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Title

Thermoregulatory and cardiovascular responses in the elderly towards a broad range of gradual air temperature changes

Authors

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Abstract

This study aimed to determine age-related differences in thermoregulatory and cardiovascular responses to a wide range of gradual ambient temperature (T_a) changes. Morphologically matched normotensive elderly and young males participated. The participants wearing only shorts rested during the 3-hour experiment. After 30 minutes of baseline at 28°C, T_a increased linearly to 43°C in 30 min (warming) and then gradually decreased to 13°C in 60 min (cooling). T_a was rewarmed to 28°C in 30 min (rewarming), and that temperature was maintained for an additional 30 min (second baseline). During the warming phase, there were no age-related differences in blood pressure (BP) and rectal temperature (T_{re}), despite a significantly lower cutaneous vascular conductance and heart rate in the elderly ($P<0.05$). At the end of the cooling phase, systolic blood pressure (SBP) in the elderly was significantly higher than the young (155.8±16.1 and 125.0±12.5 mmHg, $P<0.01$). There was a consistent age group difference in SBP during rewarming. Mean skin temperature was significantly lower in the elderly during rewarming ($P<0.05$). T_{re} decreased more in the elderly and was significantly lower at the end of the experiment than the younger participants (36.78±0.34 and 37.01±0.15°C, $P<0.05$). However, there were no age group differences in thermal sensation. In conclusion, even normotensive elderly participants have a greater and more persistent BP response to cold than younger adults, suggesting that the elderly might be at a higher risk of cardiac events during cooling and subsequent rewarming.

Keywords

Elderly, Ambient temperature change, Blood pressure, Cutaneous vascular conductance, Rectal temperature, Skin temperature

Abbreviations

Ad	Body surface area
BP	Blood pressure
CVC	Cutaneous vascular conductance
DBP	Diastolic blood pressure
HR	Heart rate
MAP	Mean arterial blood pressure
RH	Relative humidity
SBP	Systolic blood pressure
SkBF	Skin blood flow
T_a	Ambient temperature
$T_\mathrm{f\text{-}f}$	Skin temperature difference between forearm and finger
T_hand	Hand skin temperatures
T_re	Rectal temperature
$\bar{T}_\mathrm{sk}$	Mean skin temperature
TS	Thermal sensation
WHO	World Health Organization

1. Introduction

Field and epidemiological studies demonstrate that air temperature affects human health, especially in the elderly (e.g., Yu et al. 2012). Many experimental studies have focused on the physiological and subjective responses of the elderly to heat and cold exposure. Thermoregulatory responses to cold and heat load are sluggish and weakened in the elderly compared to the young (e.g., Kenney and Munce 2003). Core temperatures increase more in older adults than younger individuals during heat exposure mainly due to reduced sweat gland output and skin blood flow (Inoue et al. 1996; Kenney and Munce 2003; Kenny et al. 2017). During cold exposure, the core temperature in the elderly decreases more due to an attenuated vasoconstrictor response (Inoue and Shibasaki 1996; Frank et al. 2000; Kenney and Munce 2003; DeGroot et al. 2007) and/or less heat production (Frank et al. 2000; Kingma et al. 2011) compared to the young.

Cardiovascular responses to heat and cold stress deteriorate in older adults. During heat exposure, cardiac output decreased in older more than younger people (Minson et al. 1998; Gagnon et al. 2016). During cold exposure, systolic blood pressure (SBP) increases more in the elderly than in the young (Wagner and Horvath 1985; Tochihara et al. 1993; Collins et al. 1995; Jansen et al. 2001; Hess et al. 2009; Hashiguchi et al. 2011). Many previous studies on age-related differences in thermoregulatory and cardiovascular responses were conducted during sudden and steady state exposure to cold and heat, since it has been well known that the temperature disparity between warm living room and cold bedroom or dressing room would be a risk of cardiac events in the elderly people (Umishio et al. 2019; Tochihara et al. 2012).

Whereas, daily fluctuation of the ambient temperature (T_a) in one room could also induce larger variation in blood pressure (BP), which is associated with cardiovascular disease (Kario 2016). Despite WHO recommends indoor T_a should be above 18 °C (WHO 2018), a recent nationwide survey in Japan revealed that the lowest living room temperature in winter is only 12.6 °C on average and below 18 °C in 90 % of houses (Umishio et al. 2020). The room temperature fall at night in poorly insulated house with local heating might induce morning hypertension (Umishio et al. 2019), which is strongly associated with cardiovascular events (Karino 2016). However, physiological responses during slow gradual T_a changes have only been investigated in limited number of studies (Ohnaka et al. 1993; DeGroot and Kenney 2007; Schellen et al. 2010). Moreover, in previous studies, T_a was altered within a relatively narrow range of mild cold and warm temperatures (19–28 °C, Ohnaka et al. 1993; 17–25 °C, Schellen et al. 2010) or between neutral and hot (21.5–39.5 °C, Ogawa et al. 1993). Thus, in older adults, the response to a wide range of gradual T_a changes, especially to severe cold environment below the recommended lowest indoor T_a (WHO 2018), is unclear. Additionally, persistent high BP in the elderly during rewarming after mild cold exposure was reported (Kingma et al. 2011). Thus, age-related differences in the cardiovascular responses after severe cold exposure are another concern that needs further investigation.

Physiological responses to heat and cold are affected by anthropological characteristics, including body fat and body surface area to mass ratio (Ad/mass) (Inoue et al. 2009; Kenny and Munce 2003). Additionally, basal function of the cardiovascular system, such as resting blood pressure, affect physiological responses to heat and cold exposure (Shigeomi et al. 2001; Kenny et al. 2010; Hintsala et al. 2014). In general, the elderly have more body fat, higher body mass index (BMI) and Ad/mass ratio, and higher basal blood pressure than the young (Umemura et al. 2019). Thus, thermoregulatory and cardiovascular responses in the elderly are often confounded by morphological characteristics and higher resting blood pressure. Controlling for these confounding factors when making age group comparisons will clarify the thermoregulatory and cardiovascular response per se to hot and cold in older adults.

The purpose of this study was to determine age-related differences in thermoregulatory and cardiovascular response during a wide range of T_a changes from severe heat to cold and subsequent rewarming. Morphologically matched normotensive older and younger participants were compared to remove the confounding bias of body fat difference, Ad/mass ratio, and BP in the elderly. We hypothesized that even in the normotensive elderly, impairment in thermoregulatory and cardiovascular response to wide range of ambient temperature would be observed compared to the younger counterparts with matched morphological characteristics. In addition, persistent hypertension would be observed during rewarming after severe cold exposure even in the normotensive elderly.

2. Methods

2.1. Participants

Nine healthy young males and nine healthy elderly males participated in this study. Table 1 shows the physical characteristics of the subjects for both groups in Mean±SD. Body surface area (Ad) was estimated according to the equation of Takahira (1925). The percentage of body fat (%fat) was estimated from the sum of skinfold thickness on the back and upper arms (Nagamine and Suzuki 1964). Although, there were significant differences ($P < 0.01$) in age and height between the young and elderly groups, other morphological characteristics, including mass, BMI, %fat, Ad/mass and three points skinfold thickness were not significantly different. Before enrolling in the study, all participants were examined by a medical doctor to confirm that they were normotensive (systolic and diastolic blood pressure were less than 140 and 90 mmHg, respectively), with no medication, and no history of cardiovascular disease. Participants were selected by matching their basal blood pressure and morphological characteristics between the groups. A medical doctor attended in all experiments involving the elderly to check their health condition. All volunteers provided written informed consent after receiving a full explanation of the study requirements and the risks involved. The Institutional Review Board of Kyushu University approved the experimental protocol (#108).

2.2. Procedures

The experiments were conducted during the summer, beginning around 10 a.m. At the beginning of each experiment, T_a, the relative humidity (RH), and air velocity of the climatic chamber were set at 28 °C, 65%, and less than 0.15 m/sec, respectively. Participants wore shorts, and sensors and devices for physiological measurements were attached. Participants stayed in the chamber at rest in a sitting position for at least 30 min (baseline). Then, T_a was increased to 43 °C linearly over 30 min at a rate of 0.5 °C/min (warming phase) followed by cooling to 13 °C over 60 min at a rate of -0.5 °C/min (cooling phase). Then, T_a was rewarmed to 28 °C over 30 min at a rate of 0.5 °C/min (rewarming phase) and maintained for an additional 30 min (second baseline) as shown in Figure 1. T_a changes in the climatic chamber was measured at 10, 40, 80, and 120 cm height from the floor. RH could not be controlled during the T_a changes but was in a similar pattern in all experiments. In general, gradually decreased to around 35% RH during the warming phase and increased to 55-60% RH during the cooling phase. The RH data was not available during rewarming phase due to sensor trouble.

2.3. Measurements

Rectal temperature (T_{re}) was measured at a depth of 13 cm from the anal sphincter using a thermistor probe (ITPO10-11, Nikkiso-YSI CO., Ltd., Japan). Skin temperatures at different body locations (forehead, back, abdomen, forearm, hand, finger, thigh, calf, and instep) were measured with thermistor probes (ITPO10-12, Nikkiso-YSI CO., Ltd., Japan). Rectal and skin temperatures were recorded every minute using data loggers (LT8A, Gram Corporation, Japan), and 10-minute averages were used for the analysis. Mean skin temperature ($\bar{T}_{sk}$) was calculated using the following modified Hardy-DuBois formula (1937).

$$\bar{T}_{sk} = 0.07T_{forehead} + 0.175T_{back} + 0.175T_{abdomen} + 0.14T_{forearm} + 0.05T_{hand}$$
$$+ 0.19T_{thigh} + 0.13T_{calf} + 0.07T_{instep}$$

The difference in skin temperature between the forearm and finger ($T_{f\text{-}f}$) was calculated to assess vasoconstriction and vasodilation (House and Tipton 2002; Schellen et al. 2010).

Systolic and diastolic blood pressures (SBP and DBP) were measured every 10 minutes from the left upper arm using an automatic tonometer (HEM-737, OMRON, Japan). The mean arterial blood pressure (MAP) was estimated as DBP, plus one-third of the pulse pressure (SBP - DBP). Skin blood flow in the forearm (SkBF) was monitored using laser Doppler flowmetry (FLO-C1, Omegawave Inc., Japan). During the experiment, changes in SkBF (%SkBF) were normalized relative to the baseline (baseline was 100%). The forearm's cutaneous vascular conductance (CVC) was calculated by dividing the %SkBF by MAP (%/mmHg). The heart rate (HR) was measured using an electrocardiogram (AU-512, Fukuda Denshi, Japan) with chest leads. The slopes of the regression line between cardiovascular parameters (BP, CVC and HR) and $\bar{T}_{sk}$ during cooling phase were calculated in each participant to evaluate sensitivity of cardiovascular responses to skin cooling. Shivering was detected based on the observations of the investigator. Bodyweight loss was estimated by weighing nude subjects before and after the experimental session using a precision body scale with a 1-gram resolution (ID2, Mettler-Toledo, Germany).

Thermal sensation (TS) was rated every 10 min during the protocol using a 9-point scale (+4: very hot, +3: hot, +2: warm, +1: slightly warm, 0: neutral, −1: slightly cool, −2: cool, −3: cold, −4: very cold).

2.4. Statistical analysis

Physiological parameters were compared using a two-way repeated-measures analysis of variance (ANOVA), where the factors were age group and time. Age group differences in physiological parameters were compared using an unpaired Student's *t*-test. The group difference in TS was analyzed using a Mann-Whitney *U*-test. The relationships between $\bar{T}_{sk}$ and blood pressure, CVC, and HR were analyzed using Pearson's correlation coefficient. All data are presented as mean ± SD. Differences at $P < 0.05$ were considered significant for all statistical analyses. Analyses were conducted using a statistical software (IBM SPSS Statistics version 20, IBM).

3. Results

3.1. Body temperatures

Changes in mean (SD) T_{re}, $\bar{T}_{sk}$, hand skin temperatures (T_{hand}), and $T_{f\text{-}f}$ every 10 min for both groups are shown in Figure 2. The ANOVA showed significant main effects of time and interaction between age group and time for T_{re}, $\bar{T}_{sk}$, T_{hand}, and $T_{f\text{-}f}$ ($P < 0.05$). The T_{re} time course in both groups showed similar trends from the baseline to the heating and cooling phases (Fig. 2A). However, T_{re} decreased more in the elderly during the rewarming phase, and T_{re} was significantly lower in elderly participants than young participants at the end of the experiment ($P < 0.05$).

There were no significant differences in $\bar{T}_{sk}$ (Fig. 2B) between the groups during the first 20 min of the experiment, but $\bar{T}_{sk}$ was significantly lower in the elderly compared with the young at 30 and 40 min during warming phase ($P < 0.05$). During the cooling phases, $\bar{T}_{sk}$ did not differ significantly between the two groups. However, $\bar{T}_{sk}$ was significantly lower in the elderly compared with the young during the last 60 min of the experiment (rewarming phase and second baseline) ($P < 0.05$). Similar trends were also found in $T_{forehead}$, $T_{abdomen}$, T_{thigh}, and T_{calf}.

The time course and age-related differences in T_{hand} (Fig. 2C) showed specific trends compared with other skin regions. There were no differences in T_{hand} between the groups for the first 80 min (from baseline to warming phase) of the experiment. However, during the cooling period, T_{hand} in the elderly was significantly higher than T_{hand} in the young ($P < 0.05$). During the rewarming phase at 130 min, T_{hand} reached the lowest value, and the average difference in T_{hand} between groups was 1.56 °C ($P < 0.01$). After that, T_{hand} of the young rewarmed by an average of 3.81 °C at the end of the experiment, but the elderly rewarmed by only 1.07 °C. There were no age-related differences in $T_{f\text{-}f}$ during the baseline, warming, cooling, and rewarming periods (Fig. 2D). However, $T_{f\text{-}f}$ of the elderly was significantly greater during the second baseline than the young ($P < 0.05$).

3.2. Thermoregulatory and cardiovascular responses

The mean SBP, DBP, MAP, %SkBF, CVC, and HR at 10 min intervals are shown in Figure 3. The ANOVA showed significant main effects of time ($P < 0.05$) and significant interactions between age groups and time ($P < 0.01$) for SBP, DBP, MAP, %SkBF, CVC, and HR. There were no differences in SBP between the groups for the first 100 min of the experiment (Fig. 3A). However, during the cooling phase, the SBP of the elderly was significantly higher than the young participants ($P < 0.05$). SBP in the young decreased to the first baseline level during the rewarming period. In contrast, SBP in the elderly remained elevated and the significant group differences continued through the second baseline until the end of the experiment ($P < 0.05$). Significant group differences in DBP were observed during the cooling phase at 110 min and during the rewarming phase at 140 min ($P < 0.05$, Fig. 3B). Changes in MAP were similar to

SBP (Fig. 3C).

%SkBF during the warming phase was significantly higher in the young group compared with the elderly group ($P < 0.05$, Fig. 3D), which peaked at the end of the phase and was 1.7-fold higher in the young. During the cooling phase, %SkBF decreased in both groups to less than the baseline level; there were no age-related differences at the latter half of the phase. During the rewarming phase and the second baseline, %SkBF was still less than the baseline in both groups. Time course changes in CVC were similar to %SkBF (Fig. 3E).

HR was significantly lower in the elderly than in the young from the baseline to the first half of the experiment's cooling phase ($P < 0.05$, Fig. 3F). During the first 30-min of baseline, the average HR was 67.3 ± 12.3 beats/min and 76.7 ± 6.2 beats/min in the elderly and the young, respectively. The increase in HR from the baseline was significantly less in the elderly (2.9 ± 3.4 beats/min) than in the young participants (5.9 ± 1.5 beats/min) during the warming phase ($P < 0.05$). The reduction of HR during the cooling phase was significantly less in the elderly (-10.2 ± 2.0 beats/min) than in the young participants (-15.6 ± 4.1 beats/min) ($P < 0.05$). During the rewarming phase and the second baseline, there were slight recoveries in HR for both groups and no significant differences between groups.

Total body weight loss during the 3-hour experiment tended to be smaller in the elderly (103 ± 13 g/m^2) than in the young participants (123 ± 3 g/m^2), but group differences were not statistically significant. No visible shivering was observed during the experiments for any subjects.

3.3. Sensitivity of the cardiovascular response to mean skin temperature reduction

The slope of the SBP, DBP, MAP, CVC, and HR versus $\bar{T}_{sk}$ during the cooling phase (60 to 120 min) were assessed in each individual. Table 2 summarizes the mean values in both groups. The sensitivity of SBP and MAP to $\bar{T}_{sk}$ reduction was significantly greater in the elderly than the young participants ($P < 0.01$). In contrast, there was no group difference in the sensitivity of DBP to $\bar{T}_{sk}$. CVC and HR decreased significantly less in response to the $\bar{T}_{sk}$ reduction in the elderly than the young group ($P < 0.01$).

3.4. Subjective response

Changes in mean TS are shown in Figure 4. TS changed as T_a changed in both groups; no group differences were detected throughout the experiment.

4. Discussion

Several reports focused on age-related differences in BP and body temperature regulation during cooling and rewarming. The elderly generally have greater body fat (Inoue et al. 1992; Kingma et al. 2001; Ohlendorf et al. 2020) and higher baseline blood pressure (DeGroot and Kenney 2007; Uemura et al. 2019) than younger individuals. However, these reports do not account for the confounding effects of morphological characteristics and resting blood pressure on the response to temperature changes. Therefore, in this study, the participants were selected to minimize differences between the young and elderly groups in their body fatness, Ad/mass ratio, BMI, and basal blood pressure. This selection enabled us to focus on the age-related differences in thermoregulatory and cardiovascular responses to dynamic changes in ambient temperatures.

4.1. Cardiovascular and thermal responses during warming

In this study, despite the similar baseline blood pressures, the significantly lower forearm %SkBF and CVC in the elderly during heat exposure (Fig. 3DE), was in line with previous studies reporting smaller increases in skin blood flow in the elderly (Kenney and Munce 2003; Kenny et al. 2017). This result suggests that dry heat loss (vasodilation response to the heat) is impaired in the elderly.

There were significant age-related differences in cardiac response (HR) to heat in addition to the %SkBF and CVC. From baseline to the hot environment period, HR was significantly lower, and HR increased less in response to heat stress in the elderly compared with the young group (Fig. 3F). In agreement with this result, previous research demonstrated a lower HR response to passive heating in the elderly than young participants (Inoue and Shibasaki 1996; Miwa et al. 2002; Gagnon et al. 2015; Gagnon et al. 2016). Recently, Kenny et al. (2017) reported significantly lower cardiac output, HR, and limb blood flow in the elderly after 3 hours of heat exposure (44 °C) compared with the young. Young people have sufficient cardiac output to support greater skin vasodilation in hot environment; whereas, both the cardiac response and skin vasodilation are impaired in older adults during heat exposure (Inoue et al. 2009).

Despite the lower %SkBF, CVC and HR in the elderly group, there were no group differences in core body temperature (T_{re}) during warming and the subsequent cooling phase (Fig. 2A). Previous reports demonstrate a slight increase in T_{re} (37.8 and 37.6 °C in the elderly and young, respectively) and a moderate increase in HR (18–20 beats/min) after 3 hours of heat exposure at 44 °C (Kenny et al. 2017). In the present study, the increase in HR during the 30-min gradual warming period to 43 °C was only 3–6 beats/min. Furthermore, total body weight loss during the 3-hour experiment was only 103–123 g/m^2. These results indicate that the heat stress induced by our protocol might not be severe enough to evaluate age-related difference in sudomotor response to elevated core body temperature.

During the gradual warming phase, blood pressure (SBP, DBP, and MAP) did not change significantly from the baseline in either age group (Fig. 3ABC). This tendency continued during the beginning of the cooling phase (until 90 min) when T_a was higher than the baseline. Since there was greater skin vasodilation (%SkBF and CVC) in the young participants, one might expect lower blood pressure. However, blood pressure was maintained in both groups during the warming phase. In line with the present study, previous studies reported that MAP was maintained when young or elderly individuals were exposed to long periods of moderate (Kenny et al. 2017) or severe heat (Minson et al. 1998).

4.2. Cardiovascular and thermal responses during cooling and rewarming

During the cooling phase (60–120 min), $\bar{T}_{sk}$ decreased in both groups with no group differences (Fig. 2B). However, T_{hand} was significantly higher in the elderly group during the latter half of cooling (Fig. 2C). The difference in T_{hand} may be due to less vasoconstriction in the extremities in the elderly (Richardson et al. 1992; Tochihara et al. 1993; Frank et al. 2000). The higher T_{hand} in the elderly continued during the substantial rewarming phase, which may have led to greater heat loss and a drop in T_{re} (Fig. 2A). However, during rewarming and the second baseline, $\bar{T}_{sk}$ was significantly lower in the elderly group (Fig. 2B). Also, the elderly participants showed significantly greater $T_{f\text{-}f}$, a surrogate index of vasoconstriction (House and Tipton et al. 2002), at the second baseline (Fig. 2D). This data suggests that vasoconstriction in the elderly during the second baseline was greater than in the young. Even with less heat loss in the elderly, indicated by the lower $\bar{T}_{sk}$ and greater $T_{f\text{-}f}$, the decrease in T_{re} was greater than in the young during the rewarming and second baseline periods (Fig. 2A). One of the potential mechanisms for explaining the continuous drop in T_{re} during rewarming phase would be greater venous return in the elderly from cooler extremities to the core body region (Natsume et al. 1992).

Considering heat balance regulating core body temperature and the matched morphological characteristics in this study, the elderly group likely had less cold-induced thermogenesis (CIT) during the cooling phase. Several reports demonstrate less metabolic heat production in older adults and their core body temperature decreases more during mild cold exposure (DeGroot and Kenney 2007; Kingma et al. 2011). One limitation of the present study is that metabolic heat production was not measured. However, considering previous studies' findings (Kingma et al. 2011; Chen et al. 2013), the greater core temperature drop in the elderly can be at least partly explained by less CIT, which might be associated with less brown adipose tissue activity in older adults (Yoneshiro et al. 2011; Chen et al., 2013).

BP in hypertensive elderly individuals increases more in response to cold exposure (Shigeomi et al. 2001) or reaches higher level with similar BP change from baseline compared to normotensive counterparts (Hintsala et al. 2014). This study's major finding is that even in non-hypertensive elderly individuals, BP increased more during the cooling phase than in the young (Fig. 3ABC). Especially, BP increased rapidly in the last 20 min of the phase and significant age-group difference was observed at 110 and 120 min when T_a was below 18 °C, which is the lowest indoor temperature of the WHO guideline (WHO 2018). The average forearm %SkBF in the elderly group was maintained at baseline level at 100 min (T_a = 23 °C), then decreased to 65.8% of baseline at 110 min when T_a reached 18 °C. Thus, it is suggested that the rapid increase in BP in the elderly would be induced when T_a dropped below the threshold for cutaneous vasoconstriction. This rapid increase in BP during gradual cooling may also increase the risk of cardiac events. The age-related difference in BP response to cold would be explained by the greater sensitivity of SBP and MAP to the reduction in $\bar{T}_{sk}$ in the elderly (Table 2). In contrast, the reduction in HR in response to $\bar{T}_{sk}$ cooling was significantly less in the elderly (Table 2). These results indicate that HR downregulation might be dampened in older adults due to impaired baroreflex for maintaining BP (Laitinen et al. 1998).

In general, skin temperature cooling induces cutaneous and visceral vasoconstriction, resulting in increased BP (Hess et al. 2009; Wilson et al. 2007). In this study, there were no group differences in %SkBF and CVC in the forearm, $\bar{T}_{sk}$, or $T_{f\text{-}f}$ during the latter half of the cooling phase; the level of cutaneous vasoconstriction may be similar in the two groups. Therefore, the age-related difference in BP regulation during cold exposure can be explained by the reduced sensitivity of the baroreflex in the elderly (Laitinen et al. 1998; O'Mahony et al. 2000; Monahan 2007; Okada et al. 2012) and/or greater vascular resistance due to stiffer blood vessels (Hess et al. 2009). At the thermoneutral baseline, the non-hypertensive elderly participants in this study, who may have higher vascular stiffness, could maintain their basal BP with downregulation of resting HR. However, the elderly participants could not regulate their BP in a cold environment as their younger counterparts, probably because of the increased blood vessel stiffness and limitations in HR reduction.

During the rewarming period, BP in the young participants returned to baseline levels, whereas BP in the elderly did not completely recover. Differences between the groups were highly significant, especially in the SBP. A large age-related gap in SBP remained throughout the recovery period. During rewarming and the second baseline, %SkBF and CVC in the forearm was similar in both groups. However, significantly lower $\bar{T}_{\mathrm{sk}}$ and larger $T_{\mathrm{f\text{-}f}}$ (Fig. 2BD) in the elderly reflected greater cutaneous vasoconstriction. Wilson et al. (2007) reported that vasoconstriction in both peripheral and visceral arteries results in increased BP during skin cooling. T_{re} was significantly lower in the elderly at the end of the experiment (Fig. 2A). Thus, the central integration of cold stimuli from deep body and skin receptors may have enhanced cutaneous and visceral vasoconstriction to maintain a higher BP.

A study similar to the present study focused on persistent high BP in the elderly during rewarming after mild cold exposure (Kingma et al. 2011). In line with the present study, they reported higher SBP in the elderly during cooling and rewarming. Moreover, Kingma et al. (2011) suggested a greater risk of increased SBP after rewarming in the elderly, especially when body fat was lower. In the present study, morphological factors were excluded since morphological characteristics were matched between age groups. Therefore, the observed age-related differences in BP can be explained by the thermoregulatory responses, cardiovascular responses, and blood vessels' stiffness.

4.3. Thermal sensation during the experiment

The time course of TS was similar to dynamic changes of T_a in both groups (Fig. 4). There were no age-related differences in TS during the warming phase. This result is in line with a previous report demonstrating similar TS in young and elderly females during 49 min of heat exposure at 35 °C (Tochihara et al. 1993). The time course of TS in both groups was also similar during cooling, rewarming and the second baseline. Previously, Tochihara et al. (1993) investigated TS of young and elderly females after sudden cold exposure at 10 °C for 49 min. The elderly felt less coldness than the young immediately after entering the cold chamber; they then gradually reached similar cold sensation as the young at the end of the exposure. Based on the results, they suggested that elderly people would have delayed sensitivity to cold (Tochihara et al. 1993). Opposed to their result, similar TS in young and elderly groups in the present study might be due to the protocol of the gradual temperature change. However, a gap between the subjective TS and body temperature change in the elderly was observed in this study. During rewarming and the second baseline, the elderly group showed significantly lower $\bar{T}_{sk}$ than the young, and T_{re} decreased continuously throughout the experiment (Fig. 2AB), whereas, TS in both groups was similar. This might lead to blunted behavioral thermoregulation in the elderly (Natsume et al. 1992; Ohnaka et al. 1993). Additionally, during cooling and rewarming phase, the elderly showed substantial and persistent rise in their BP (Fig. 3ABC). These results might indicate a relatively blunted subjective thermal sensitivity to the reduction in body temperature in older adults, with higher risk of cardiac events. This could partly be supported by the evidence reporting blunted cutaneous thermal sensitivity thresholds in the elderly to warm and cold stimuli on their skin (Tochihara et al. 2011; Inoue et al. 2016). The gap between body temperature and TS, the large pressor response to cold, and a persistently higher BP during rewarming was observed even in the normotensive elderly participants in this study. The greater cold-induced cardiovascular strain and lower $\bar{T}_{sk}$ with similar cold sensation as young adults could be another potential cause for the higher risk of cardiac events in the elderly, since their thermal behavior for regulating appropriate thermal environment might be impaired.

4.4. Limitation

Since metabolic rate was not measured in this study, the discussion on the age-related difference in their metabolic thermogenesis and BAT activity was speculative.

Physical fitness is known as one of the factors affecting physiological response to heat and cold stress (Havenith 1995; Yoshida et al. 1998). Since no group difference was observed in BMI and basal BP, the elderly participants in this study might be physically fit relative to the general elderly people. However, since the fitness level in both age groups was not measured and controlled in this study, it was not able to distinguish the confounding effect of physical fitness.

There was limitation to extend the finding to different season, since the experiments were conducted in summer. Especially, physiological response to T_a reduction might differ in winter when participants are acclimatized to cold.

5. Conclusions

We investigated age-related differences in thermoregulatory and cardiovascular responses during a wide range of T_a changes by comparing morphologically matched normotensive elderly and young participants. Despite the lower CVC and HR observed in the elderly during the warming phase, there were no age-related differences in BP and T_{re}. During the cooling phase, BP in the elderly was significantly higher than the young, and the persistently higher BP continued during rewarming. Although $\bar{T}_{sk}$ decreased similarly in both groups during cooling, $\bar{T}_{sk}$ recovered slower in the elderly during rewarming. T_{re} decreased more in the elderly, and group difference reached significance at the end of the experiment. However, there was no age group difference in their TS. These results indicated that, even in the normotensive older adults, there could be a latent risk of cardiac events during gradual cold exposure and subsequent rewarming, with similar thermal sensation as young adults.

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Author contributions

YT, KY, KF, and HK conceived and designed research. KY, KF, YK, and HK conducted the experiments. YT, KY, KF, and HW analyzed data. YT and HW wrote the draft of the manuscript. All authors read and approved the manuscript.

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Figures captions

Fig. 1 Time course of gradual ambient temperature change during the experiment.

Fig. 2 Time course of rectal temperature (A), mean skin temperature (B), hand skin temperature (C), and skin temperature difference between forearm and finger (D). Values are means and standard deviation. * and ** indicate significant differences between groups ($P < 0.05$ and $P < 0.01$, respectively).

Fig. 3 Time course of systolic blood pressure (A), diastolic blood pressure (B), mean arterial blood pressure (C), skin blood flow in the forearm (D), cutaneous vascular conductance in the forearm (E), and heart rate (F). Values are means and standard deviation. * and ** indicate significant differences between groups ($P < 0.05$ and $P < 0.01$, respectively).

Fig. 4 Time course of thermal sensation. Values are means and standard deviation. Thermal sensation is assessed using 9-point scale (4: very hot, 3: hot, 2: warm, 1: slightly warm, 0: neutral, −1: slightly cool, −2: cool, −3: cold, −4: very cold).

Table 1 Physical characteristics of the subjects (Mean ± SD).

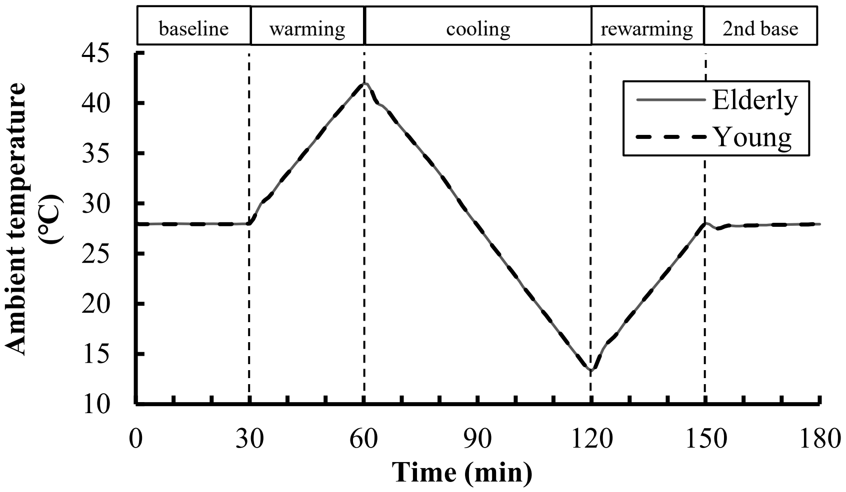
	Elderly (n = 9)		Young (n = 9)
Age (years)	69.6 ± 3.2	**	22.3 ± 1.2
Height (cm)	161.7 ± 3.8	**	171.0 ± 5.6
Mass (kg)	56.4 ± 9.6		62.9 ± 7.6
Body mass index	21.5 ± 3.2		21.6 ± 3.4
Body fat (%)	14.6 ± 6.3		15.0 ± 4.8
Ad/mass (m^2/kg)	277.8 ± 23.7		270.0 ± 18.3
SF$_{abdomen}$ (mm)	17.3 ± 10.2		14.8 ± 9.4
SF$_{arm}$ (mm)	8.4 ± 4.5		9.2 ± 4.5
SF$_{back}$ (mm)	13.4 ±4.2		13.6 ± 6.5

Ad: body surface area, SF: skinfold thickness; ** $P < 0.01$

Table 2 Sensitivity of the cardiovascular response to mean skin temperature reduction during the cooling phase (Mean ± SD).

	Elderly		Young
Sensitivity of SBP to $\bar{T}_{sk}$ (mmHg/°C)	−5.65 ± 1.82	**	−1.36 ± 1.23
Sensitivity of DBP to $\bar{T}_{sk}$ (mmHg/°C)	−2.10 ± 0.61		−1.20 ± 1.16
Sensitivity of MAP to $\bar{T}_{sk}$ (mmHg/°C)	−3.28 ± 0.63	**	−1.25 ± 1.12
Sensitivity of CVC to $\bar{T}_{sk}$ (%/mmHg/°C)	0.21 ± 0.08	**	0.45 ± 0.20
Sensitivity of HR to $\bar{T}_{sk}$ (bpm/°C)	1.64 ± 0.30	**	2.28 ± 0.58

The values are group averaged slopes of cardiovascular response versus $\bar{T}_{sk}$ assessed in each participant. SBP, DBP, and MAP: systolic, diastolic, and mean arterial blood pressure; CVC: cutaneous vascular conductance; HR: heart rate; $\bar{T}_{sk}$: mean skin temperature; ** $P < 0.01$


baseline
warming
cooling
rewarming
2nd base
Elderly
Young
Ambient temperature (°C)
45
40
35
30
25
20
15
10
0
30
60
90
120
150
180
Time (min)

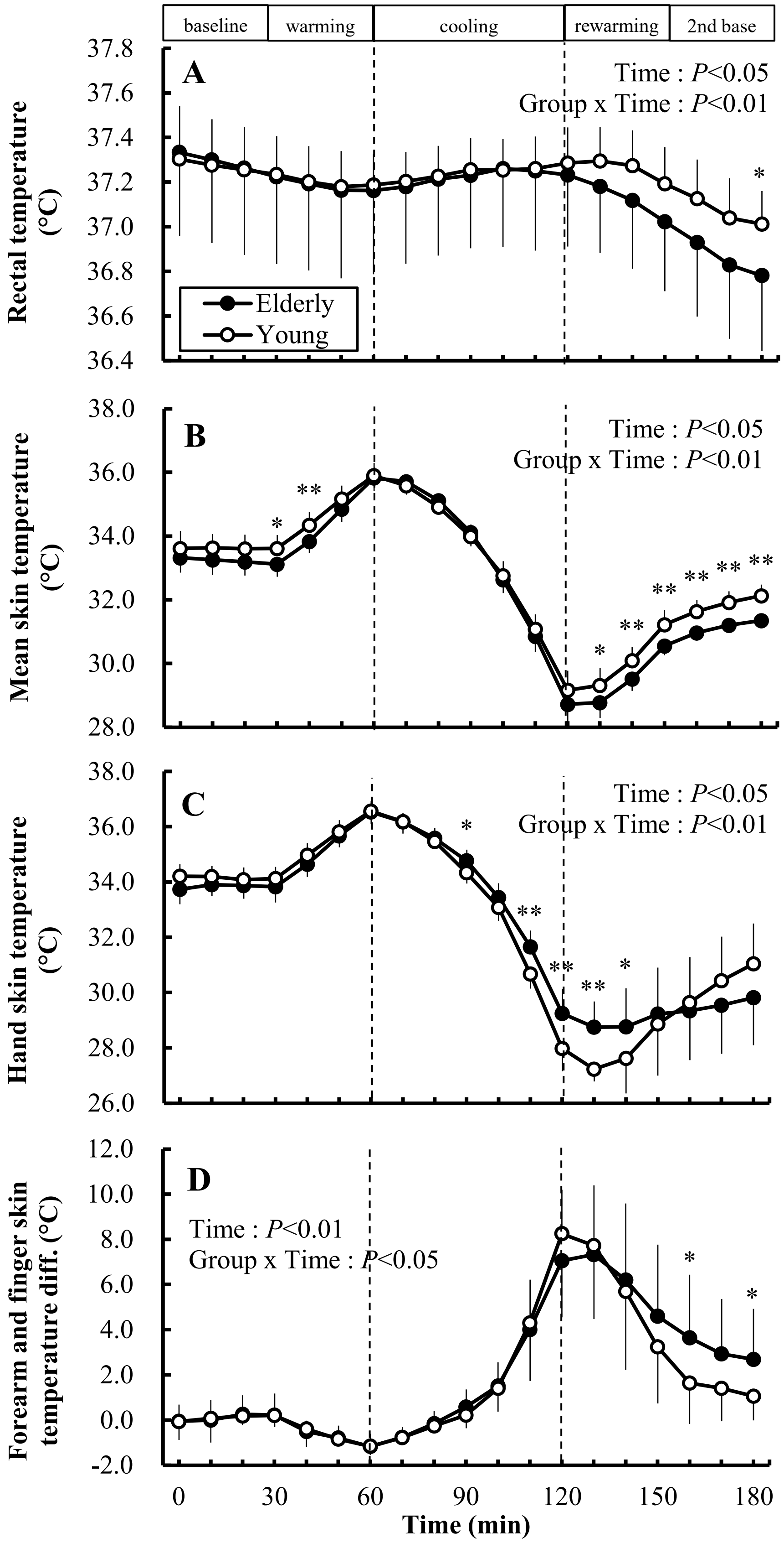
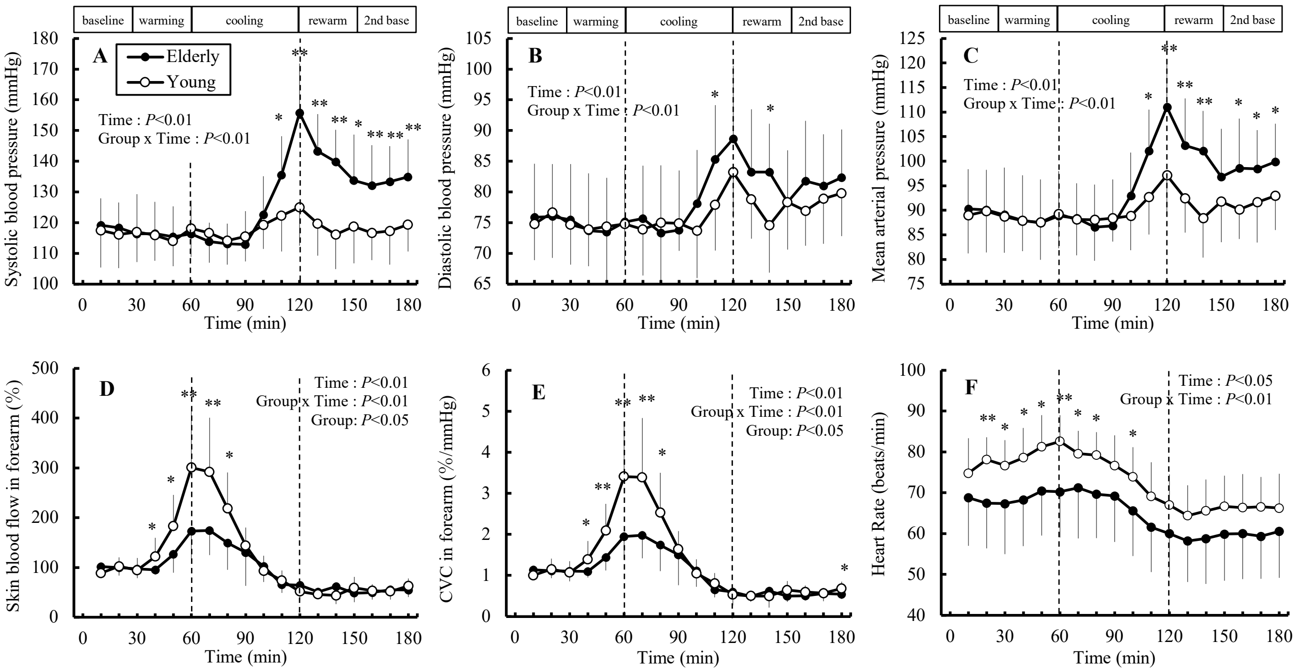
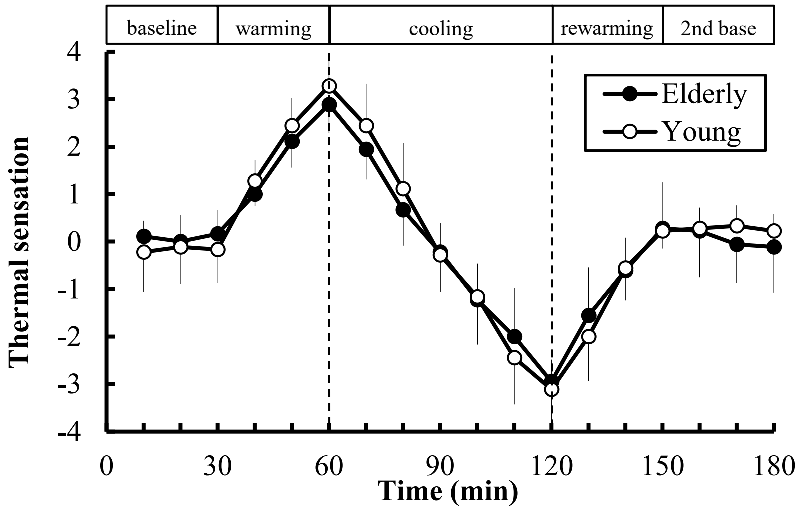

baseline
warming
cooling
rewarming
2nd base
A
Time : *P*<0.05
Group x Time : *P*<0.01
Rectal temperature (°C)
37.8
37.6
37.4
37.2
37.0
36.8
36.6
36.4
Elderly
Young
*
B
Mean skin temperature (°C)
38.0
36.0
34.0
32.0
30.0
28.0
*
**
C
Hand skin temperature (°C)
26.0
D
Forearm and finger skin temperature diff. (°C)
Time : *P*<0.01
Group x Time : *P*<0.05
12.0
10.0
8.0
6.0
4.0
2.0
0.0
-2.0
0
30
60
90
120
150
180
Time (min)

Figure 3


baseline
warming
cooling
rewarm
2nd base
A
Elderly
Young
Systolic blood pressure (mmHg)
Time : P<0.01
Group x Time : P<0.01
Time (min)
B
Diastolic blood pressure (mmHg)
Time : P<0.01
Group x Time : P<0.01
C
Mean arterial pressure (mmHg)
Time : P<0.01
Group x Time : P<0.01
D
Skin blood flow in forearm (%)
Time : P<0.01
Group x Time : P<0.01
Group: P<0.05
E
CVC in forearm (%/mmHg)
Time : P<0.01
Group x Time : P<0.01
Group: P<0.05
F
Heart Rate (beats/min)
Time : P<0.05
Group x Time : P<0.01
0
30
60
90
120
150
180


baseline
warming
cooling
rewarming
2nd base
Thermal sensation
4
3
2
1
0
-1
-2
-3
-4
0
30
60
90
120
150
180
Time (min)
Elderly
Young

Author Statement

Author contributions

YT, KY, KF, and HK conceived and designed research. KY, KF, YK, and HK conducted the experiments. YT, KY, KF, and HW analyzed data. YT and HW wrote the draft of the manuscript. All authors read and approved the manuscript.