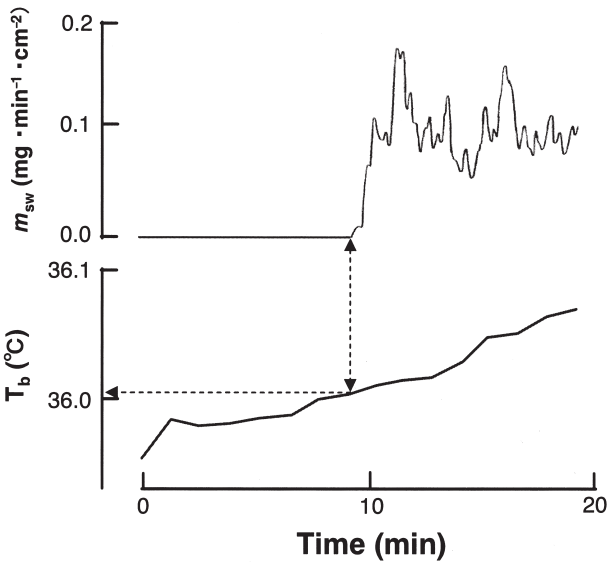

Fig. 1. Representative example showing changes in mean body temperature (T_b) and sweating rate (m_{sw}) in one subject before and during warm water immersion. Data are plotted every min. Warm water immersion started at time 0. Arrows indicate the onset of sweating and threshold T_b for m_{sw}.

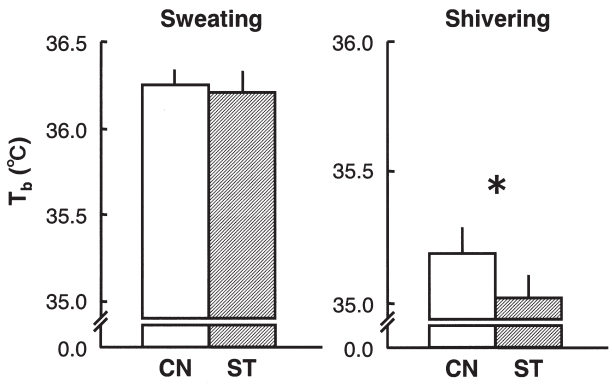

Fig. 2. Threshold mean body temperature (T_b) for sweating (left) and shivering (right) in the fed (CN, open bars) and starved (ST, hatched bars) conditions. Values are means + SE. *, significant difference between two conditions.

starvation significantly lowered the threshold T_b for shivering by 0.17°C (p=0.029). Similar results were obtained in threshold T_{re}, i.e., food deprivation did not affect the threshold T_{re} for sweating (37.17 ± 0.13 and 37.10 ± 0.11°C in the CN and ST, respectively), while it significantly reduced threshold T_{re} for shivering (36.85 ± 0.13 and 36.70 ± 0.12°C in the CN and ST, respectively; p=0.017).

The blood analysis data are shown in Table 2. The 24-hour starvation significantly elevated the RBC number, Ht and plasma levels of TP and albumin, suggesting a slight hemoconcentration in the ST. Indeed, the subjects reported that they did not feel thirsty and did not want to consume beverages during the starvation period. In contrast, the plasma levels of Na, Cl and K in the ST were significantly lower than those in the CN. During the food deprivation period, the subjects did not take any salts, but lost electrolytes via urine. Thus, the electrolytes balance should have been negative, which resulted in the decreases in plasma Na and Cl levels. Such changes in the salt balance may have contributed to the significantly lower levels of plasma osmolality and then to the absence of thirst in the ST. As expected, the plasma concentrations of glucose and TG were depressed and the FFA level was significantly elevated by fasting. In addition, the plasma levels of leptin were decreased after one-day starvation in subjects tested, although statistical significant difference was not seen due to great inter-individual variations.

DISCUSSION

Consistent with the previous studies in various species of animals (2, 5, 6), the present study showed that in humans, food deprivation shifted threshold T_b for thermogenesis to a lower level. However, little attention has been paid to the impact of starvation on heat loss threshold. In rats, we reported that threshold T_{cor} for heat loss response was hardly affected by a 3-day food deprivation (8). A new finding of the present study was that starvation did not affect the threshold T_b for m_{sw}, i.e., evaporative heat loss, in humans. Thus, similarly to the case in starved rats, the zone between the thresholds for heat loss and heat production, the interthreshold zone, could be widened by food deficiency due to a downward shift of thermogenic threshold associated with a minimal change in heat loss threshold in humans.

The thermoeffector thresholds are well known to shift under various physiological and pathological conditions. Takamata *et al.* (2001) have shown that the onset of sweating is strongly modified by plasma osmolality, e.g., the elevation of osmolality by about 13 mOsm raised the threshold T_{cor} for m_{sw} by about 0.5°C (12). In the starved subjects, the plasma osmolality was significantly decreased by 8 mOsm due to the negative electrolyte balance caused by the limitation of food intake (Table 2). If the report of Takamata *et al.* (2001) could be applicable to humans under hypotonic conditions, the threshold T_{cor}s

Table 2. Blood parameters, plasma levels of electrolytes, energy substrates and leptin, and plasma osmolality

	CN	ST	p
Red blood cell, x10^3 /μl	463 ± 19.3	482 ± 21.6*	0.019
Hematocrit, %	42.4 ± 2.0	44.5 ± 2.3*	0.029
Na, mEq/l	141 ± 1	139 ± 1*	0.027
K, mEq/l	4.1 ± 0.1	4.3 ± 0.1*	0.045
Cl, mEq/l	103 ± 1	99 ± 1*	0.035
Osmolality, mOsm l/kg	287 ± 1	279 ± 2*	0.006
Glucose, mg/dl	105 ± 5	72 ± 2*	0.002
Total protein, g/dl	7.2 ± 0.2	7.9 ± 0.2*	0.007
Albumin, g/dl	4.7 ± 0.1	5.0 ± 0.2*	0.036
Triglyceride, mg/dl	91 ± 23	51 ± 8	n.s.
Free fatty acid, μEq/l	221 ± 38	1762 ± 156*	<0.001
Leptin, ng/ml	4.7 ± 1.5	2.1 ± 0.4	n.s.

Values are means ± SEs. CN, control condition; ST, fasting condition. *, significant difference from corresponding values of the CN; n.s., no significant difference.

for m_{sw} in the ST might have been estimated at lower values because of the plasma hypo-osmolality (12). In the present study, there were no significant differences in sweating thresholds between the CN and ST. Thus, it is reasonably concluded that short-term food deprivation, at least, may not reduce the threshold T_bs for m_{sw} in humans.

Food deprivation has been shown to decrease T_{cor} (2-5). In general, T_{cor} of endotherms is preferably controlled within the interthreshold zone by the thermoregulatory system. When T_{cor} is shifted for some reason and reaches either the heat loss or heat production threshold, the corresponding effector mechanism is activated and T_{cor} is returned to a temperature between the two thresholds. When T_a is low enough and a sufficient amount of heat loss is maintained, T_{cor} may fall until the threshold for thermogenesis is reached, i.e., T_{cor} may stay near to the threshold for heat production within the interthreshold zone (9). Thus, the magnitude of drop in T_{cor} may depend on the degree of the shift of threshold T_{cor} for heat production and T_a. In the previous studies in animals (13), the period of starvation was more than 2 days and the magnitudes of shifts in T_{cor} and thermogenic threshold were 0.5-1.2℃, e.g., in rats, a 3-day food deprivation lowered T_{cor} by about 0.7℃ and the threshold by approximately 0.8 ℃ (8). Considering the subjects' physical condition, we adopted only one day starvation in the present study, which may have resulted in a smaller degree of shift in shivering threshold and therefore T_{cor}.

The mechanism of the starvation-induced downward shift of thermogenic threshold has not been elucidated. Starvation is shown to stimulate or inhibit secretions of various humoral factors to control energy balance in animals and humans (14, 15). Among them, leptin, released from the adipose tissue, may be one of the most effective factors, i.e., it contributes to stabilizing the fat mass in the body by depressing food intake and facilitating energy expenditure (heat production). In animal studies, the thermogenic hormone has been shown to raise T_{cor} when injected centrally or peripherally (16, 17). Thus, leptin might have a role in the control of T_{cor} through modifying the thermogenic system. Consistent with the previous report (18), the plasma levels of leptin were obviously decreased by the one-day fasting in the present subjects. It is therefore possible that the starvation-induced drop in threshold T_{cor} for shivering could partly be attributable to the reduction of plasma leptin level.

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