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1 **Title**

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

5 **Authors**

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1
2 **21 Abstract**
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5 22 This study aimed to determine age-related differences in thermoregulatory and cardiovascular
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7 23 responses to a wide range of gradual ambient temperature (T_a) changes. Morphologically
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10 24 matched normotensive elderly and young males participated. The participants wearing only
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13 25 shorts rested during the 3-hour experiment. After 30 minutes of baseline at 28°C, T_a increased
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16 26 linearly to 43°C in 30 min (warming) and then gradually decreased to 13°C in 60 min (cooling).
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19 27 T_a was rewarmed to 28°C in 30 min (rewarming), and that temperature was maintained for an
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22 28 additional 30 min (second baseline). During the warming phase, there were no age-related
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25 29 differences in blood pressure (BP) and rectal temperature (T_{re}), despite a significantly lower
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27 30 cutaneous vascular conductance and heart rate in the elderly ($P<0.05$). **At the end of the cooling**
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30 31 phase, systolic blood pressure (SBP) in the elderly was significantly higher than the young
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33 32 (**155.8±16.1 and 125.0±12.5 mmHg**, $P<0.01$). There was a consistent age group difference in
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36 33 SBP during rewarming. Mean skin temperature was significantly lower in the elderly during
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39 34 rewarming ($P<0.05$). T_{re} decreased more in the elderly and was significantly lower at the end of
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42 35 the experiment than the younger participants (**36.78±0.34 and 37.01±0.15°C**, $P<0.05$). However,
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45 36 there were no age group differences in thermal sensation. In conclusion, even normotensive
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48 37 elderly participants have a greater and more persistent BP response to cold than younger adults,
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51 38 suggesting that the elderly might be at a higher risk of cardiac events during cooling and
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53 39 subsequent rewarming.
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58 **41 Keywords**
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2 42 Elderly, Ambient temperature change, Blood pressure, Cutaneous vascular conductance, Rectal
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5 43 temperature, Skin temperature
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10 45 **Abbreviations**
11
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13 46 Ad Body surface area
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16 47 BP Blood pressure
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19 48 CVC Cutaneous vascular conductance
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22 49 DBP Diastolic blood pressure
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24 50 HR Heart rate
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27 51 MAP Mean arterial blood pressure
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30 52 RH Relative humidity
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33 53 SBP Systolic blood pressure
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36 54 SkBF Skin blood flow
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39 55 T_a Ambient temperature
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41 56 T_{f-f} Skin temperature difference between forearm and finger
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44 57 T_{hand} Hand skin temperatures
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47 58 T_{re} Rectal temperature
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50 59 \bar{T}_{sk} Mean skin temperature
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53 60 TS Thermal sensation
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55 61 **WHO World Health Organization**
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2 **63 1. Introduction**
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5 64 Field and epidemiological studies demonstrate that air temperature affects human health,
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7 65 especially in the elderly (e.g., Yu et al. 2012). Many experimental studies have focused on the
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10 66 physiological and subjective responses of the elderly to heat and cold exposure.
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13 67 Thermoregulatory responses to cold and heat load are sluggish and weakened in the elderly
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16 68 compared to the young (e.g., Kenney and Munce 2003). Core temperatures increase more in
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19 69 older adults than younger individuals during heat exposure mainly due to reduced sweat gland
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22 70 output and skin blood flow (Inoue et al. 1996; Kenney and Munce 2003; Kenny et al. 2017).
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25 71 During cold exposure, the core temperature in the elderly decreases more due to an attenuated
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28 72 vasoconstrictor response (Inoue and Shibasaki 1996; Frank et al. 2000; Kenney and Munce
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31 73 2003; DeGroot et al. 2007) and/or less heat production (Frank et al. 2000; Kingma et al. 2011)
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33 74 compared to the young.

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36 75 Cardiovascular responses to heat and cold stress deteriorate in older adults. During heat
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39 76 exposure, cardiac output decreased in older more than younger people (Minson et al. 1998;
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42 77 Gagnon et al. 2016). During cold exposure, systolic blood pressure (SBP) increases more in the
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45 78 elderly than in the young (Wagner and Horvath 1985; Tochiara et al. 1993; Collins et al. 1995;
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48 79 Jansen et al. 2001; Hess et al. 2009; Hashiguchi et al. 2011). Many previous studies on
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51 80 age-related differences in thermoregulatory and cardiovascular responses were conducted
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54 81 during sudden and steady state exposure to cold and heat, since it has been well known that the
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57 82 temperature disparity between warm living room and cold bedroom or dressing room would be
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60 83 a risk of cardiac events in the elderly people (Umishio et al. 2019; Tochiara et al. 2012).
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2 84 Whereas, daily fluctuation of the ambient temperature (T_a) in one room could also induce larger
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5 85 variation in blood pressure (BP), which is associated with cardiovascular disease (Kario 2016).
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7 86 Despite WHO recommends indoor T_a should be above 18 °C (WHO 2018), a recent nationwide
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10 87 survey in Japan revealed that the lowest living room temperature in winter is only 12.6 °C on
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12
13 88 average and below 18 °C in 90 % of houses (Umishio et al. 2020). The room temperature fall at
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16 89 night in poorly insulated house with local heating might induce morning hypertension (Umishio
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18
19 90 et al. 2019), which is strongly associated with cardiovascular events (Karino 2016). However,
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22 91 physiological responses during slow gradual T_a changes have only been investigated in limited
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25 92 number of studies (Ohnaka et al. 1993; DeGroot and Kenney 2007; Schellen et al. 2010).
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27 93 Moreover, in previous studies, T_a was altered within a relatively narrow range of mild cold and
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30 94 warm temperatures (19–28 °C, Ohnaka et al. 1993; 17–25 °C, Schellen et al. 2010) or between
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33 95 neutral and hot (21.5–39.5 °C, Ogawa et al. 1993). Thus, in older adults, the response to a wide
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36 96 range of gradual T_a changes, especially to severe cold environment below the recommended
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39 97 lowest indoor T_a (WHO 2018), is unclear. Additionally, persistent high BP in the elderly during
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42 98 rewarming after mild cold exposure was reported (Kingma et al. 2011). Thus, age-related
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45 99 differences in the cardiovascular responses after severe cold exposure are another concern that
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47 100 needs further investigation.

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49 101 Physiological responses to heat and cold are affected by anthropological characteristics,
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52 102 including body fat and body surface area to mass ratio (Ad/mass) (Inoue et al. 2009; Kenny and
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55 103 Munce 2003). Additionally, basal function of the cardiovascular system, such as resting blood
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58 104 pressure, affect physiological responses to heat and cold exposure (Shigeomi et al. 2001; Kenny
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2 105 et al. 2010; Hintsala et al. 2014). In general, the elderly have more body fat, higher **body mass**
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4 106 **index (BMI) and** Ad/mass ratio, and higher basal blood pressure than the young (Umemura et al.
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6
7 107 2019). Thus, thermoregulatory and cardiovascular responses in the elderly are often confounded
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9
10 108 by morphological characteristics and higher resting blood pressure. **Controlling for** these
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13 109 confounding factors when making age group comparisons will clarify the **thermoregulatory and**
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16 110 **cardiovascular response per se** to hot and cold in older adults.

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18 111 The purpose of this study was to determine age-related differences in thermoregulatory and
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21 112 cardiovascular response during a wide range of T_a changes from severe heat to cold and
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24 113 subsequent rewarming. Morphologically matched normotensive older and younger participants
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27 114 were compared to remove the confounding bias of body fat **difference**, Ad/mass ratio, and BP in
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30 115 the elderly. We hypothesized that even in the normotensive elderly, impairment in
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33 116 thermoregulatory and cardiovascular response to wide range of ambient temperature would be
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36 117 **observed** compared to the younger counterparts with matched **morphological** characteristics. In
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39 118 addition, **persistent** hypertension would be **observed** during rewarming after severe cold
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42 119 exposure even in the normotensive elderly.

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45 46 121 **2. Methods**

47 48 49 122 *2.1. Participants*

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52 123 Nine healthy young males and nine healthy elderly males participated in this study. Table 1
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55 124 shows the physical characteristics of the subjects for both groups in Mean±SD. Body surface
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58 125 area (Ad) was estimated according to the equation of Takahira (1925). The percentage of body
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2 126 fat (%fat) was estimated from the sum of skinfold thickness on the back and upper arms
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4 127 (Nagamine and Suzuki 1964). Although, there were significant differences ($P < 0.01$) in age and
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7 128 height between the young and elderly groups, other morphological characteristics, including
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10 129 mass, BMI, %fat, Ad/mass and three points skinfold thickness were not significantly different.
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13 130 Before enrolling in the study, all participants were examined by a medical doctor to confirm that
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16 131 they were normotensive (systolic and diastolic blood pressure were less than 140 and 90 mmHg,
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18 132 respectively), with no medication, and no history of cardiovascular disease. Participants were
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21 133 selected by matching their basal blood pressure and morphological characteristics between the
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24 134 groups. A medical doctor attended in all experiments involving the elderly to check their health
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27 135 condition. All volunteers provided written informed consent after receiving a full explanation of
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30 136 the study requirements and the risks involved. The Institutional Review Board of Kyushu
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33 137 University approved the experimental protocol (#108).

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37 38 139 2.2. Procedures

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41 140 The experiments were conducted during the summer, beginning around 10 a.m. At the
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44 141 beginning of each experiment, T_a , the relative humidity (RH), and air velocity of the climatic
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47 142 chamber were set at 28 °C, 65%, and less than 0.15 m/sec, respectively. Participants wore shorts,
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49
50 143 and sensors and devices for physiological measurements were attached. Participants stayed in
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52
53 144 the chamber at rest in a sitting position for at least 30 min (baseline). Then, T_a was increased to
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55
56 145 43 °C linearly over 30 min at a rate of 0.5 °C/min (warming phase) followed by cooling to
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58 146 13 °C over 60 min at a rate of -0.5 °C/min (cooling phase). Then, T_a was rewarmed to 28 °C

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2 147 over 30 min at a rate of 0.5 °C/min (rewarming phase) and maintained for an additional 30 min
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4 148 (second baseline) as shown in Figure 1. T_a changes in the climatic chamber was measured at 10,
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6
7 149 40, 80, and 120 cm height from the floor. RH could not be controlled during the T_a changes but
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10 150 was in a similar pattern in all experiments. In general, gradually decreased to around 35% RH
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12
13 151 during the warming phase and increased to 55-60% RH during the cooling phase. The RH data
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16 152 was not available during rewarming phase due to sensor trouble.

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20 21 154 2.3. Measurements

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24 155 Rectal temperature (T_{re}) was measured at a depth of 13 cm from the anal sphincter using a
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27 156 thermistor probe (ITPO10-11, Nikkiso-YSI CO., Ltd., Japan). Skin temperatures at different
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30 157 body locations (forehead, back, abdomen, forearm, hand, finger, thigh, calf, and instep) were
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33 158 measured with thermistor probes (ITPO10-12, Nikkiso-YSI CO., Ltd., Japan). Rectal and skin
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36 159 temperatures were recorded every minute using data loggers (LT8A, Gram Corporation, Japan),
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39 160 and 10-minute averages were used for the analysis. Mean skin temperature (\bar{T}_{sk}) was calculated
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41 161 using the following modified Hardy-DuBois formula (1937).

$$42
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44 162 \bar{T}_{sk} = 0.07T_{forehead} + 0.175T_{back} + 0.175T_{abdomen} + 0.14T_{forearm} + 0.05T_{hand} \\ 45
46
47 163 + 0.19T_{thigh} + 0.13T_{calf} + 0.07T_{instep}$$

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49 164 The difference in skin temperature between the forearm and finger (T_{f-f}) was calculated to assess
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52 165 vasoconstriction and vasodilation (House and Tipton 2002; Schellen et al. 2010).
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54
55 166 Systolic and diastolic blood pressures (SBP and DBP) were measured every 10 minutes from
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58 167 the left upper arm using an automatic tonometer (HEM-737, OMRON, Japan). The mean
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2 168 arterial blood pressure (MAP) was estimated as DBP, plus one-third of the pulse pressure (SBP -
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5 169 DBP). Skin blood flow in the forearm (SkBF) was monitored using laser Doppler flowmetry
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7 170 (FLO-C1, Omegawave Inc., Japan). During the experiment, changes in SkBF (%SkBF) were
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10 171 normalized relative to the baseline (baseline was 100%). The forearm's cutaneous vascular
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13 172 conductance (CVC) was calculated by dividing the %SkBF by MAP (%/mmHg). The heart rate
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16 173 (HR) was measured using an electrocardiogram (AU-512, Fukuda Denshi, Japan) with chest
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19 174 leads. The slopes of the regression line between cardiovascular parameters (BP, CVC and HR)
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22 175 and \bar{T}_{sk} during cooling phase were calculated in each participant to evaluate sensitivity of
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24 176 cardiovascular responses to skin cooling. Shivering was detected based on the observations of
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26
27 177 the investigator. Bodyweight loss was estimated by weighing nude subjects before and after the
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30 178 experimental session using a precision body scale with a 1-gram resolution (ID2, Mettler-Toledo,
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33 179 Germany).

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35 180 Thermal sensation (TS) was rated every 10 min during the protocol using a 9-point scale (+4:
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38 181 very hot, +3: hot, +2: warm, +1: slightly warm, 0: neutral, -1: slightly cool, -2: cool, -3: cold,
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41 182 -4: very cold).

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45 46 47 184 *2.4. Statistical analysis*

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49 185 Physiological parameters were compared using a two-way repeated-measures analysis of
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52 186 variance (ANOVA), where the factors were age group and time. Age group differences in
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55 187 physiological parameters were compared using an unpaired Student's *t*-test. The group
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58 188 difference in TS was analyzed using a Mann-Whitney *U*-test. The relationships between \bar{T}_{sk} and

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2 189 blood pressure, CVC, and HR were analyzed using Pearson's correlation coefficient. All data are
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5 190 presented as mean \pm SD. Differences at $P < 0.05$ were considered significant for all statistical
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7 191 analyses. Analyses were conducted using a statistical software (IBM SPSS Statistics version 20,
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10 192 IBM).

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14 15 16 194 **3. Results**

17 18 19 195 *3.1. Body temperatures*

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22 196 Changes in mean (SD) T_{re} , \bar{T}_{sk} , hand skin temperatures (T_{hand}), and T_{f-f} every 10 min for both
23
24 197 groups are shown in Figure 2. The ANOVA showed significant main effects of time and
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26
27 198 interaction between age group and time for T_{re} , \bar{T}_{sk} , T_{hand} , and T_{f-f} ($P < 0.05$). The T_{re} time course
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30 199 in both groups showed similar trends from the baseline to the heating and cooling phases (Fig.
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32
33 200 2A). However, T_{re} decreased more in the elderly during the rewarming phase, and T_{re} was
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35
36 201 significantly lower in elderly participants than young participants at the end of the experiment
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38 202 ($P < 0.05$).

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40
41 203 There were no significant differences in \bar{T}_{sk} (Fig. 2B) between the groups during the first 20
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44 204 min of the experiment, but \bar{T}_{sk} was significantly lower in the elderly compared with the young
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47 205 at 30 and 40 min during warming phase ($P < 0.05$). During the cooling phases, \bar{T}_{sk} did not differ
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50 206 significantly between the two groups. However, \bar{T}_{sk} was significantly lower in the elderly
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53 207 compared with the young during the last 60 min of the experiment (rewarming phase and
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55 208 second baseline) ($P < 0.05$). Similar trends were also found in $T_{forehead}$, $T_{abdomen}$, T_{thigh} , and T_{calf} .

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58 209 The time course and age-related differences in T_{hand} (Fig. 2C) showed specific trends compared

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2 210 with other skin regions. There were no differences in T_{hand} between the groups for the first 80
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4 211 min (from baseline to warming phase) of the experiment. However, during the cooling period,
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7 212 T_{hand} in the elderly was significantly higher than T_{hand} in the young ($P < 0.05$). During the
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10 213 rewarming phase at 130 min, T_{hand} reached the lowest value, and the average difference in T_{hand}
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12
13 214 between groups was 1.56 °C ($P < 0.01$). After that, T_{hand} of the young rewarmed by an average
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16 215 of 3.81 °C at the end of the experiment, but the elderly rewarmed by only 1.07 °C. There were
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19 216 no age-related differences in $T_{\text{f-f}}$ during the baseline, warming, cooling, and rewarming periods
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22 217 (Fig. 2D). However, $T_{\text{f-f}}$ of the elderly was significantly greater during the second baseline than
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24
25 218 the young ($P < 0.05$).

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27 219

28 29 30 220 *3.2. Thermoregulatory and cardiovascular responses*

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33 221 The mean SBP, DBP, MAP, %SkBF, CVC, and HR at 10 min intervals are shown in Figure 3.
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36 222 The ANOVA showed significant main effects of time ($P < 0.05$) and significant interactions
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38
39 223 between age groups and time ($P < 0.01$) for SBP, DBP, MAP, %SkBF, CVC, and HR. There
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41
42 224 were no differences in SBP between the groups for the first 100 min of the experiment (Fig. 3A).
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44
45 225 However, during the cooling phase, the SBP of the elderly was significantly higher than the
46
47
48 226 young participants ($P < 0.05$). SBP in the young decreased to the first baseline level during the
49
50
51 227 rewarming period. In contrast, SBP in the elderly remained elevated and the significant group
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54 228 differences continued through the second baseline until the end of the experiment ($P < 0.05$).
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57 229 Significant group differences in DBP were observed during the cooling phase at 110 min and
58
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60 230 during the rewarming phase at 140 min ($P < 0.05$, Fig. 3B). Changes in MAP were similar to

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2 231 SBP (Fig. 3C).
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4 232 %SkBF during the warming phase was significantly higher in the young group compared with
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7 233 the elderly group ($P < 0.05$, Fig. 3D), which peaked at the end of the phase and was 1.7-fold
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10 234 higher in the young. During the cooling phase, %SkBF decreased in both groups to less than the
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13 235 baseline level; there were no age-related differences at the latter half of the phase. During the
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16 236 rewarming phase and the second baseline, %SkBF was still less than the baseline in both groups.
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19 237 Time course changes in CVC were similar to %SkBF (Fig. 3E).
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22 238 HR was significantly lower in the elderly than in the young from the baseline to the first half of
23
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25 239 the experiment's cooling phase ($P < 0.05$, Fig. 3F). During the first 30-min of baseline, the
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27
28 240 average HR was 67.3 ± 12.3 beats/min and 76.7 ± 6.2 beats/min in the elderly and the young,
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30
31 241 respectively. The increase in HR from the baseline was significantly less in the elderly (2.9 ± 3.4
32
33
34 242 beats/min) than in the young participants (5.9 ± 1.5 beats/min) during the warming phase ($P <$
35
36
37 243 0.05). The reduction of HR during the cooling phase was significantly less in the elderly (-10.2
38
39
40 244 ± 2.0 beats/min) than in the young participants (-15.6 ± 4.1 beats/min) ($P < 0.05$). During the
41
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43 245 rewarming phase and the second baseline, there were slight recoveries in HR for both groups
44
45
46 246 and no significant differences between groups.
47
48
49 247 Total body weight loss during the 3-hour experiment tended to be smaller in the elderly ($103 \pm$
50
51
52 248 13 g/m²) than in the young participants (123 ± 3 g/m²), but group differences were not
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55 249 statistically significant. No visible shivering was observed during the experiments for any
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58 250 subjects.
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252 *3.3. Sensitivity of the cardiovascular response to mean skin temperature reduction*

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

259

260 *3.4. Subjective response*

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

263

264 **4. Discussion**

265 Several reports focused on age-related differences in BP and body temperature regulation during
266 cooling and rewarming. The elderly generally have greater body fat (Inoue et al. 1992; Kingma
267 et al. 2001; Ohlendorf et al. 2020) and higher baseline blood pressure (DeGroot and Kenney
268 2007; Uemura et al. 2019) than younger individuals. However, these reports do not account for
269 the confounding effects of morphological characteristics and resting blood pressure on the
270 response to temperature changes. Therefore, in this study, the participants were selected to
271 minimize differences between the young and elderly groups in their body fatness, Ad/mass ratio,
272 **BMI**, and basal blood pressure. This selection enabled us to focus on the age-related differences

1
2 273 in thermoregulatory and cardiovascular responses to dynamic changes in ambient temperatures.
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6
7 275 *4.1. Cardiovascular and thermal responses during warming*
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10 276 In this study, despite the similar baseline blood pressures, the significantly lower
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12
13 277 forearm %SkBF and CVC in the elderly during heat exposure (Fig. 3DE), was in line with
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16 278 previous studies reporting smaller increases in skin blood flow in the elderly (Kenney and
17
18
19 279 Munce 2003; Kenny et al. 2017). This result suggests that dry heat loss (vasodilation response
20
21
22 280 to the heat) is impaired in the elderly.
23
24 281 There were significant age-related differences in cardiac response (HR) to heat in addition to
25
26
27 282 the %SkBF and CVC. From baseline to the hot environment period, HR was significantly lower,
28
29
30 283 and HR increased less in response to heat stress in the elderly compared with the young group
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32
33 284 (Fig. 3F). In agreement with this result, previous research demonstrated a lower HR response to
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36 285 passive heating in the elderly than young participants (Inoue and Shibasaki 1996; Miwa et al.
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39 286 2002; Gagnon et al. 2015; Gagnon et al. 2016). Recently, Kenny et al. (2017) reported
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42 287 significantly lower cardiac output, HR, and limb blood flow in the elderly after 3 hours of heat
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45 288 exposure (44 °C) compared with the young. Young people have sufficient cardiac output to
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48 289 support greater skin vasodilation in hot environment; whereas, both the cardiac response and
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51 290 skin vasodilation are impaired in older adults during heat exposure (Inoue et al. 2009).
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53 291 Despite the lower %SkBF, CVC and HR in the elderly group, there were no group differences
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56 292 in core body temperature (T_{re}) during warming and the subsequent cooling phase (Fig. 2A).
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58 293 Previous reports demonstrate a slight increase in T_{re} (37.8 and 37.6 °C in the elderly and young,
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1
2 294 respectively) and a moderate increase in HR (18–20 beats/min) after 3 hours of heat exposure at
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5 295 44 °C (Kenny et al. 2017). In the present study, the increase in HR during the 30-min gradual
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7 296 warming period to 43 °C was only 3–6 beats/min. Furthermore, total body weight loss during
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10 297 the 3-hour experiment was only 103–123 g/m². These results indicate that **the heat stress**
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13 298 **induced by our protocol might not be severe enough to evaluate age-related difference in**
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16 299 **sudomotor response to elevated core body temperature.**

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18 300 During the gradual warming phase, blood pressure (SBP, DBP, and MAP) did not change
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21 301 significantly from the baseline in either age group (Fig. 3ABC). This tendency continued during
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24 302 the beginning of the cooling phase (until 90 min) when T_a was higher than the baseline. Since
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27 303 there was greater skin vasodilation (**%SkBF and CVC**) in the young participants, **one** might
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30 304 expect lower blood pressure. However, blood pressure was maintained in both groups during the
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33 305 warming phase. In line with the present study, previous studies reported that MAP was
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36 306 maintained when young or elderly individuals were exposed to long periods of moderate
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39 307 (Kenny et al. 2017) or severe heat (Minson et al. 1998).

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42 43 44 309 *4.2. Cardiovascular and thermal responses during cooling and rewarming*

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47 310 During the cooling phase (60–120 min), \bar{T}_{sk} decreased in both groups with no group differences
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50 311 (Fig. 2B). However, T_{hand} was significantly higher in the elderly group during the latter half of
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53 312 cooling (Fig. 2C). The difference in T_{hand} may be due to less vasoconstriction in the extremities
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56 313 in the elderly (Richardson et al. 1992; Tochiara et al. 1993; Frank et al. 2000). The higher T_{hand}
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59 314 in the elderly continued during the substantial rewarming phase, which may have led to greater

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2 315 heat loss and a drop in T_{re} (Fig. 2A). However, during rewarming and the second baseline, \bar{T}_{sk}
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4 316 was significantly lower in the elderly group (Fig. 2B). Also, the elderly participants showed
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7 317 significantly greater T_{f-f} , a surrogate index of vasoconstriction (House and Tipton et al. 2002), at
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10 318 the second baseline (Fig. 2D). This data suggests that vasoconstriction in the elderly during the
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13 319 second baseline was greater than in the young. Even with less heat loss in the elderly, indicated
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16 320 by the lower \bar{T}_{sk} and greater T_{f-f} , the decrease in T_{re} was greater than in the young during the
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19 321 rewarming and second baseline periods (Fig. 2A). One of the potential mechanisms for
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22 322 explaining the continuous drop in T_{re} during rewarming phase would be greater venous return in
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25 323 the elderly from cooler extremities to the core body region (Natsume et al. 1992).
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27 324 Considering heat balance regulating core body temperature and the matched morphological
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30 325 characteristics in this study, the elderly group likely had less cold-induced thermogenesis (CIT)
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33 326 during the cooling phase. Several reports demonstrate less metabolic heat production in older
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36 327 adults and their core body temperature decreases more during mild cold exposure (DeGroot and
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39 328 Kenney 2007; Kingma et al. 2011). One limitation of the present study is that metabolic heat
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42 329 production was not measured. However, considering previous studies' findings (Kingma et al.
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44 330 2011; Chen et al. 2013), the greater core temperature drop in the elderly can be at least partly
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47 331 explained by less CIT, which might be associated with less brown adipose tissue activity in
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50 332 older adults (Yoneshiro et al. 2011; Chen et al., 2013).
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53 333 BP in hypertensive elderly individuals increases more in response to cold exposure (Shigeomi et
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56 334 al. 2001) or reaches higher level with similar BP change from baseline compared to
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59 335 normotensive counterparts (Hintsala et al. 2014). This study's major finding is that even in
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2 336 non-hypertensive elderly individuals, BP increased more during the cooling phase than in the
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5 337 young (Fig. 3ABC). Especially, BP increased rapidly in the last 20 min of the phase and
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7 338 significant age-group difference was observed at 110 and 120 min when T_a was below 18 °C,
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10 339 which is the lowest indoor temperature of the WHO guideline (WHO 2018). The average
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13 340 forearm %SkBF in the elderly group was maintained at baseline level at 100 min ($T_a = 23$ °C),
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16 341 then decreased to 65.8% of baseline at 110 min when T_a reached 18 °C. Thus, it is suggested
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19 342 that the rapid increase in BP in the elderly would be induced when T_a dropped below the
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22 343 threshold for cutaneous vasoconstriction. This rapid increase in BP during gradual cooling may
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25 344 also increase the risk of cardiac events. The age-related difference in BP response to cold would
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28 345 be explained by the greater sensitivity of SBP and MAP to the reduction in \bar{T}_{sk} in the elderly
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31 346 (Table 2). In contrast, the reduction in HR in response to \bar{T}_{sk} cooling was significantly less in
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34 347 the elderly (Table 2). These results indicate that HR downregulation might be dampened in older
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37 348 adults due to impaired baroreflex for maintaining BP (Laitinen et al. 1998).
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40 349 In general, skin temperature cooling induces cutaneous and visceral vasoconstriction, resulting
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43 350 in increased BP (Hess et al. 2009; Wilson et al. 2007). In this study, there were no group
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46 351 differences in %SkBF and CVC in the forearm, \bar{T}_{sk} , or T_{f-f} during the latter half of the cooling
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49 352 phase; the level of cutaneous vasoconstriction may be similar in the two groups. Therefore, the
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52 353 age-related difference in BP regulation during cold exposure can be explained by the reduced
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55 354 sensitivity of the baroreflex in the elderly (Laitinen et al. 1998; O'Mahony et al. 2000; Monahan
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58 355 2007; Okada et al. 2012) and/or greater vascular resistance due to stiffer blood vessels (Hess et
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61 356 al. 2009). At the thermoneutral baseline, the non-hypertensive elderly participants in this study,

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2 357 who may have higher vascular stiffness, could maintain their basal BP with downregulation of
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4 358 resting HR. However, the elderly participants could not regulate their BP in a cold environment
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7 359 as their younger counterparts, probably because of the increased blood vessel stiffness and
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10 360 limitations in HR reduction.
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12 361 During the rewarming period, BP in the young participants returned to baseline levels, whereas
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14 362 BP in the elderly did not completely recover. Differences between the groups were highly
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16 363 significant, especially in the SBP. A large age-related gap in SBP remained throughout the
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18 364 recovery period. During rewarming and the second baseline, %SkBF and CVC in the forearm
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20 365 was similar in both groups. However, significantly lower \bar{T}_{sk} and larger T_{f-f} (Fig. 2BD) in the
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22 366 elderly reflected greater cutaneous vasoconstriction. Wilson et al. (2007) reported that
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24 367 vasoconstriction in both peripheral and visceral arteries results in increased BP during skin
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26 368 cooling. T_{re} was significantly lower in the elderly at the end of the experiment (Fig. 2A). Thus,
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28 369 the central integration of cold stimuli from deep body and skin receptors may have enhanced
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30 370 cutaneous and visceral vasoconstriction to maintain a higher BP.
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32 371 A study similar to the present study focused on persistent high BP in the elderly during
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34 372 rewarming after mild cold exposure (Kingma et al. 2011). In line with the present study, they
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36 373 reported higher SBP in the elderly during cooling and rewarming. Moreover, Kingma et al.
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38 374 (2011) suggested a greater risk of increased SBP after rewarming in the elderly, especially when
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40 375 body fat was lower. In the present study, morphological factors were excluded since
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42 376 morphological characteristics were matched between age groups. Therefore, the observed
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44 377 age-related differences in BP can be explained by the thermoregulatory responses,
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378 cardiovascular responses, and blood vessels' stiffness.

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380 *4.3. Thermal sensation during the experiment*

381 The time course of TS was similar to dynamic changes of T_a in both groups (Fig. 4). There were

382 no age-related differences in TS during the warming phase. This result is in line with a previous

383 report demonstrating similar TS in young and elderly females during 49 min of heat exposure at

384 35 °C (Tochihara et al. 1993). The time course of TS in both groups was also similar during

385 cooling, rewarming and the second baseline. Previously, Tochihara et al. (1993) investigated TS

386 of young and elderly females after sudden cold exposure at 10 °C for 49 min. The elderly felt

387 less coldness than the young immediately after entering the cold chamber; they then gradually

388 reached similar cold sensation as the young at the end of the exposure. Based on the results,

389 they suggested that elderly people would have delayed sensitivity to cold (Tochihara et al. 1993).

390 **Opposed to their result, similar TS in young and elderly groups in the present study might be**

391 **due to the protocol of the gradual temperature change.** However, a gap between the subjective

392 TS and body temperature change in the elderly was observed in this study. During rewarming

393 and the second baseline, the elderly group showed significantly lower \bar{T}_{sk} than the young, and

394 T_{re} decreased continuously throughout the experiment (Fig. 2AB), whereas, TS in both groups

395 was similar. **This might lead to blunted behavioral thermoregulation in the elderly (Natsume et**

396 **al. 1992; Ohnaka et al. 1993).** Additionally, during cooling and rewarming phase, the elderly

397 showed substantial and persistent rise in their BP (Fig. 3ABC). These results might indicate a

1
2 398 relatively blunted subjective thermal sensitivity to the reduction in body temperature in older
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4 399 adults, with higher risk of cardiac events. This could partly be supported by the **evidence**
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7 400 reporting blunted cutaneous thermal sensitivity thresholds in the elderly to warm and cold
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10 401 **stimuli** on their skin (Tochihara et al. 2011; Inoue et al. 2016). The gap between body
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13 402 temperature and TS, the **large** pressor response to cold, and a persistently higher BP during
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16 403 rewarming was observed even in the normotensive elderly participants in this study. The greater
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19 404 cold-induced cardiovascular strain and lower \bar{T}_{sk} with similar cold sensation as young adults
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22 405 could be another potential cause for the higher risk of cardiac events in the elderly, **since their**
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24 406 **thermal behavior for regulating appropriate thermal environment might be impaired.**

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28 29 408 *4.4. Limitation*

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33 409 Since metabolic rate was not measured in this study, the discussion on the age-related difference
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36 410 in their metabolic thermogenesis **and BAT activity** was speculative.

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38 411 **Physical fitness is known as one of the factors affecting physiological response to heat and cold**
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41 412 **stress (Havenith 1995; Yoshida et al. 1998). Since no group difference was observed in BMI and**
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44 413 **basal BP, the elderly participants in this study might be physically fit relative to the general**
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47 414 **elderly people. However, since the fitness level in both age groups was not measured and**
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50 415 **controlled in this study, it was not able to distinguish the confounding effect of physical fitness.**

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52 416 **There was limitation to extend the finding to different season, since the experiments were**
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55 417 **conducted in summer. Especially, physiological response to T_a reduction might differ in winter**
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58 418 **when participants are acclimatized to cold.**

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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

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440 experiments. YT, KY, KF, and HW analyzed data. YT and HW wrote the draft of the manuscript.

441 All authors read and approved the manuscript.

442

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583 **Figures captions**

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

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586 **Fig. 2** Time course of rectal temperature (A), mean skin temperature (B), hand skin temperature
587 (C), and skin temperature difference between forearm and finger (D). Values are means and
588 standard deviation. * and ** indicate significant differences between groups ($P < 0.05$ and $P <$
589 0.01 , respectively).

590

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

595

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

599

600 **Table 1** Physical characteristics of the subjects (Mean \pm SD).

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

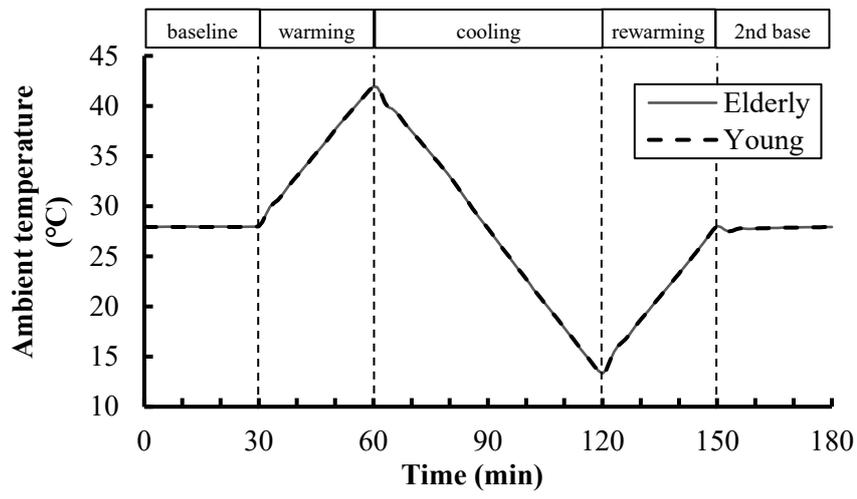
601 Ad: body surface area, SF: skinfold thickness; ** $P < 0.01$

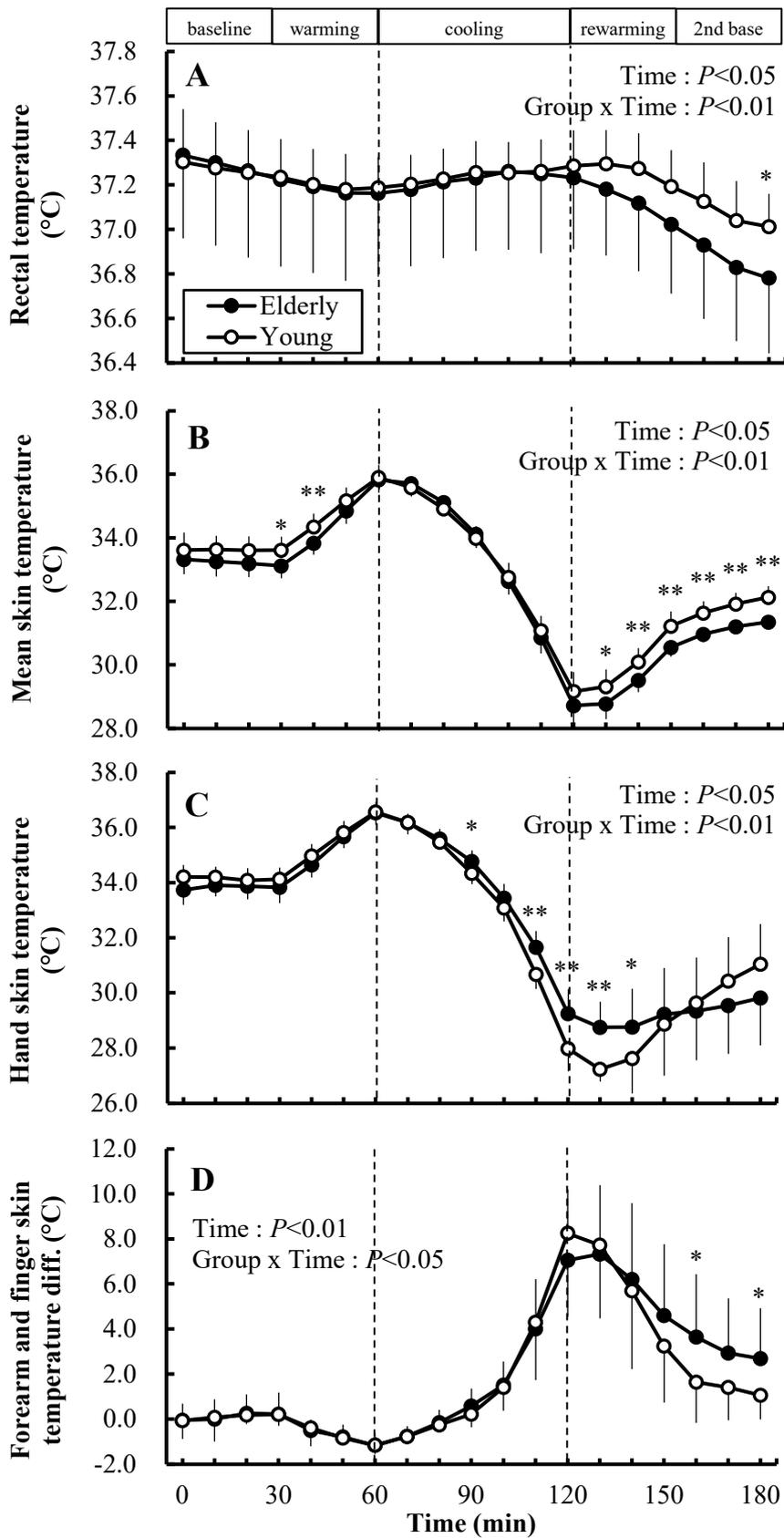
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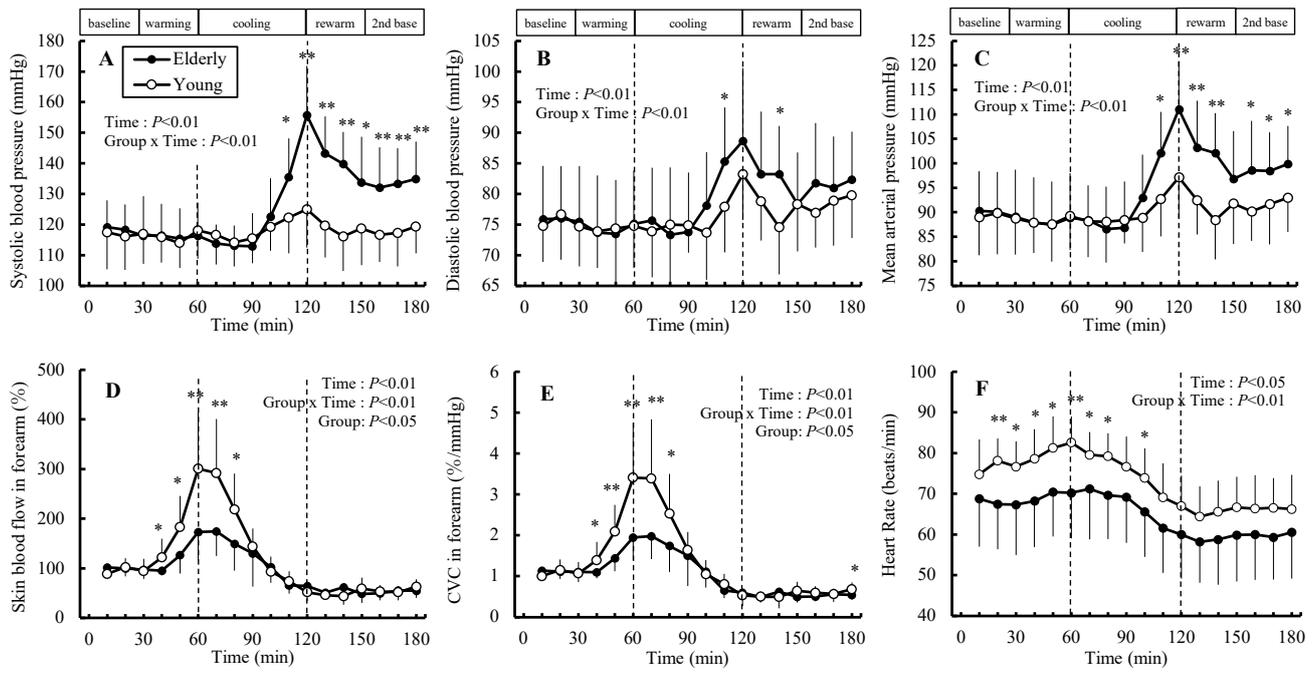
603 **Table 2** Sensitivity of the cardiovascular response to mean skin temperature reduction during
604 the cooling phase (Mean \pm SD).

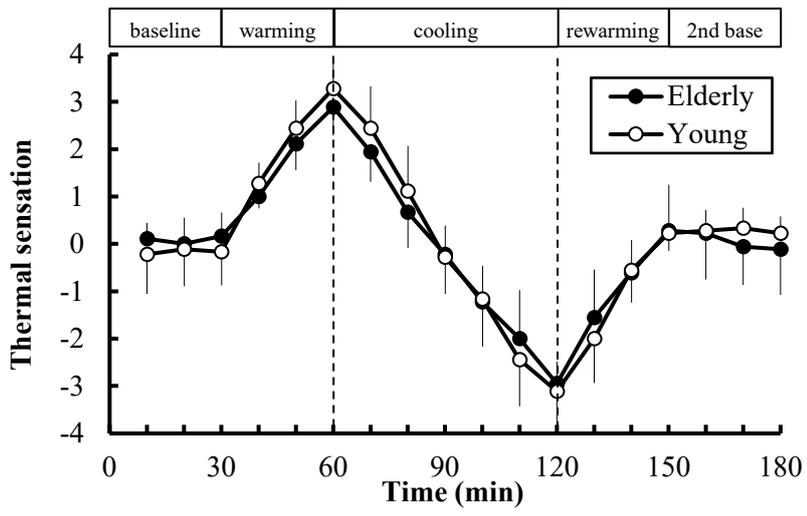
	Elderly		Young
Sensitivity of SBP to \bar{T}_{sk} (mmHg/ $^{\circ}$ C)	-5.65 \pm 1.82	**	-1.36 \pm 1.23
Sensitivity of DBP to \bar{T}_{sk} (mmHg/ $^{\circ}$ C)	-2.10 \pm 0.61		-1.20 \pm 1.16
Sensitivity of MAP to \bar{T}_{sk} (mmHg/ $^{\circ}$ C)	-3.28 \pm 0.63	**	-1.25 \pm 1.12
Sensitivity of CVC to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

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









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.