Effects of fasting on thermoregulatory processes and the daily oscillations in rats

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Submitted 26 August 2002; accepted in final form 10 January 2003

Nagashima, Kei, Sadamu Nakai, Kenta Matsue, Masahiro Konishi, Mutsumi Tanaka, and Kazuyuki Kanosue. Effects of fasting on thermoregulatory processes and the daily oscillations in rats. Am J Physiol Regul Integr Comp Physiol 284: R1486–R1493, 2003. First published January 23, 2003; 10.1152/ajpregu.00515.2002.—To investigate the mechanism involved in the reduction of body core temperature (Tcore) during fasting in rats, which is selective in the light phase, we measured Tcore, surface temperature, and oxygen consumption rate in fed control animals and in fasted animals on day 3 of fasting and day 4 of recovery at an ambient temperature (Ta) of 23°C by biotelemetry, infrared thermography, and indirect calorimetry, respectively. On the fasting day, 1) Tcore in the light phase decreased (P < 0.05) from the control; however, Tcore in the dark phase was unchanged, 2) tail temperature fell from the control (P < 0.05, from 30.7 ± 0.1 to 23.9 ± 0.1°C in the dark phase and from 29.4 ± 0.1 to 25.2 ± 0.2°C in the light phase), 3) oxygen consumption rate decreased from the control (P < 0.05, from 24.37 ± 1.06 to 16.24 ± 0.69 ml·min⁻¹·kg body wt⁻⁰.⁷⁵ in the dark phase and from 18.91 ± 0.64 to 14.00 ± 0.41 ml·min⁻¹·kg body wt⁻⁰.⁷⁵ in the light phase). All these values returned to the control levels on the recovery day. The results suggest that, in the fasting condition, Tcore in the dark phase was maintained by suppression of the heat loss mechanism, despite the reduction of metabolic heat production. In contrast, the response was weakened in the light phase, decreasing Tcore greatly. Moreover, the change in the regulation of tail blood flow was a likely mechanism to suppress heat loss.

IN HOMEOTHERMIC ANIMALS, body core temperature (Tcore) oscillates daily: it is higher in the active phase and lower in the inactive phase in diurnal and nocturnal animals. It has been reported that the amplitude of the Tcore rhythm is largely influenced by feeding condition and/or nutritional state (6, 11, 17, 27). In addition, thermal conductance from the body core to peripheral sites is increased during fasting (11, 17, 27), which indicates suppression of the heat loss mechanism. Thus suppression of the heat loss mechanism may compensate for the lowered heat production during fasting, maintaining Tcore in the dark phase at the normal level. In contrast, such a response may not work in the light phase, resulting in a greater reduction of Tcore. However, there is no direct evidence to support this speculation.

Animals have several mechanisms to change the efficiency of heat loss in a short period: 1) skin circulation, 2) fur and feather positioning, affecting heat insulation, and 3) postural adjustment, altering effective body surface area. In rats, the tail is a crucial site for regulation of heat loss, with its physiological and anatomic characteristics, i.e., high density of arteriovenous anastomosis (6), no fur, and a greater surface-to-volume ratio than elsewhere in the body. Young and Dawson (33) reported that rats could dissipate ~25% of basal metabolic heat production through the tail by changing tail blood flow. In addition, tail blood flow is controlled by sympathetic nerve activity (14, 19). It is known that fasting modulates sympathetic nerve activity in some organs such as the liver, adrenal gland, and adipose tissue (2, 23, 34–36). Thus we surmised that fasting also has an influence on tail blood flow.

The purpose of the present study is to examine how the daily change of Tcore during fasting is generated in rats. Thus we assessed the effect of 3 days of fasting on metabolic heat production in free-moving rats. Re-
Regional body surface temperature as an index of heat loss was also evaluated by infrared thermography. We hypothesized that 1) 3 days of fasting changed the daily oscillation of T\textsubscript{core} by affecting heat production and loss mechanisms and 2) tail blood flow was closely associated with suppression of the heat loss mechanism during fasting.

**METHODS**

Adult male crj-Wistar rats (n = 17, Charles River Japan, Osaka, Japan) were individually housed in a cage (45 x 25 x 20 cm) at an ambient temperature (T\textsubscript{a}) of 23°C in a 12:12-h light-dark cycle (lights on at 0700, 200 lx in the light and 0 lx in the dark). All experimental protocols were approved by the Institutional Animal Care and Use Committee of the School of Allied Health Sciences, Osaka University Faculty of Medicine.

**Surgery.** For the measurements of T\textsubscript{core} and locomotor activity, a radio transmitter (15 x 30 x 8 mm; Physiotel TA107A-F40, DataScience, St. Paul, MN) was placed in the abdominal cavity of each rat under general anesthesia with pentobarbital sodium (5 mg/100 g body wt ip). The rats were allowed to recover for >3 wk before the experiments.

All the experimental protocols consisted of 4 days in the control condition, 3 days of fasting, and 4 days of recovery from fasting. Rats had free access to food (57.2 g carbohydrate, 23.8 g protein, 5.1 g fat, and 357 kcal/100 g; Oriental Yeast, Tokyo, Japan) during the control and recovery periods. Water was available ad libitum during each feeding condition. Food deprivation and refeeding were started at 1800. In all the rats, T\textsubscript{core} and counts of locomotor activity were recorded every 5 min with a data collection system, which consisted of a receiver board (model CTR86, DataScience) under the cage connected to a personal computer. The locomotor activity counts reflected positional movements but did not show other movements such as grooming or food intake. The rats were weighed every day at 1700.

**Experiment 1: measurement of metabolic rate.** In six rats, oxygen consumption rate (\(\dot{V}O_2\), measured by indirect open-circuit calorimetry) was measured for 24 h on the last day of the fasting, control, and recovery periods. At 1500, each rat was placed in a plastic box (40 cm long x 30 cm wide x 70 cm high) at 1500 on the last day of the control, fasting, and recovery periods. The box was well ventilated and had an open window on the top (25 x 20 cm). T\textsubscript{a} in the box was monitored with a thermometer and was kept at 23.0 ± 0.2°C.

**Experiment 2: measurement of body surface temperature.** In another group of five rats, the body surface temperature was determined by thermography (model L31RD-S270A, Nikon, Tokyo, Japan). Each rat was placed in a plastic box (40 cm long x 30 cm wide x 70 cm high) at 1500 on the last day of the control, fasting, and recovery periods. The box was well ventilated and had an open window on the top (25 x 20 cm). T\textsubscript{a} in the box was monitored with a thermometer and was kept at 23.0 ± 0.2°C during the experimental period. An infrared charge-coupled device camera was placed 20 cm above the box, and a digital image was taken every 5 min through the window. The surface temperatures of five areas [head, middle parts of the upper and lower back, and proximal and distal parts of the tail (one-third of the length of the tail from the root and tip, respectively)] were determined using an image analyzer program (FAIRIS, Nikon). The temperatures of the head and back were averaged as trunk temperature (T\textsubscript{trunk}), and those of the tail as tail temperature (T\textsubscript{tail}). T\textsubscript{tail} was measured only when the previous and subsequent tail images could be seen: the data were excluded when the tail was under the body within the 15-min period. Those values were calibrated on the basis of our preliminary data, because the radiation rate of infrared rays differs among body sites; the actual values of skin temperature at the skin sites were measured with thermocouples in a warm or cool environment, and the values were compared with those obtained by thermography. The accuracy of the measurement was ±0.2°C.

**Blood sampling.** A blood sample was taken in another group of six rats at 1700 on the last day of each feeding condition; after local anesthetic (2% lidocaine gel) was applied to the tail surface, 150 μl blood were collected in microcapillary tubes through a tiny cut of the tail. Hematocrit (microcentrifuge), blood glucose (colorimetry; Arkray, Tokyo, Japan), and plasma concentrations of total protein (refractometry; Atago, Tokyo, Japan) and triglyceride (colorimetry; Wako, Osaka, Japan) were determined from the samples.

**Statistics.** Differences in mean values among the three feeding conditions were evaluated by ANOVA for repeated measures. A post hoc test at a specific time point was conducted by the Newman-Keuls procedure. The null hypothesis was rejected at P < 0.05. Regression analysis was conducted by the standard least squares method. Difference in slopes and intercepts for the regression lines was assessed by Student's t-test. The circadian rhythm of each physiological parameter was analyzed by fitting a cosine curve [cosinor rhythmometry (13)], and its mesor (mean level), amplitude, and acrophase (the time when the rhythm peaks) were estimated. All variables were averaged over 30 min and are shown as means ± SE.

**RESULTS**

Figure 1 illustrates T\textsubscript{core}, counts of locomotor activity, and \(\dot{V}O_2\) on the last days in the control, fasting, and recovery periods in experiment 1. There were no significant differences in the three parameters between the control and recovery conditions. In addition, the locomotor activity counts in the fasting condition remained unchanged from the control. The arithmetic means and medians of the three parameters were always higher (P < 0.05) in the dark phase than in the light phase. For example, in the control condition, 1) the arithmetic means in the dark and light phases were 37.8 ± 0.1 and 37.1 ± 0.1°C in T\textsubscript{core}, 24.37 ± 1.06 and 18.91 ± 0.64 ml·min\(^{-1}\)·kg body wt\(^{-0.75}\) in \(\dot{V}O_2\), and 7.3 ± 1.4 and 2.4 ± 0.5 arbitrary units in locomotor activity, respectively, and 2) the medians in the dark and light phases were 37.8 ± 0.1 and 37.1 ± 0.1°C in T\textsubscript{core}, 24.51 ± 1.07 and 18.10 ± 0.56 ml·min\(^{-1}\)·kg body wt\(^{-0.75}\) in \(\dot{V}O_2\), and 6.9 ± 1.3 and 1.3 ± 0.4 units in locomotor activity, respectively.

In the fasting condition, T\textsubscript{core} in the dark phase remained unchanged from the control. However, T\textsubscript{core} was lower than in the control condition at 0700–1300
The reduction of $T_{\text{core}}$ was significant soon after light onset, reaching its nadir at 0800 ($36.0 \pm 0.2^\circ$C, in contrast to control of $37.1 \pm 0.1^\circ$C). The difference in $T_{\text{core}}$ between the control and fasting conditions was $0.2 \pm 0.1$, $0.7 \pm 0.1$, and $0.4 \pm 0.1^\circ$C at 0400–0700, 0700–1000, and 1000–1300, respectively, with the greatest difference at 0700–1000 ($P < 0.05$).

$V_{\text{O}_2}$ was lower than the control condition throughout the fasting day ($P < 0.05$; Fig. 1C). The arithmetic mean and median were $16.24 \pm 0.69$ and $16.05 \pm 0.58$ ml·min$^{-1}$·kg body wt$^{-0.75}$ in the dark phase and $14.00 \pm 0.41$ and $13.32 \pm 0.36$ ml·min$^{-1}$·kg body wt$^{-0.75}$ in the light phase, respectively. The reduction of $V_{\text{O}_2}$ after light onset was attenuated: the difference between the control and fasting conditions was lower at 0700–1000 than at 0400–0700 ($P < 0.05$, 5.24 ± 0.63 and 9.67 ± 0.93 ml·min$^{-1}$·kg body wt$^{-0.75}$, respectively).

Table 1 summarizes the analysis by cosinor rhythmometry for the circadian changes in $T_{\text{core}}$, locomotor activity, and $V_{\text{O}_2}$. We assumed that the circadian period was constantly 24 h (the value in a normal 12:12-h light-dark cycle), because those parameters were not measured for successive days in the same conditions.

The regression coefficients of the cosine curves (data not shown) were significant ($P < 0.05$) in any feeding condition, and the acrophases were in the middle of the dark phase. In the fasting condition, the amplitude increased in $T_{\text{core}}$ and decreased in $V_{\text{O}_2}$ with reductions of both mesors, and both acrophases advanced by 1.8 h from the controls. However, there were no changes in the three parameters in locomotor activity.

Figure 2 shows thermograms for one rat in the control condition and on day 3 of fasting in experiment 2. The thermograms are illustrated as 256-grade pseudocolor images. The tail temperature decreased to environmental temperature in the dark phase on the fasting day. The tail images could always be distinguished from the background by the difference in radiation rate: the signals from the background were always weaker than those from the tail.
Figure 3 illustrates T_tail and T_trunk in the three feeding conditions in experiment 2. T_core was not different from that in experiment 1, so those data were not presented. Rats occasionally hid their tails under their bodies, and these T_tail data were not recorded or were excluded (e.g., on the control day, 4/110062 and 11/110064 of 144 data in the dark and light phases, respectively, and on the fasting day, 11/110062 and 22/110061 in the dark and light phases, respectively). There were no differences in T_tail and T_trunk between the control and recovery conditions. In the control condition, the arithmetic means and medians of T_tail and T_trunk were higher (P < 0.05) in the dark phase (30.7 ± 0.5 and 30.7 ± 0.1°C in T_tail and 28.8 ± 0.1 and 28.8 ± 0.1°C in T_trunk, respectively) than in the light phase (29.4 ± 0.1 and 29.4 ± 0.1°C in T_tail and 28.2 ± 0.1 and 28.2 ± 0.1°C in T_trunk, respectively).

T_tail was lower than the control throughout the fasting day (P < 0.05; Fig. 3A); however, T_trunk was lower (P < 0.05) than in the control condition only at 0600–

Table 1. Analysis of cosinor rhythmsometry for daily changes in core temperature, V˙O2, and locomotor activity

<table>
<thead>
<tr>
<th></th>
<th>Fed</th>
<th>Fast</th>
<th>Rec</th>
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<tbody>
<tr>
<td>Tcore, °C</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mesor</td>
<td>37.5±0.1</td>
<td>37.3±0.1</td>
<td>37.4±0.1</td>
</tr>
<tr>
<td>Amplitude</td>
<td>0.5±0.1</td>
<td>0.7±0.1</td>
<td>0.4±0.1*</td>
</tr>
<tr>
<td>Acrophase</td>
<td>18.2±0.2</td>
<td>16.4±0.3*</td>
<td>17.5±0.3*</td>
</tr>
<tr>
<td>r</td>
<td>0.76–0.91†</td>
<td>0.80–0.85†</td>
<td>0.56–0.91†</td>
</tr>
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</table>

Values are means ± SE. V˙O2, oxygen consumption rate; Au, arbitrary unit; Tcore, core temperature; Fed, day 4 of fed control period; Fast, day 3 of fasting period; Rec, day 4 of recovery from fasting. Acrophase is shown in zeitgeber time (ZT; ZT 0 = 0700). *Significantly different from control, P < 0.05. †Significant regression coefficient (r) for fitted cosine curve for daily change of variable, P < 0.05. ‡Significantly different from fasting period, P < 0.05.

Fig. 2. Thermograms in fed and fasting conditions. Thermograms are shown as 256-grade pseudocolor images every 4 h in fed control condition and on day 3 of fasting. Lights were off between 1900 and 0700.
1000 (Fig. 3B). In contrast to the control condition, Ttail in the fasting condition increased after light onset and remained at a higher level (P < 0.05) than at 0400 for 4 h. Ttail at 2300, 0400, 0700, and 1300 was 30.8 ± 0.1, 29.1 ± 0.2, 27.5 ± 0.1, and 25.0 ± 0.1°C in the control condition and 23.1 ± 0.1, 24.5 ± 0.4, 27.5 ± 0.1, and 25.0 ± 0.1°C in the fasting condition, respectively. The arithmetic mean and median were lower (P < 0.05) in the dark phase (23.9 ± 0.2 and 24.0 ± 0.1°C, respectively) than in the light phase (25.2 ± 0.2 and 25.0 ± 0.2°C, respectively).

The regression coefficients of the fitted cosine curves for daily changes of Ttail and Ttrunk (data not shown) were significant in any feeding condition (P < 0.05, r = 0.41–0.72 in Ttail and 0.32–0.82 in Ttrunk). In the fasting condition, the mesors of both temperatures decreased from the control (P < 0.05, from 29.1 ± 0.2 to 23.8 ± 0.2°C in Ttail and from 28.8 ± 0.1 to 27.1 ± 0.1°C in Ttrunk). Moreover, the amplitude of Ttail increased from the control (P < 0.05, 0.9 ± 0.1°C) by 0.6°C; however, the amplitude of Ttrunk remained unchanged (0.4 ± 0.1°C). The acrophase of Ttail was delayed by -12 h from the control [P < 0.05, from zeitgeber time (ZT, ZT 0 = 0700) 17.8 ± 0.3 to 4.4 ± 0.3 h]; however, the acrophase of Ttrunk advanced (P < 0.05) from ZT 18.8 ± 0.1 to 15.8 ± 0.1 h.

Figure 4 shows the relation between V̇O₂ and Tcore in the control and fasting conditions in experiment 1. The relation was linear in each feeding condition (P < 0.05, r = 0.96 and 0.75 in the control and fasting conditions, respectively). However, the regression slope became greater (P < 0.05) in the fasting condition: Tcore at the given V̇O₂ shifted above the control condition in the dark phase; however, the shift was less in the light phase. As time passed, the circled points denoting the period during which Tcore decreased moved leftward along the regression line of the fasting condition, and the shift above the control line was totally cancelled at the end.

Figure 5 illustrates the relation between Tcore and Ttail and Ttrunk in the control and fasting conditions in experiment 2. Tcore and Ttail had a positive and linear correlation in the control condition (P < 0.05, r = 0.72; Fig. 5A); however, the correlation became negative on day 3 of fasting (P < 0.05, r = -0.64). The relation between Tcore and Ttrunk (Fig. 5B) was positive and linear in the control and fasting conditions (P < 0.05, r = 0.73 and 0.53, respectively), although the regression line shifted downward in the fasting condition. At the beginning of the period denoted by the circled points during which Tcore decreased, Tcore-Ttail shifted upward and then moved leftward along the control regression line.

Figure 6 shows the relation between the locomotor activity counts and V̇O₂ in the control and fasting conditions in experiment 1. There was a linear (P < 0.05) relation between the two parameters in each condition. There were no differences among the regression slopes, except in the light phase on the fasting day. However, the activity in the light phase on the fasting day did not increase as much as in the other condition, mostly <2.0 units. The intercept (estimated V̇O₂ at zero activity) in the control condition was higher in the dark phase than in the light phase (P < 0.05, 21.20 and
DISCUSSION

To clarify the mechanism involved in the reduction of $T_{\text{core}}$ in fasted rats, which occurs selectively in the inactive phase, we assessed the daily changes in $T_{\text{core}}$ and $V_{\text{O}_2}$ in fed and fasting conditions. In addition, regional body surface temperature as an index of heat loss was assessed by thermography. In fed conditions, $T_{\text{core}}, V_{\text{O}_2}, T_{\text{trunk}},$ and $T_{\text{tail}}$ showed a clear daily oscillation: higher in the dark phase and lower in the light phase. However, in the fasting condition, $V_{\text{O}_2}$ decreased from the control condition in the dark and light phases, and its circadian rhythm amplitude was reduced. Moreover, $T_{\text{tail}}$ decreased from the control greatly in the light phase of the fasting period.

Homeothermic animals regulate $T_{\text{core}}$ by heat production and loss mechanisms. In the fed condition, $T_{\text{core}}$ is highly correlated with $V_{\text{O}_2}$, i.e., metabolic heat production (Fig. 4). On the assumption that heat balance was equilibrated and evaporative heat loss was small enough, the thermal conductance from the body core to the environment was calculated as $V_{\text{O}_2}/(T_{\text{core}} - T_a)$ (9). The value was higher in the dark phase than in the light phase ($P < 0.05$, 1.65 and 1.28 ml·min⁻¹·kg body wt⁻¹°C⁻¹, respectively). The result indicates that heat loss mechanisms were activated in the dark phase. Thus, in the control condition, metabolic heat production was the factor causing $T_{\text{core}}$ to be higher in the dark phase than in the light phase.

Several studies have shown that fasting decreases the metabolic rate (3, 7, 12, 15, 18, 20, 24, 30, 31). In the present study, $V_{\text{O}_2}$ was lower in fasted rats during the active and inactive periods (Fig. 1C, Table 1). Despite the reduction of $V_{\text{O}_2}$, i.e., heat production, $T_{\text{core}}$ in the dark phase on the fasting day was well maintained. The linear relation between $V_{\text{O}_2}$ and $T_{\text{core}}$ (Fig. 4) in the fasting condition indicates that $V_{\text{O}_2}$ was a factor determining $T_{\text{core}}$ as in the control condition. However, the increase in $T_{\text{core}}$ at the given $V_{\text{O}_2}$ in the dark phase may suggest that $T_{\text{core}}$ was maintained mainly by the suppression of heat loss mechanisms. In support of this speculation, the assumed thermal con-

### Table 2. Changes in body weight, hematocrit, and circulating nutrients

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Fast</th>
<th>Rec</th>
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<tbody>
<tr>
<td>Body wt, g</td>
<td>325 ± 10</td>
<td>275 ± 10*</td>
<td>324 ± 7</td>
</tr>
<tr>
<td>Hematocrit, %</td>
<td>40.0 ± 0.2</td>
<td>42.1 ± 0.2*</td>
<td>40.6 ± 0.3</td>
</tr>
<tr>
<td>Blood glucose, mg/dl</td>
<td>102 ± 7</td>
<td>86 ± 3*</td>
<td>95 ± 5</td>
</tr>
<tr>
<td>Total protein, g/dl</td>
<td>6.6 ± 0.3</td>
<td>6.3 ± 0.2*</td>
<td>7.1 ± 0.5</td>
</tr>
<tr>
<td>Triglyceride, mg/dl</td>
<td>55 ± 3</td>
<td>42 ± 2*</td>
<td>72 ± 3*</td>
</tr>
</tbody>
</table>

Values are means ± SE. *Significantly different from control, $P < 0.05$. 

triglyceride in six rats. Hematocrit in the fasting condition was greater ($P < 0.05$) than in the control condition. The other variables decreased ($P < 0.05$) on day 3 of fasting; however, they returned to the control level on day 4 of the recovery, except for the augmented value of triglyceride.

17.89 ml·min⁻¹·kg body wt⁻⁰·⁷⁵, respectively). Moreover, those values were higher than in the fasting condition ($P < 0.05$, 14.64 and 13.87 ml·min⁻¹·kg body wt⁻⁰·⁷⁵ in the dark and light phase, respectively).

Table 2 shows body weight, hematocrit, and concentrations of blood glucose and plasma total protein and
ductance in the dark phase of the fasting period decreased from the control value \( P < 0.05, 1.10 \) and \( 1.65 \) ml \( \cdot \) min\(^{-1}\) \( \cdot \) kg body wt \( -0.75 \cdot ^\circ \)C\(^{-1}\), respectively).

\( T_{core} \) in the light phase on the fasting day decreased strongly from the control for 3 h after light onset. However, in the fasted animals, the decrease in \( V_{O2} \) during the period was less than in control condition, and the circadian rhythm amplitude decreased (Fig. 1C, Table 1). Thus we suppose that heat production was not a dominant factor generating the \( T_{core} \) rhythm in the fasting condition, in contrast to the control condition. The regression analysis of \( T_{core} \) and \( V_{O2} \) (Fig. 4) may show that the suppression of heat loss mechanisms was attenuated in the light phase on the fasting day compared with that in the dark phase. Moreover, the suppression was completely abolished at the beginning of the light phase, which may be a mechanism for the significant reduction of \( T_{core} \) at that time. Thus it is supposed that heat loss mechanisms primarily determine the \( T_{core} \) rhythm in the fasting condition.

Body surface temperature reflects the magnitude of heat loss. At \( T_{a} \) below the thermoneutral zone, i.e., 28–32°C in Wistar rats, nonevaporative processes dissipate body heat (18, 35). The change in tail blood flow is an important process regulating heat loss in rats (33). \( T_{tail} \) in the dark phase on the fasting day decreased to the level of \( T_{a} \) (23°C) and was lower than that in the light phase (Fig. 3A). The regression analysis for \( T_{core} \) and \( T_{tail} \) (Fig. 5A) may indicate that tail blood flow increased with the rise in \( T_{core} \) in the control condition; the increase in \( T_{tail} \) in response to the increase in \( T_{core} \) was \( >1 ^\circ \)C). In the fasting condition, \( T_{tail} \) at the given \( T_{core} \) decreased; this decrease was greater in the dark phase than in the light phase. Although the results strongly suggest an attenuation of tail blood flow, it is notable that the attenuation was blunted at the beginning of the light phase (circled points in Fig. 5A), at which \( T_{core} \) greatly decreased. In contrast, the attenuation of the skin blood flow of the trunk may have been similar between the dark and light phases (Fig. 5B). Thus it is believed that tail blood flow was a key process determining heat loss from the body in the fasting condition, which was the factor regulating the \( T_{core} \) rhythm.

Despite the fact that locomotor activity was unchanged from the control condition (Fig. 1B, Table 1), \( V_{O2} \) greatly decreased in the fasting condition. In addition, the decrease was greater in the dark phase than in the light phase (\( P < 0.05, 8.13 \pm 0.13 \) and \( 4.78 \pm 0.71 \) ml \( \cdot \) min\(^{-1}\) \( \cdot \) kg body wt \( -0.75 \cdot ^\circ \)C\(^{-1}\), respectively). The regression analysis for activity and \( V_{O2} \) (Fig. 6) also indicated that the estimated \( V_{O2} \) at zero activity decreased in the fasting condition. Furthermore, the reduction in the estimated \( V_{O2} \) at zero activity could explain \( \sim 80\% \) of the decrease in measured \( V_{O2} \) in the dark and light phases. These results may show that the reduction of resting metabolic rate contributed to the decrease in \( V_{O2} \). One possible factor for the reduction of resting metabolic rate is a lack of food intake. Food intake itself induces an increase in metabolism, known as postprandial-derived thermogenesis and/or diet-induced thermogenesis (21, 22, 29, 30). Another possible factor is a decrease in energy stores and/or circulating nutrients. Recent studies have clarified that elevations in leptin and/or insulin in response to increases in body fat mass and/or blood glucose facilitate energy expenditure (3, 5, 16, 26). The 3-day fast induced a 15% reduction of body weight. Furthermore, the plasma concentrations of circulating nutrients decreased on day 3 of fasting, despite dehydration, as estimated by the increase in hematocrit (Table 1). Thus it is speculated that the reductions in energy stores and/or circulating nutrients were factors decreasing \( V_{O2} \) in the fasting condition. We did not assess the daily changes in plasma nutrients, because blood sampling greatly disturbs the circadian rhythm of \( T_{core} \). However, the daily rhythm of plasma nutrients might be associated with the metabolic rhythm.

The significant difference in the regulation of tail blood flow between the dark and light phases may indicate that the circadian system such as the suprachiasmatic nucleus, which is known as a central oscillator in various physiological functions, was involved in the mechanism (4, 8, 10, 25, 28). Liu et al. (10) reported that \( T_{core} \) remained unchanged during 4 days of fasting in suprachiasmatic nucleus-lesioned rats. In addition, Alfoldi et al. (1) reported that \( T_{core} \) decreased and \( T_{tail} \) increased after sleep onset and during non-rapid eye movement sleep. The result might suggest that changes in pattern and/or amount of sleep are associated with changes in \( T_{core} \) and \( T_{tail} \) in the daytime of the fasting period. However, the locomotor activity rhythm was not influenced by fasting (Fig. 1, Table 1). Although we did not assess sleep itself, it is unlikely that the sleep-wake cycle was involved in the circadian rhythm of \( T_{tail} \) to any great extent.

In summary, fasting alters thermoregulatory mechanisms involved in heat production and loss in rats. Metabolic heat production decreased in the dark and light phases of the fasting period. However, \( T_{core} \) in the dark phase was well maintained by a suppression of heat loss, which was closely related to the decrease in tail blood flow. In contrast, the decrease in tail blood flow was abolished or attenuated in the light phase of the fasting period, which could be a mechanism involved in the augmented reduction of \( T_{core} \).

**Perspectives**

The thermoregulatory system has been considered a simple input-output system; e.g., skin blood flow increases as \( T_{core} \) and/or \( T_{a} \) rises. However, this study has clarified that the concept is not the case in the fasting condition. This study indicates that tail blood flow is a primary process in determining \( T_{core} \) during fasting. In addition, in contrast to the fed condition, nonthermal signals, such as plasma nutrients and energy stores, likely regulate tail blood flow. Furthermore, the circadian system seems to modulate the response. Thus we suppose that animals utilize feedback and feedforward thermoregulatory systems depending on food availability.
REFERENCES


