Thermal regulation and comfort during a mild-cold exposure in young Japanese women complaining of unusual coldness

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Received 26 April 2001; accepted in final form 9 November 2001

Nagashima, Kei, Tamae Yoda, Tomoko Yagishita, Aki Taniguchi, Takayoshi Hosono, and Kazuyuki Kanosue. Thermal regulation and comfort during a mild-cold exposure in young Japanese women complaining of unusual coldness. J Appl Physiol 92: 1029–1035, 2002. First published November 16, 2001; 10.1152/japplphysiol.00399.2001.—We examined body core and skin temperatures and thermal comfort in young Japanese women suffering from unusual coldness (C, n = 6). They were selected by interview asking whether they often felt severe coldness even in an air-conditioned environment (20–26°C) and compared with women not suffering from coldness (N, n = 6). Experiments were conducted twice for each subject: 120-min exposure at 23.5°C or 29.5°C after a 40-min baseline at 29.5°C. Mean skin temperature decreased (P < 0.05) from 33.6 ± 0.1°C (mean ± SE) to 31.1 ± 0.1°C and from 33.5 ± 0.1°C to 31.1 ± 0.1°C in C and N during the 23.5°C exposure. Fingertip temperature in C decreased more than in N (P < 0.05; from 35.2 ± 0.1°C to 23.6 ± 0.2°C and from 35.5 ± 0.1°C to 25.6 ± 0.6°C). Those temperatures during the 29.5°C exposure remained at the baseline levels. Rectal temperature during the 23.5°C exposure was maintained at the baseline level in both groups (from 36.9 ± 0.2°C to 36.8 ± 0.1°C and 37.1 ± 0.1°C to 37.0 ± 0.1°C in C and N). The rating scores of cold discomfort for both the body and extremities were greater (P < 0.05) in C than in N. Thus the augmented thermal sensitivity of the body to cold and activated vasoconstriction of the extremities during cold exposure could be the mechanism for the severe coldness felt in C.

thermal sensation; metabolism; thyroid function

IT IS WELL KNOWN THAT AUTONOMIC THERMOREGULATION and thermal comfort in response to cold stimuli differ even among healthy individuals (10, 24, 28, 29, 34). In Japan, we often encounter women complaining of persistent and intolerable coldness in their bodies and/or fingertips and toes even in a heated room (20–23°C) in winter. Those women also suffer from coldness even in summer in an air-conditioned room (23–26°C), where most people feel thermally comfortable (2). This unusual feeling of coldness in women is commonly called hi-e-sho in Japanese (18, 23), meaning “cold syndrome.” However, the mechanism for cold syndrome remains unknown, and there is no medical definition for it. Our primary question is whether the women complaining of the unusual coldness really feel colder than normal women in the same environment due to some specific mechanisms.

Several factors possibly involved in cold syndrome were proposed. They are briefly summarized as follows (18, 23): 1) gender (more than 30% of women in all age groups suffer from cold syndrome, however, the syndrome is rare in men) and 2) body composition (both thin and obese women tend to have the syndrome). These factors are known to influence thermoregulation and/or thermal sensitivity in a cold environment (24, 28, 29). Moreover, it has already been suggested that body core and/or skin temperatures are basic determinants for thermal comfort of cold (5, 9, 10, 12, 13, 16). Thus we assume that differences in body temperature per se and/or thermal sensitivity to cold are fundamental mechanisms in those suffering from the unusual coldness. In this study, we assessed the differences between young nonobese Japanese women with and without the feeling of unusual coldness during a mild-cold exposure. We tested two hypotheses: 1) whether body core and/or skin temperatures decrease more in women who suffer from unusual coldness than those who do not and/or 2) whether women who suffer from unusual coldness feel discomfort from the cold more than those who do not for any given reduction in those temperatures.

METHODS

Twelve Japanese female subjects participated in the present study. They gave informed consent for the experimental protocol, which was approved by the Human Investigation Committee of Osaka University Faculty of Medicine. We selected young (19–26 yr of age) women whose body weight and height were close to the average for Japanese young women (51 kg and 159 cm, respectively) to exclude any

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possible direct effects of age (10) and body composition (29) on body temperature and thermal comfort. In addition, because there is no medical definition of cold syndrome, we chose the subjects based on the 10-question interview shown in Table 1, which contained typical complaints of those suffering from unusual coldness. Subjects were those who answered yes more than seven times in the interview [n = 6, cold-sensitive group (C)] and those who answered yes less than three times in the interview [n = 6, normal group (N)]. Those who answered yes three to seven times were excluded from this study. Selected subjects proved to be healthy by medical examination and had regular menstruation cycles. Subjects in the present study were selected from 66 applicants. One person conducted this selection. The subjects for both groups grew up and currently live in a similar climatic environment. Their physical characteristics are shown in Table 2. All values were similar between the two groups.

Two different experimental sessions were conducted for each subject: 1) an exposure of 23.5°C (cold session) and 2) a time-control session at the ambient temperature of 29.5°C (control session). The order of the two sessions was randomly chosen with a 2-day interval. The temperatures were chosen, based on the comfort chart of Fanger (7), in which the neutral range of 29.5°C is within the neutral range of thermal comfort and that of 23.5°C induces a mild cold feeling in naked individuals. Before this experiment, we also verified similar findings in Japanese women, wearing similar clothes, who suffer from unusual coldness and those who do not (i.e., I) they felt neither cold nor cool nor hot or warm at 29.5°C, and 2) the temperature of 23.5°C was not too cold to induce shivering or sudden reduction in body temperature. All experiments were conducted during the early follicular phase, determined by the day of menstruation cycle, and in summer in Japan (from July to September) to avoid seasonal acclimation to a cold environment. Subjects fasted from 8:00 PM on the day before the experiment. They came to the laboratory at 8:00 AM on the experimental day. Dressed in sleeveless shirts and short pants, they entered the environmental chamber maintained at 29.5°C with a relative humidity of 50%. Subjects rested in a sitting position for 1.5 h while all measuring devices were applied. A Teflon catheter (20 gauge) was placed in a left forearm vein for blood sampling. Subjects rested for another 40 min to obtain baseline data in both sessions. Then, in the cold session, room temperature was decreased to 23.5°C within 40 min and kept at this level for another 80 min. In the control session, the chamber temperature was kept at 29.5°C for the entire period. Rectal temperature (Tre) was measured with a thermister probe (NEC Sanei) placed 12 cm from the anal sphincter. Skin temperatures at eight sites (forehead, chest, back, abdomen, upper arm, forearm, thigh, and calf) were measured with copper-constantan thermocouples. Temperatures were recorded every 10 s and averaged over 10 min. Mean temperatures for the eight skin sites (Tsk) were calculated on the basis of the regional area (17). In addition, temperature at the ventral surface of the left first fingertip (Tnm) was also measured as an index temperature of the extremities. The accuracy for all the measurements was ±0.1°C. Heart rate (HR) and blood pressure were measured every 10 min (CH-611C, Citizen). Mean arterial pressure (MAP) was calculated as ([systolic arterial pressure + 2 × diastolic arterial pressure]/3). Laser-Doppler flow (LDF) on the right forearm was measured by laser Doppler flowmetry (ALF 21, Advance) as an index of skin blood flow and averaged every 10 min. Cutaneous vascular conductance (CVC) was calculated as LDF/MAP. Changes in LDF and CVC were expressed as percent changes from the averaged values during the last 20 min of each baseline period (100% LDF and CVC). Metabolic rate was assessed by indirect calorimetry to evaluate heat production process; expiratory gas of a subject was collected through a face mask (Hans Rudolph, Kansas City, MO), then oxygen and carbon dioxide concentrations and flow rate of the expiratory gas were analyzed every 30 s (AE280s, Minato Medical Science). Metabolic rate was calculated by the values for nonprotein respiration quotient and oxygen consumption rate, and expressed as kilocalories per body surface area (m²) per hour.

Subjects were asked to report thermal comfort for the body and extremities (fingertips and toes) separately every 10 min by marking on a 15-cm line rating scale, which was labeled “cold” 2.5 cm from the left end and “not at all” 2.5 cm from the right end (22). We instructed the subjects to mark on the scale how strong they felt cold discomfort, thus cold meant that they felt severe discomfort due to the cold environment or due to cold extremities. In addition, subjects were allowed to mark the comfort beyond the not-at-all point if necessary. Then the length from the point of not at all to the marked point was measured as the rating score of thermal comfort (shown as a negative value if subjects marked their comfort beyond the not-at-all point).

A 10-ml blood sample was taken at 40, 90, and 160 min after the onset of the baseline period for each session. The blood was divided into plain and EDTA-containing tubes and then centrifuged to serum and plasma. The samples were stored at −80°C until assay. Plasma concentrations of norepinephrine and epinephrine were measured by high-pressure liquid chromatography (model HLC-725CA, Tosoh). Intra-assay coefficients of variation were 0.7 and 2.4% at 174 and 380 pg/ml standards for norepinephrine and 2.5 and 2.7% at 28 and 246 pg/ml standards for epinephrine, respectively. Serum total thyroxine (T4) level was determined by enzyme immunnoassay (ICN, Orangeburg, NY), and the intra-assay coefficients of variation were 2.0 and 2.5% for 2.0 and 25 µ/dl standards, respectively. Serum cortisol concentration was determined by radioimmunoassay, and the intra-assay coefficients of variation were 4.2 and 2.9% for 3.0 and 25.0 µ/dl standards, respectively.

Table 2. Age and physical characteristics of subjects

<table>
<thead>
<tr>
<th>Age, yr</th>
<th>Body Weight, kg</th>
<th>Height, cm</th>
<th>Body Fat, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>C group</td>
<td>22.8 ± 0.8</td>
<td>50.9 ± 2.0</td>
<td>160.8 ± 1.3</td>
</tr>
<tr>
<td>N group</td>
<td>22.0 ± 0.3</td>
<td>54.0 ± 2.2</td>
<td>160.0 ± 2.0</td>
</tr>
</tbody>
</table>

Values are means ± SE (n = 6 for each group). C group, group that suffers from unusual coldness; N group, group that does not suffer from unusual coldness.

Table 1. 10-question interview

<table>
<thead>
<tr>
<th>Question</th>
<th>C Group</th>
<th>N Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. sensitive to a reduction in environmental temperature?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>2. feel colder in a cold environment than others do?</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>3. sometimes feel cold even in summer?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>4. dislike being barefoot even in summer due to coldness?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>5. feel cold in an air-conditioned room in summer when most people feel comfortable?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>6. need thicker clothes than others do?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>7. need an electric blanket for better sleep in winter?</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>8. wear socks while sleeping in winter?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>9. often wake up due to coldness or cold extremities in winter?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>10. often have pain or color changes in the fingertips or toes due to bad circulation in cold?</td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>

Do you or are you
The differences in physical characteristics between the two groups were compared by t-test. Differences in the measurement values between the C and N groups or the cold and control sessions were assessed by ANOVA with repeated measures. A significant difference of means between the two groups or sessions at a specific time point was subsequently identified by the Newman-Keuls procedure. Statistical differences in slopes or intercepts for the regression lines between the C and N groups were assessed by t-test. All values are presented as means ± SE, and a null hypothesis was rejected at the level of \( P < 0.05 \).

RESULTS

Baseline \( T_{re} \) ranged from 36.2 to 37.2°C and from 36.2 to 37.6°C in both sessions in the C and N groups, respectively (Fig. 1B). There was no difference in \( T_{re} \) between the two groups in each session or between the cold and control sessions in each group. \( T_{re} \) remained unchanged during the 160-min measurement except for in the control session in the C group, which increased (\( P < 0.05 \)) from the baseline value at 140–160 min. Baseline values for \( T_{sk} \) and \( T_{fin} \) were similar between the C and N groups (Fig. 1, C and D). Both \( T_{sk} \) and \( T_{fin} \) in the cold session in both groups were lower (\( P < 0.05 \)) than those in the control session at 50–160 min and 70–160 min, respectively. \( T_{sk} \) in the cold session decreased with the reduction in ambient temperature without any difference between the two groups, reaching 31.1 ± 0.1 and 31.1 ± 0.2°C at the end in the C and N groups, respectively. In contrast, \( T_{fin} \) in the C group decreased more (\( P < 0.05 \)) than in the N group at 120–160 min, reaching 23.6 ± 0.2 and 25.6 ± 0.5°C in \( T_{fin} \) at the end in the C and N group, respectively. Differences in baseline \( T_{re} \), \( T_{sk} \), and \( T_{fin} \) between the control and cold sessions in each subject were ~0.3°C in \( T_{re} \) and ~0.2°C in \( T_{sk} \) and \( T_{fin} \).

HR remained unchanged in the control sessions in both groups. However, HR in the C group gradually decreased (\( P < 0.05 \)) from baseline in the cold session and from baseline in the control session (Fig. 2A). MAP remained unchanged for all sessions (Fig. 2B) in both groups. The percentages of both LDF and CVC in the cold session were lower (\( P < 0.05 \)) than those in the control session at 70–110 min and 80–160 min in the C and N groups, respectively (Fig. 2, C and D).
Figure 3 illustrates the metabolic rate estimated by indirect calorimetry. The metabolic rate in the C group was higher ($P < 0.05$) than in the N group both in the cold and control sessions. There was no significant difference in the metabolic rate between the cold and control sessions in each group.

Figure 4 shows plasma norepinephrine (Fig. 4A), epinephrine (Fig. 4B), serum $T_4$ (Fig. 4C), and cortisol levels (Fig. 4D) in all experimental sessions. Those baseline values were similar in all experimental sessions except for a lower ($P < 0.05$) $T_4$ level in the C group than in the N group (5.9 ± 0.4 and 8.8 ± 0.7 μg/dl in the C and N groups, respectively). Plasma norepinephrine level in both groups was greater ($P < 0.05$) during the cold session compared with the control session (at 90 min only in the C group and 160 min in both groups) without any significant difference between the two groups. However, neither cortisol nor $T_4$ levels were different between the cold and control sessions in each group.

The rating score of thermal comfort for the body was greater in the C group than in the N group at 50–160 min in the cold session (Fig. 5A). The score for the extremities was also greater in the C group than in the N group at 90–160 min in the cold session (Fig. 5B). The scores for both body and extremities in the cold session were greater than in the control session at 50–160 min in the C group and 80–160 min in the N group. There were no significant differences in the scores between the C and N groups in the control session. In addition, the scores did not change throughout the control session in each group.

Figure 6 shows the relationships between $T_{sk}$ and the rating score of thermal comfort for the body (Fig. 6A) and between $T_{fin}$ and the rating score of thermal comfort for the extremities (Fig. 6B) at 30–130 min in the cold session (while both $T_{sk}$ and $T_{fin}$ gradually decreased). The relationships were linear ($P < 0.05$) both in the C and N groups. The slope and intercept of the regression line for $T_{sk}$ and the rating score for the body were greater ($P < 0.05$) in the C group than in the N group. However, there were no differences in the regression slope and intercept for $T_{fin}$ and the rating score for the extremities between the C and N groups.

**DISCUSSION**

In the present study, we assessed changes in body core and skin temperatures, and thermal comfort during a mild-cold exposure in young Japanese women complaining of unusual coldness in their daily lives. Those women reported stronger thermal sensitivity of the body and extremities to cold than normal women.

**Thermal comfort for the body.** The rating score of thermal comfort for the body was greater ($P < 0.05$) in the C group than in the N group (Fig. 5A). It is well known that the body core and/or skin temperatures are prime inputs both for thermal comfort for the body and autonomic thermoregulatory responses (5, 9, 10, 12, 13, 16, 25, 26, 33), and several attempts have been made to determine the relative contribution of core and skin temperatures (5, 9, 12, 13, 16). Chatonnet and Cabanac (5) suggested that thermal comfort during a cold exposure was primarily derived from skin temperature in humans. Frank et al.
demonstrated that core and skin temperatures contributed equally to thermal comfort in humans. Tre, the index of core temperature, was not changed in the cold session in the C and N groups (Fig. 1B). Therefore, a reduction in Tsk was the prime stimulus affecting thermal comfort for the body in the present experimental conditions (Fig. 1C). However, there was no difference in Tsk between the C and N groups during the cold session. These results show that a greater decrease in body temperature was not the mechanism for the stronger cold discomfort for the body in the C group.

There was a linear relationship between Tsk and the rating score of thermal comfort for the body in both groups (Fig. 6A). Moreover, the regression slope for Tsk and the rating score was greater in the C group than in the N group. The results suggest that the C group had a higher thermal sensitivity of the body to cold than the N group, which could be the mechanism for the greater rating score in the C group.

HR decreased from the baseline in the cold session only in the C group (Fig. 2). Raven et al. (30) showed that surface cooling increased stroke volume of the heart, followed by a decrease in HR via baroreflexes. In addition, they suggested that the increase in stroke volume was caused by a redistribution of blood from the periphery to the core due to vasoconstriction of the skin. Thus the vasoconstriction during the cold exposure may have been stronger in the C group than in the N group despite the same cold stimuli to the skin.

Metabolic rate, skin blood flow, and body temperature. Metabolic rate, assessed to evaluate autonomic heat-production process, was lower in the C group than in the N group (Fig. 3). Despite the difference in metabolic rate, there were no statistical differences in Tre.

Reduction in the extremity temperature could have primarily attributed to the greater cold discomfort of the extremities in the C group (Fig. 5B).

An increase in vasoconstrictor activity of the skin during a cold exposure is closely associated with the sympathetic nerve activity, especially in acral sites such as the fingertips and toes, resulting in a decrease in skin temperature (19, 21, 27). In fact, Tfin appeared to be inversely correlated to plasma norepinephrine levels in the cold session in both groups (Fig. 4A). The result may suggest greater sympathetic nerve activity in the C group; however, there was no statistical difference in plasma norepinephrine between the groups. Thus an augmentation of vascular sensitivity to the sympathetic input may also be a mechanism for the greater reduction in Tfin in the C group.

Thermal comfort for the extremities. A reduction in Tfin in the cold session was greater in the C group than in the N group (Fig. 1D). In contrast, there was no statistical difference in the regression slope for Tfin and the rating score of thermal comfort for the extremities between the two groups. The factors generating thermal comfort for the extremities remain unclear, and the temperature of the extremities was measured only at the tip of the first finger. However, an augmented reduction in the extremity temperature could have primarily attributed to the greater cold discomfort of the extremities in the C group (Fig. 5B).

Fig. 5. Scores of thermal comfort of cold for body (A) and extremities (B) during the cold and control sessions in the C and N groups. Score 10 indicates cold and the score 0 indicates not cold at all. Values are means ± SE (n = 6). *Significantly different between the C and N groups in each session (P < 0.05). †Significantly different between the cold and control sessions within a group (P < 0.05).

Fig. 6. Relationships between Tsk and thermal comfort for the body (A) and Tfin and thermal comfort of cold for the extremities (B) at 30–130 min in the cold session. Values are means ± SE (n = 6).
However, $T_{re}$ in the control session gradually increased (~0.2°C) in the C group, which may suggest the baseline $T_{re}$ in the C group was rather reduced and restored to the desired level at the end. The exposure of 23.5°C did not increase metabolic heat production in both groups. Because the body composition, one of the heat-insulation mechanisms, was similar among the subjects in this study (Table 2), the reduction in skin blood flow could have kept $T_{re}$ unchanged by attenuating heat dissipation through the skin.

Thyroid and adrenal functions affect metabolism (1, 4, 11). Moreover, the sympathetic nerve activity and thyroid function are closely associated with heat production during a cold exposure (6, 8, 15, 32). Although $T_4$ level did not change in the cold session in both groups, the baseline values were split between the two groups (Fig. 4C). $T_4$ levels in both groups were within the normal range for women based on the clinical laboratory data of Osaka University Hospital. However, a close relationship between thyroid function and resting metabolic rate was reported even in euthyroid individuals (3). Thus the small but clear difference in $T_4$ level between the two groups may have resulted in the difference in metabolic rate.

It has been reported that aging (10), body composition (29), and menstruation cycle (20) affect thermal comfort of cold for the body. Because we selected subjects without differences in those factors, other factors are likely to be involved in the mechanism for the higher sensitivity of thermal comfort for the body in the C group (Fig. 6A). Gordon and colleagues (14, 15) reported that rats with drug-induced hypothyroidism preferred a higher ambient temperature, although the rats actively regulated and lowered their core temperature. There was no difference in thermal comfort for the body between the two groups during the 29.5°C exposure; however, the results may suggest that lower thyroid function and/or reduced $T_{re}$ in the C group increased thermal sensitivity of the body to cold, interacting with thermal inputs from the skin. Another possible mechanism may be the influence of thermal inputs from the extremities, although we asked the subjects to report thermal comfort for the body and extremities separately. In addition, although the total area of the extremities is too small to decrease the mean temperature of the body surface, there may be a close and significant interaction between thermal inputs and/or comfort of the extremities and thermal comfort for the body.

We estimated thermal comfort with a line rating scale. It has been reported that scores on the line rating scale are well correlated to the intensity of some stimuli such as taste, smell, and thirst (22, 31). In our unpublished findings, the line rating scale showed higher repeatability than ordinary point scales in estimating thermal comfort within an individual. However, it still remains unknown whether those rating scales, including the scale we used, linearly correlate to the absolute intensity of cold discomfort, i.e., a neuronal activation in the center of thermal comfort. Thus there are some limitations to assess the difference between subjects.

In summary, cold discomfort during a mild-cold exposure was stronger in young Japanese women complaining of severe coldness in their daily lives despite their body core and skin temperatures being similar to women not suffering from unusual coldness. One mechanism for the strong cold discomfort is an augmented thermal sensitivity of the body to cold, which may be associated with low thyroid function. Another mechanism is a greater reduction in extremity temperature due to greater activation of the sympathetic nerve.

Perspectives. Despite the findings of this study, all factors decreasing body temperature and increasing thermal sensitivity to cold are still likely mechanisms for cold syndrome in general. Thus cold syndrome may just indicate problems in thermoregulation and/or thermal perception in women. However, there is no specific factor to explain the high rate of cold syndrome in Japanese women (although an epidemiological survey has not been done so far). Our findings may be associated with a specific mechanism for cold syndrome.

We thank Dr. Nina Stachenfeld for her valuable comments. We also appreciate Motoe Ogawa for her reception work and technical assistance.

This study was in part supported by grant-inaids for scientific research from the Ministry of Education, Science, and Culture of Japan (11557003 and 12307001).

REFERENCES