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PLEASE CITE THE PUBLISHED VERSION

https://doi.org/10.1016/j.jtherbio.2021.103174

PUBLISHER

Elsevier BV

VERSION

AM (Accepted Manuscript)

PUBLISHER STATEMENT

This paper was accepted for publication in the journal Journal of Thermal Biology and the definitive published version is available at https://doi.org/10.1016/j.jtherbio.2021.103174

Age Comparison of Changes in Local Warm and Cold Sensitivity due to Whole Body Cooling

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Highlights:

- During body cooling, cold sensitivity is blunted but warm sensitivity is maintained
- Warm and cold sensitivity differences may relate to activation of different TRP channels
- Age-related declines in warm sensitivity are evident in neutral and cold conditions
- Older males have impaired cold defence mechanisms during cold exposure
- Ageing is associated with increasing thermoregulatory risk with short duration cold exposure

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Funding: Loughborough University (Design School)

Ethical Approval: Loughborough Research Ethics Committee

Abstract

Purpose: This study investigated the influence of whole body cooling on local thermal sensitivity to warm (40°C) and cold (20°C) stimuli in 10 young (age: 24 ± 2 yrs) and 10 older males (age: 69 ± 4 yrs). **Methods:** Local warm and cold sensitivity was assessed at eight body regions using a 25 cm^2 pressure controlled thermal probe after 40 min of whole body exposure to a thermoneutral (NEUT: 25°C/40% RH) and a cold (COLD: 12°C/50% RH) environment. Gastrointestinal temperature (T_{gi}), mean and local skin temperature, heart rate, whole body thermal sensation and comfort, and skin blood flow were also measured. **Results:** Whole body cooling blunted local cold sensitivity but warm sensitivity was maintained in both age groups. Furthermore, a significant age-related decline (from young to older group) in sensitivity to a warm stimulus was observed in both NEUT and COLD conditions. Older males also had a greater ΔT_{gi} compared to the young but had similar thermal sensation and comfort responses. **Conclusion:** The observed interaction effect of local cold stimulation and whole body cooling may be related to both stimuli triggering similar TRP channels, whereas the lack of interaction between local warm stimuli and whole body cooling may be related to these two stimuli triggering different TRP channels. The findings reiterate the potential thermoregulatory risks (e.g. cold injury and hypothermia) associated with ageing, even with such short exposure times.

Key words: Thermal sensitivity; ageing; regional; warm; cold; cooling

Abbreviations

COLD	Cold condition
CVC	Cutaneous vascular conductance
NEUT	Neutral condition
RH	Relative humidity
SkBF	Skin blood flow
T_{gi}	Gastrointestinal (core) temperature
TRP	Transient receptor potential
T_{sk}	Skin temperature
$\bar{T}_{sk}$	Weighted mean skin temperature

1. Introduction

The way in which humans sense temperature change has been extensively investigated, with previous studies focusing on age (Dufour and Candas, 2007; Harju, 2002; Inoue et al., 2016; Kenshalo, 1986; Lautenbacher and Strian, 1991a; Meh and Denislic, 1994; Seah and Griffin, 2008; Stevens and Choo, 1998; Tochihara et al., 2011), sex (Filingeri et al., 2018; Gerrett et al., 2014; Golja et al., 2003; Inoue et al., 2016; Lautenbacher and Strian, 1991b; Luo et al., 2020) and ethnic (Havenith et al., 2020; Lee et al., 2010) differences in thermal sensitivity over the body surface. Predominantly, these investigations have been conducted in what the authors describe as 'thermoneutral' environments, ranging from 21 to 28°C. Thus it is not fully understood if altering the overall thermal state of the body affects our ability to sense local warm and cold temperatures.

Regional variations in warm and cold sensitivity are known to exist when we are exposed to thermoneutral environments within comfort limits; however there is limited knowledge on the influence of more extreme environmental exposures, such as whole body cooling. As older individuals are more susceptible to hypothermia (Collins et al., 1977; Degroot and Kenney, 2007), it is also of interest to investigate how behavioural thermoregulation and subjective responses may alter with age, during cold exposure. Thermal sensitivity and comfort are suggested to be the drivers of behavioural thermoregulation in both hot and cold environments, preceded by a change in T_{sk} and thus are vital influencers in the control and maintenance of core body temperature (Schlader et al., 2011, 2009; Vargas et al., 2019). As behavioural adjustments limit the requirement for autonomic responses, a decline in thermal sensitivity may consequently put a greater strain on the body (Schlader et al., 2017). This would be particularly detrimental during exposure to cold stress and may increase the likelihood of cold-induced injury or illness (Smolander, 2001; Watts, 1972).

Two previous studies assessed the influence of mild whole body heating on local sensitivity responses (thresholds) to warm and cold stimuli (Nakamura et al., 2008; Takeda et al., 2016). Nakamura *et al.*, (2008) focused primarily on thermal comfort responses and showed that during whole body heating, face cooling was preferable and during whole body cooling, the torso was the preferred location for warming. Takeda et al. (2016) assessed warm and cold thresholds at the forearm and chest, during thermoneutral and mild-hyperthermic conditions in young and older adults. They observed age-related declines in warm sensitivity at the forearm in both conditions, but local cold sensitivity only diminished with age in the thermoneutral condition. Furthermore, Tochihara *et al.*, (2011) assessed warm thresholds at nine body regions in 'thermoneutral' (28°C) and 'cool' (22°C) conditions and also observed non-uniform, age-related declines in warm sensitivity. Warm sensitivity was also blunted during the 'cool' condition and this was more noticeable in the older group. Most of these studies were conducted with Japanese individuals in which the thermoneutral zone and definitions of 'warm' and 'cool differ compared to European individuals, purely due to ethnic differences and habitual acclimatisation (Havenith et al., 2020, 2017; Schweiker et al., 2020). Hence, these factors must be considered when comparing findings within the literature.

A later study investigated the influence of progressive cooling on local thermal sensitivity (warm and cold magnitudes) of the hands and feet in young males (Filingeri et al., 2017). Using a water perfused suit (5°C water temperature), whole body skin temperature (T_{sk}) was decreased over a 30 min period. A thermal stimulator increased or decreased in temperature (± 8°C at 2.43°C/s) from a baseline of 30°C and individuals immediately rated their sensation using a visual analogue scale. Filingeri *et al.*, (2017), concluded that progressive decreases in whole body T_{sk} increased local warm sensitivity of the hands and feet in a dose dependent manner; however the response to local cold stimuli remained unchanged. They proposed that this was likely a result of enhanced 'warm seeking' behaviour in an attempt to regain homeostasis when cold. However, in real world situations, exposure to cold would not decrease T_{sk} in a uniform manner as it would within a water perfused suit. Thus, it is yet to be established if this same phenomenon still occurs during whole body exposure to cold air and whether other body regions respond in the same way as the hands and feet. For this reason the present study will focus on air exposure and include regions beyond the hands and feet.

Due to the growing aged population and the prevalent impact of severe cold spells in older adults, this area of research requires expanding to gain a better understanding of the effect of ageing on thermal responses during extreme weather events. Therefore, the aim of this study was to investigate the influence of whole body cooling on thermal sensitivity to local warm and cold stimuli in young and older males. It was hypothesised that whole body cooling would increase local warm sensitivity due to the increased temperature difference between the stimulus and skin, while cold sensitivity would remain the same (as observed by Filingeri et al. (2017) for the hands and feet). Further, due to an assumed decrease in temperature sensitivity with ageing, it was hypothesised that these responses would be attenuated in the older males.

2. Methodology

2.1 Participants

Twenty healthy, white Western European male volunteers were recruited from two age categories: 10 young (18-30 yrs) and 10 older (60-80 yrs). Prior to taking part, all participants were provided with detailed information about the study and subsequently gave their written informed consent. Additionally, all participants were required to complete a health-screen questionnaire and were excluded from the study if they failed to meet the required health standards. Due to the nature of the study, only participants that were non-smokers and had no history of diabetes, cardiovascular disease, skin conditions or neuromuscular disorders were recruited. All protocols and procedures involved in the study were approved by the Loughborough University Research Ethics Committee (project reference: R17-P098) and are in line with the World Medical Association Declaration of Helsinki for medical research using human participants.

2.2 Experimental design

The aim of the experiment was to assess the effect of whole body cooling on local thermal sensitivity (magnitude estimation) to warm and cold stimuli in young and older males. To achieve these aims, the study followed a balanced (order of cold or warm stimulus), independent group design. Participants attended the laboratory on two separate occasions, including a pre-experimental session and the main experimental visit. During the main experimental visit, participants completed two conditions; thermoneutral (NEUT; 25°C/40% RH) and cold (COLD; 12°C/50% RH), as shown in the protocol schematic in Figure 1.

Please insert Figure 1 near here

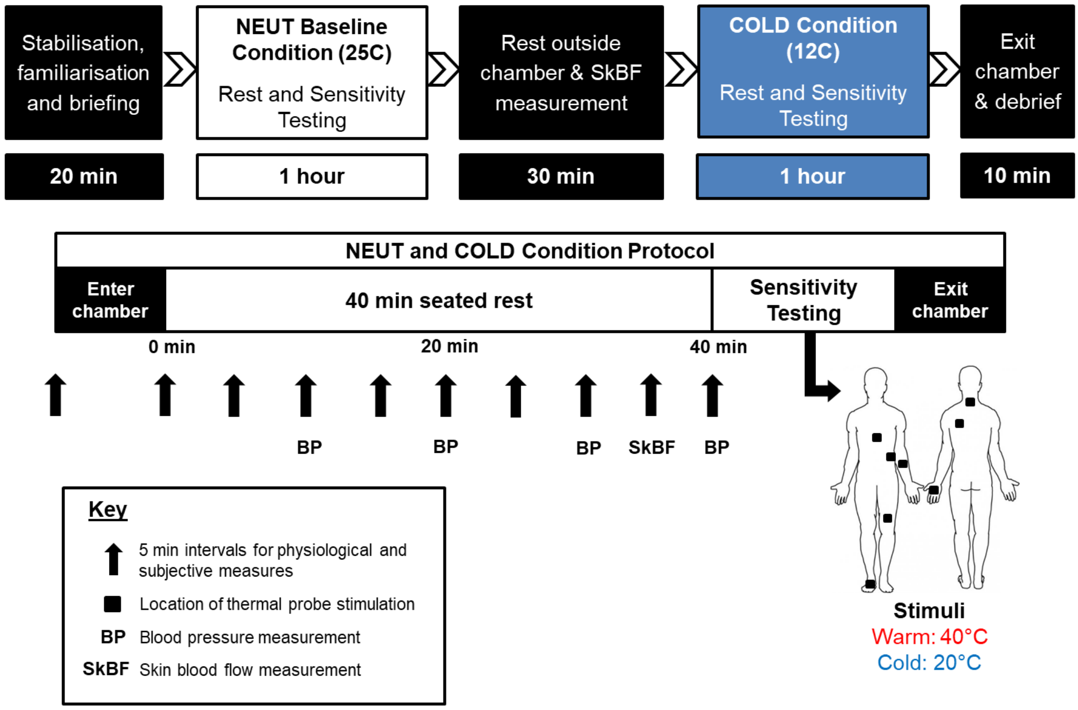

Figure 1 Study protocol schematic

2.3 Pre-experimental session

During the pre-experimental session participants were each briefed verbally, provided with written instructions detailing the requirements of the study and had the opportunity to ask any questions. Participants were instructed to refrain from alcohol 24 h prior before the main experimental visit and to avoid exercise and caffeine on the day of the visit.

Each participant was required to swallow an ingestible radio pill (e-CELSIUS® performance capsule, BodyCAP France, Inc.) for the measurement of gastrointestinal (core) temperature (T_{gi}) throughout the main experimental visit. A health screen questionnaire was completed to confirm their suitability for swallowing the pill. Before use, each pill was activated using an activator and monitor (e-Viewer® performance monitor, BodyCAP France, Inc.) which assigned a unique code for tracking. The pill was ingested 5 h before the experimental protocol was due to start.

2.4 Experimental protocol

On arrival at the laboratory for the main experimental visit, measures of participant's height in cm (Stadiometer, SECA, Leicester, UK), body mass in kg (Metter Toledo kcc150, Metter Toledo, Leicester, UK, Resolution 1g) and body fat percentage via bio-electrical impedance (Body composition analyser, Tanita, MC-780MA) were recorded. Skin fold measurements were also taken at seven sites on the body (subscapular, anterior suprailiac, anterior forearm, medial torso, knee, hand and foot), using skin fold callipers (Holtain Ltd. Crymych, Pembs, UK) to estimate skin fold thickness at specific body regions for correlation analysis.

Once all pre-test measures were recorded, participants rested in a seated position for 20 min in a thermoneutral (~22-24°C) preparation room, wearing standardised shorts and t-shirt. A step-by-step overview of the protocol order was explained to each participant including familiarisation with the custom subjective scales (Coull, 2019; Coull et al., 2020) for the rating of thermal sensation (magnitude scale ranging from -50 extremely cold to 50 extremely hot – see Figure 2A) and thermal comfort (1 comfortable to 7 very uncomfortable – see Figure 2B) (based on ISO 10551: 2019). After resting for 20 min, baseline measures of T_{gi} (e-Viewer® performance monitor, BodyCAP France, Inc.), T_{sk} at 4 body regions (Spot Infrared thermometer, FLUKE 566, IR Thermometer, Fluke Corporation, USA – calibrated using BLACKPOINT, Blackbody Calibrator, BB702, Omega, USA), heart rate (Polar wrist monitor A360, Polar Alectro Oy, FI-90440 Kempele, Finland), whole body thermal sensation/comfort and blood pressure (Omron M3 LED blood pressure monitor, HEM-7134-E, Omron Healthcare UK Ltd) were recorded.

Please insert Figure 2 near here

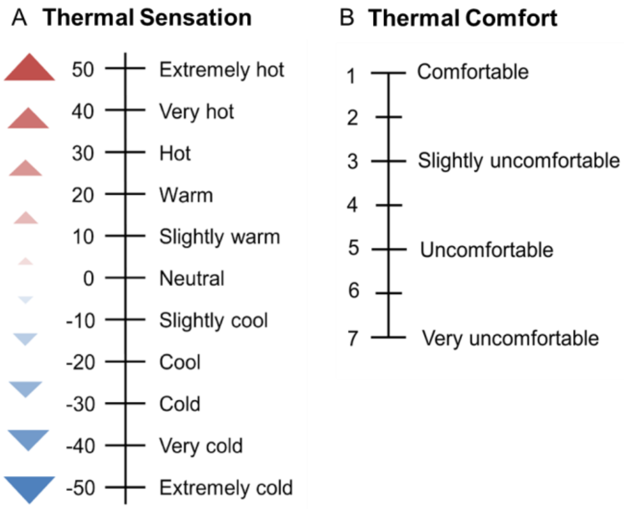

Figure 2 Custom subjective scales used for the assessment of regional and whole body thermal sensation (A) and whole body thermal comfort (B)

Participants then entered the environmental chamber (T.I.S.S. Peak Performance, Series 2009 Climate Chambers), which was set at 25°C/40% RH for the first condition (NEUT) and monitored throughout (Testo 435-2, Testo Ltd, Alton, Hampshire, UK). On entering the chamber participants rested in a seated position for 40 min. As shown in Figure 1, every 5 min during this rest period T_{gi}, local T_{sk}, heart rate, thermal sensation and comfort were recorded and blood pressure was measured every 10 min in the left arm. At 35 min, skin blood flow (SkBF) was measured for a 5 min period on the right forearm using a single fibre laser-Doppler flowmetry probe and perfusion monitor (Moor-Lab, Moor Instruments, Devon, UK). Each participant's right arm was supported in a fixed and comfortable position during the measurement to minimise movement. The area of skin used for the SkBF measurement was highlighted using washable marker pen to assure accurate placement of the probe during subsequent measurements.

Subsequently, participants were then thoroughly familiarised with the thermal sensitivity protocol and thermal probe application procedure before the test was undertaken. The thermal probe (NTE-2, Physitemp Instruments, Inc., USA) consisted of a 25 cm^2 metal surface with a capacity to cool and heat with a range of 0-50°C. Participants removed their t-shirt and a total of 8 body regions (posterior neck, upper back, medial torso, lateral torso, forearm, hand, knee and foot) were stimulated in a balanced order (between participants) with the thermal probe for both warm (fixed at 40°C) and cold (fixed at 20°C) temperatures (Figure 1). The temperatures of the probe were chosen to ensure the warm and cold stimuli were innocuous, to avoid stimulation of the pain receptors, resulting in an asymmetric stimulus pattern (Coull (2019). The pressure applied with the probe was standardised (4.1 kPa, equivalent to 1 kg over the probe surface) between participants and body regions using an inbuilt pressure system (for further details see Coull (2019)). Participants rated their thermal sensation 10 s after probe application using the magnitude scale described above and detailed in Figure 2A. The absolute magnitude of their sensation response to the fixed temperature stimuli (warm and cold) is defined in this paper as thermal sensitivity. This is in contrast to other study approaches where thermal sensitivity is defined in terms of thresholds (Dufour and Candas 2007; Tochihara et al. 2011; Inoue et al. 2016; Takeda et al. 2016) or where magnitude is divided by the ΔT_{sk} (Filingeri et al., 2018; Luo et al., 2020).

After the sensitivity test, which lasted approximately 15 min, participants exited the environmental chamber and returned to the thermoneutral preparation room for a 30 min period. During this period between the two conditions (NEUT and COLD), participants rested in a seated position. Additionally, a SkBF measurement of maximum vasodilation was taken by applying the laser-Doppler probe, housed in a heating system set at 43°C (laser-Doppler temperature monitor, Moor Instruments, Devon, UK), to the anterior forearm until a plateau was observed. This was measured during this rest period instead of at the end of the protocol due to the potential influence of whole body cold exposure on maximal vasodilation. After approximately 30 min of rest, baseline measures were recorded again and participants re-entered the environmental chamber, this time at 12°C/50% RH for the COLD condition.

The entire procedure described above for the NEUT condition was then repeated for the COLD condition. Afterwards, participants remained in the laboratory until all measures returned to baseline for safety and comfort purposes.

2.5 Calculations

Weighted mean T_{sk} ($\overline{T}_{sk}$) was calculated for both conditions and age groups using the following equation (Ramanathan, 1964):

$$Tsk = (0.3 * Triceps) + (0.3 * Chest) + (0.2 * Quadriceps) + (0.2 * Calf)$$

Cutaneous vascular conductance (CVC) was calculated using SkBF (average flux) and mean arterial pressure [1/3(systolic – diastolic)+diastolic] data collected between 35-40 min, using the following equation:

$$CVC = \frac{flux}{MAP}$$

The %Δ from NEUT to COLD was then calculated and compared across age groups.

2.6 Statistical analysis

Statistical analysis was completed using Microsoft Excel (2010) and a statistical software package (SPSS version 23.0, IBM, USA). Age group differences in local T_{sk} and regional thermal sensitivity to warm and cold were assessed using a two-way repeated measures ANOVA. The large number of regions assessed may have increased the likelihood of inflating type I error and so Bonferroni corrections were applied to account for multiple comparisons. Results are presented with and without Bonferroni corrections as the first has the risk of inflating type I error, whereas the second has the risk of inflating type II (Havenith et al., 2008). Age group differences in participant characteristics and environmental conditions were assessed using independent samples *t*-tests. Whole body thermal sensation and comfort and all other physiological measures were analysed using a two-way repeated measures ANOVA with Bonferroni post hoc tests. Pearson correlations were performed to assess relationships between regional skin fold thickness, T_{sk}, SkBF and thermal sensitivity. Unless otherwise stated, significance was set at $p < 0.05$ and all data are presented as means ± standard deviation.

3. Results

3.1 Participant characteristics

Participants recruited for this study differed in age (young: 24 ± 2 yrs Vs older: 69 ± 4 yrs, $p < 0.001$) but were matched for height (young: 179.8 ± 7.7 cm Vs older: 175.3 ± 4.6 cm, $p > 0.05$), weight (young: 78.1 ± 11.1 kg Vs older: 76.9 ± 9.7 kg, $p > 0.05$) and body surface area (young: 2.0 ± 0.2 m^2 Vs older: 1.9 ± 0.1 m^2, $p > 0.05$). The older group had a significantly higher ($p < 0.01$) body fat percentage (20.9 ± 3.6%) compared to the young (15.9 ± 2.5%), which is representative of the general population at the respective ages used (Mott et al., 1999).

3.2 Environmental conditions

There were no significant differences ($p > 0.05$) in the ambient air temperature and relative humidity between age groups in the NEUT (young: 25.1 ± 0.1°C/ 40.2 ± 0.4% RH Vs older: 25.1 ± 0.1°C/ 40.2 ± 0.7% RH) or COLD condition (young: 12.1 ± 0.1°C/ 49.2 ± 0.7% RH Vs older: 12.1 ± 0.1°C/ 48.7 ± 1.3% RH).

3.3 Gastrointestinal temperature

No significant differences in T_{gi} ($p > 0.05$) were observed between age groups in the NEUT condition, however in the COLD condition, older males had a significantly lower T_{gi} ($p < 0.05$) than the young (Figure 3A). In the young group, T_{gi} was briefly lower at the start of COLD compared to NEUT ($p < 0.05$). In the older group, T_{gi} was significantly lower in the COLD compared to NEUT ($p < 0.05$).

The ΔT_{gi} from pre-post in both conditions was compared between age groups. Older individuals had a significantly greater ΔT_{gi} than the young group (young: +0.1 ± 0.2°C Vs older: -0.2 ± 0.2°C, p = 0.003) in the COLD condition only. In the older group, this change was also significantly different from the NEUT to COLD condition (0.0 ± 0.2°C Vs -0.2 ± 0.2°C respectively, p = 0.048).

3.4 Mean skin temperature

There were no significant differences in $\bar{T}_{sk}$ between age groups in the NEUT or COLD condition ($p > 0.05$). At the PRE time point, $\bar{T}_{sk}$ was similar between age groups and conditions but between 0-40 min $\bar{T}_{sk}$ was significantly lower ($p < 0.05$) in the COLD condition, in both age groups, when compared to NEUT (Figure 3B).

Please insert Figure 3 near here

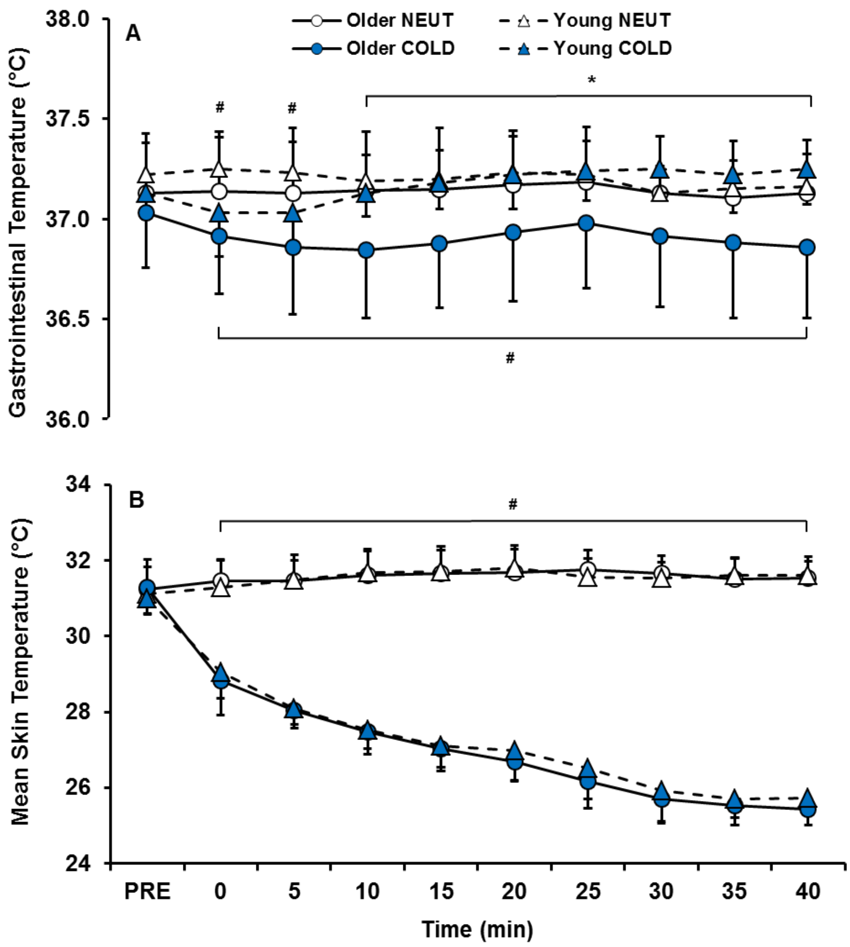

Figure 3 Gastrointestinal temperature (°C) (A) and weighted mean skin temperature (°C) (B) in the NEUT (25°C/40% RH) and COLD (12°C/50% RH) condition between young and older males. *(A) Significantly different between groups in COLD condition only. #(A)Significantly different between conditions in the young group (0 and 5 min) and in the older group (0-40 min). #(B) Significantly different between conditions at 0-40 min in both ages groups

3.5 Local skin temperature

The local T_{sk} of eight body regions were recorded before applying the thermal probe (before both warm and cold stimuli) to the skin in the NEUT and COLD condition. There were no significant differences in local T_{sk} prior to application of the warm and cold probe in either condition in both age groups ($p > 0.05$). Significant differences were observed between age groups at several body regions in both conditions (see Table 1 and 2 in supplementary materials).

3.6 Heart rate

Over time heart rate remained stable throughout the NEUT and COLD condition in both age groups and did not significantly differ between conditions ($p > 0.05$) or between age groups (NEUT: young: 73.0 ± 8.2 Vs older: 74.8 ± 6.1 average bpm, $p = 0.48$; COLD: young: 71.8 ± 8.8 Vs older: 75.9 ± 11.7 average bpm, $p = 0.33$).

3.7 Cutaneous vascular conductance

The %decrease in CVC from NEUT to COLD was not significantly different ($p = 0.33$) between the young (-28.6%) and older group (-22.2%). CVC as a % of maximum (during skin heating) was significantly higher ($p \leq 0.01$) in the older compared to young group in both the NEUT (9.3 ± 3.6 Vs 5.0 ± 1.8 %CVC_{max}) and COLD condition (7.2 ± 2.6 Vs 3.3 ± 0.9 %CVC_{max}).

3.8 Thermal sensation and comfort

Whole body thermal sensation responses were not significantly different between age groups in either condition ($p > 0.05$). In both age groups, participants felt significantly colder throughout (0-40 min) the COLD condition compared to NEUT ($p < 0.05$) as shown in Figure 4A. Whole body thermal sensation remained between ‘neutral and slightly warm’ during the NEUT condition and towards the end of the COLD condition, participants felt between ‘cold and very cold’.

The thermal comfort responses followed a similar trend to thermal sensation as there were no significant differences in whole body thermal comfort between age groups ($p > 0.05$) in either condition. In both age groups, participants felt significantly more uncomfortable throughout (0-40 min) the COLD condition compared to NEUT ($p < 0.05$) as shown in Figure 4B. In the NEUT condition participants felt ‘comfortable’, however in the COLD they reported to be between 4-5 on the comfort scale, approaching ‘very uncomfortable’.

Please insert Figure 4 near here

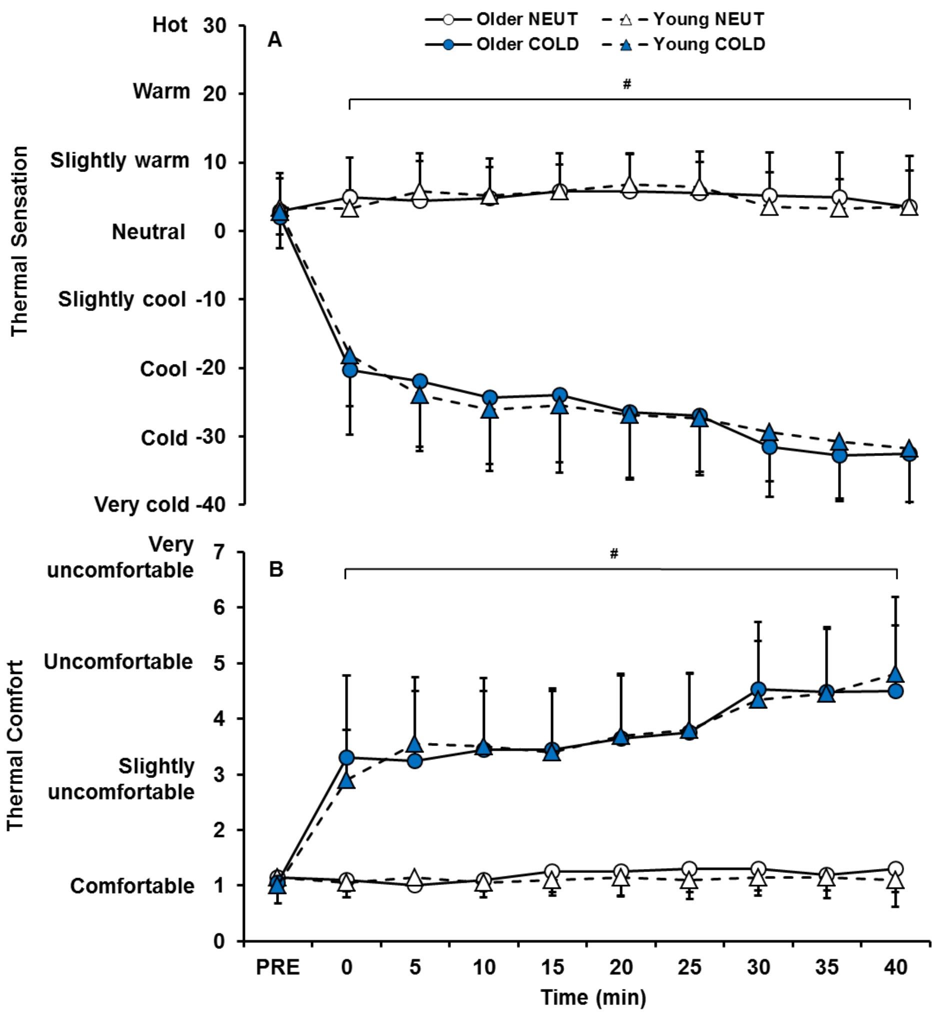

Figure 4 Whole body thermal sensation (A) and comfort (B) responses in the NEUT (25°C/40% RH) and COLD (12°C/50% RH) condition between young and older males. #Significantly different between conditions in both age groups

3.9 Overall thermal sensitivity

AGE: As shown in Figure 5, overall warm sensitivity (average of all 8 regions) was significantly greater in the young compared to older age group in both the NEUT (p = 0.001) and COLD condition (p = 0.002). However, there were no significant differences between age groups ($p > 0.05$) in cold sensitivity. CONDITION: Cold sensitivity was significantly lower in the COLD condition compared to NEUT in both age groups (p = 0.01) however there were no differences in warm sensitivity between conditions (p > 0.05).

Please insert Figure 5 near here

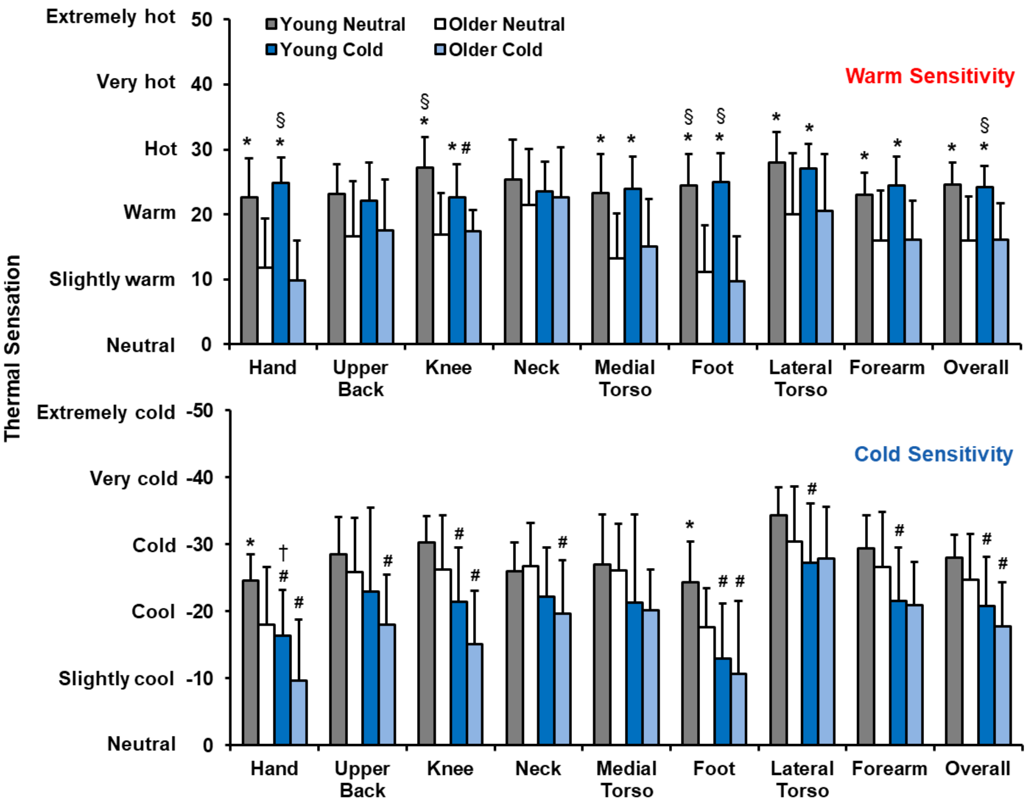

Figure 5 Warm and cold sensitivity at each body region in the NEUT (25°C/40% RH) and COLD (12°C/50% RH) condition between young and older males. *Significantly different between age groups. #Significantly different between conditions. §Significant between age groups after Bonferroni correction. †Significant between conditions after Bonferroni correction

3.10 Regional thermal sensitivity

3.10.1 Warm sensitivity

AGE: Warm sensitivity was significantly different between age groups at the same six body regions in both conditions (Figure 5); the younger group were significantly more sensitive at the hand, foot, knee, forearm, and medial and lateral torso (p < 0.05). CONDITION: Warm sensitivity was similar in the NEUT condition versus COLD for both groups, with the only exception being the knee region in the young group (p = 0.01).

The most sensitive regions were the lateral torso and knee in the young group and the lateral torso and posterior neck in the older group, in both conditions. The least sensitive body regions in the older group were the hand and foot in both conditions. However, in the young group the least sensitive regions were the hand and forearm in the NEUT condition and the upper back and knee in the COLD condition.

3.10.2 Cold sensitivity

AGE: Cold sensitivity was significantly different between age groups in only two locations in the NEUT condition only (Figure 5), with younger males reporting higher sensitivity ratings at the hand ($p = 0.04$) and the foot ($p = 0.02$). No differences were observed between age groups in the COLD condition ($p > 0.05$). CONDITION: In the young group, sensitivity was higher in the NEUT condition at the hand, foot, knee, lateral torso and forearm and in the older group at the hand, foot, knee, upper back and neck, when compared to the COLD condition.

In both conditions, the most sensitive regions to cold were the lateral torso in the young group and both the lateral torso and neck in the older group. The least sensitive regions were the hand and foot in both age groups and conditions.

3.11 ∆Thermal sensation between NEUT and COLD

The ∆sensation from the NEUT to the COLD condition was calculated for each body region in both age groups. AGE and CONDITION: Figure 6 shows that in response to a warm stimulus, there was little change in sensitivity across sites from NEUT to COLD for both age groups, but for the knee region ($p = 0.03$). However, in response to a cold stimulus a clear trend was evident, showing a decrease in sensitivity at almost all body regions from NEUT to COLD, similar for both age groups (Figure 6).

Please insert Figure 6 near here

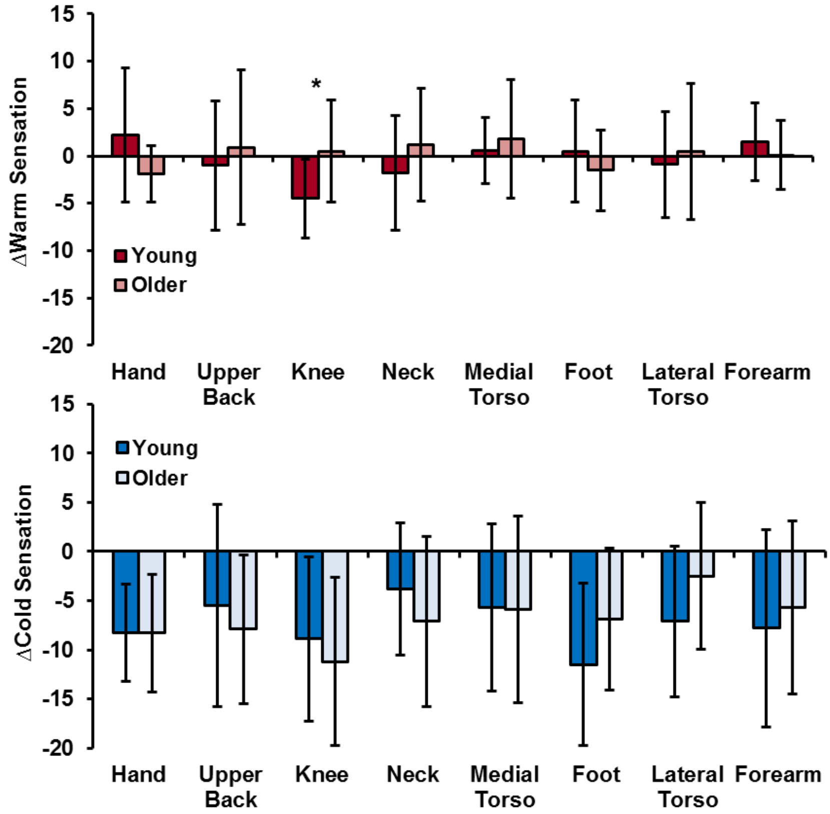

Figure 6 ΔWarm and cold sensation from the NEUT (25°C/40% RH) to the COLD (12°C/50% RH) condition between young and older males. *Significantly different between age groups. No significant differences after Bonferroni correction

3.12 Thermal sensitivity and skin fold thickness

Relationships between thermal sensitivity (warm and cold) and skin fold thickness in the NEUT and COLD condition were assessed in both age groups. No significant correlations were observed at any of the body regions assessed in either age group or condition ($p > 0.05$). The same nonsignificant finding was observed when combining both age groups to create a wider range of skin fold thickness values.

3.13 Thermal sensitivity and skin temperature

The relationship between overall thermal sensitivity and overall T_{sk} (average of 8 regions) was assessed using Pearson's correlations. No significant correlations were observed ($p > 0.05$). Further correlations were calculated to assess the relationship between local thermal sensitivity and T_{sk} at each individual body region in both age groups. In the NEUT condition (young group only), significant positive relationships were observed between local T_{sk} and warm ($r = 0.78$, $p = 0.01$) and cold sensitivity ($r = 0.66$, $p = 0.04$) at the upper back only. A similar positive relationship (young group only) was observed for cold sensitivity at the upper back ($r = 0.70$, $p = 0.02$) in the

COLD condition. This shows that participants with warmer T_{sk} had a higher thermal sensitivity score to both a warm and a cold stimulus.

3.14 Thermal sensitivity and skin blood flow

Pearson's correlations were performed to assess the relationship between overall thermal sensitivity (warm and cold) and SkBF (%CVC maximum) in both conditions and age groups. There was a significant positive correlation observed for warm sensitivity (r = 0.73, $p = 0.02$) in the older group NEUT condition only.

4. Discussion

The aim of this study was to assess the influence of whole body cooling, in a cool air environment, on local thermal sensitivity to warm and cold stimuli in young and older males relative to a neutral environment. The main finding was that whole body cooling blunted local thermal sensitivity to cold but had little to no influence on warm sensitivity, regardless of age (Figure 6). This is contrary to our hypothesis - that warm sensitivity would be affected, with greater impact in the young group. A further main finding was that the older group were less sensitive to a warm stimulus at several body regions compared to their younger counterparts.

4.1 Overall Local Thermal Sensitivity

We hypothesised that warm sensitivity would increase during whole body cooling in both age groups, due to the greater temperature difference between the stimulus and skin, while cold sensitivity would remain the same (Filingeri et al. 2017). In contrast, to the findings from Filingeri et al. (2017), overall warm sensitivity did not differ between conditions, whereas cold sensitivity was blunted during the COLD condition in both age groups. Therefore, it appears changes in stimulus and T_{sk} gradients elicited from skin cooling, affected warm sensation differently to cold.

The stable responses to a warm stimulus (from the NEUT to COLD condition) in the present study are consistent with data from West et al. (2019) and West (2019), where they conditioned feet in various ways (foot cooling and heating, exercise and thermoneutral rest), but found the same thermal sensation to a fixed warm stimulus temperature. This was despite large variations in pre-conditioning temperatures and differing T_{sk} gradients. They hypothesised that the observed responses to temperature stimuli should not be viewed as responses on a continuum (e.g. a set temperature would trigger a set response irrespective of the whole body condition), but rather they identified a need to consider this in relation to the neurological pathway that is stimulated, with a focus on the thermal transient receptor potential (thermoTRP) ion channels. That is, when the local temperature stimulus and the whole body T_{sk} stimulus are within a temperature range activating the same TRP channels (e.g. TRPM8 ranging from ~28°C down to ~8°C (Romanovsky, 2007; Ständer and Luger, 2009)), the two stimuli can interact (as observed with our cold stimulus during whole body skin cooling giving an attenuated response). However, when the local temperature stimulus triggers different TRP channels from the conditioning temperature of the skin (warm stimulus TRPV3 versus TRPM8 (Romanovsky, 2007; Ständer and Luger, 2009) for skin cooling), no attenuation or modulation took place, as they work on different, independent TRP channels. This theory is supported by the present study and observations by West at al. Further research is required to validate this theory.

4.2 Regional Thermal Sensitivity

As expected, regional differences in thermal sensitivity to warm and cold were observed within both age groups in the NEUT and COLD conditions (Figure 5). In both conditions, the most sensitive regions were predominantly the torso and neck, and the least sensitive were the hand and foot in both age groups, suggesting that whole body cold exposure did not change the regional pattern in thermal sensitivity. The high sensitivity around the head and torso was previously observed in neutral environments (Ouzzahra et al. 2012; Gerrett et al. 2014), and evidently still plays a role in thermal sensitivity during whole body cooling, since sensitivity at the neck, medial torso and lateral torso was less attenuated than other body regions from NEUT to COLD exposure.

Age-related differences in sensitivity to warm and cold were observed at several body regions. In the NEUT condition, cold sensitivity was significantly lower in the older group at the hand and foot. In response to a warm stimulus, older males were significantly less sensitive at six body regions; the hand, foot, knee, medial torso, lateral torso and forearm in both conditions. These findings align with work using threshold detection and evidence that ageing deteriorates the ability to sense temperature change (Guergova and Dufour, 2011; Inoue et al., 2016; Lautenbacher and Strian, 1991a; Tochihara et al., 2011). Our data also supports the idea (Guergova and Dufour, 2011; Inoue et al., 2016; Lautenbacher and Strian, 1991b) that age-related decline in warm sensitivity precedes a decline in cold sensitivity, which may be explained by the higher number of cold receptors over the body and their superficial location (Hensel, 1981; Romanovsky, 2007).

The change in cold sensitivity from NEUT to COLD at each body region was consistent between age groups, showing an age-related difference at the knee region only. Unexpectedly, warm sensitivity was not markedly influenced by whole body cooling across all regions (Figure 6). In addition, cold sensitivity was blunted during the COLD condition at almost every body region and this was more prominent at the extremities (hand, foot and knee; Figure 6), contradicting previous research (Filingeri et al., 2017). These findings may differ due to differences in methodology. Filingeri *et al.*, (2017) artificially clamped whole body T_{sk} and T_{sk} at the sensitivity measurement sites, thereby removing the natural T_{sk} response.

Although only measuring warm thresholds, Tochihara *et al.*, (2011), demonstrated a greater blunting in warm sensitivity at the extremities during their ‘whole body cooling’ condition (22°C air temperature). This follows a similar pattern to the present study in response to a warm stimulus/cool environment and supports a common trend that the extremities are the least sensitive body region. Moreover, Tochihara *et al.*, (2011) observed an exacerbated decrease in sensitivity at the extremities in older individuals, indicative of a deterioration in temperature affector units with increasing age. Our data did not follow the same trend as the blunted sensitivity to cold was similar in both age groups. The methodology of assessing thermal thresholds is very different from that of magnitude estimation and the study by Tochihara and colleagues was conducted in Japanese individuals. Hence comparisons of outcomes should be made with caution.

4.3 Physiological and Subjective Responses

Exposure to the COLD condition significantly altered physiological and whole body subjective responses in both age groups. $\bar{T}_{sk}$ progressively decreased from 0-35 min before reaching stability prior to the sensitivity test (Figure 4). Despite the well-known decline in older individual’s vasomotor responses (Coull et al., 2020; Holowatz et al., 2010; Holowatz and Kenney, 2010), there were no age-related differences in $\bar{T}_{sk}$ in the COLD, which is consistent with data from cool/cold exposure

(Degroot and Kenney, 2007; Falk et al., 1994; Kenney and Armstrong, 1996; Tochihara et al., 2011), and may in part be due to the large individual variation in T_{sk}.

Older individual's T_{gi} was significantly lower than the young during the COLD condition from 10 min onwards, suggesting short duration cold exposure may impair the ability to maintain a thermal balance in older males despite their higher body fat content. Although older males had a lower T_{gi}, their whole body thermal sensation and comfort responses were similar to the young group throughout the COLD condition (Figure 4). This may not be alarming in the context of this study, however if larger drops in T_{gi} during prolonged exposure to cold are not perceived by older individuals, then the consequences could be harmful. The physiological and subjective responses discussed above support the consensus that older individuals have an impaired defence during mild cold exposure (Blatteis, 2012; Degroot and Kenney, 2007; Kenney and Munce, 2003). Alongside a blunting in cold sensitivity, this impairment in cold defence mechanisms may increase the risk of cold-induced injury and illness in the older population.

4.4 Skin Temperature and Sensitivity

There was no relationship between sensitivity and local T_{sk} in the older group. In the younger group however, positive relationships were observed between local T_{sk} and sensitivity at the upper back region, for warm and cold sensitivity in the NEUT condition and cold sensitivity in the COLD condition. The significant relationship at the upper back is interesting as it is a region of high sensitivity (Coull, 2019; Gerrett et al., 2014), T_{sk} (Coull, 2019; Fournet, 2013) and sweat production (Coull et al., 2020; Smith and Havenith, 2012, 2011).

4.5 Thermal sensitivity definitions and application differences

In the present study, thermal sensitivity was defined as the magnitude response to a fixed temperature stimulus on a -50 (extremely cold) to 50 (extremely hot) thermal sensation scale (Coull, 2019; Coull et al., 2020). Verbal responses were given by the participants 10 s after application of the thermal stimulus, which resulted in a steady state response. The decision to use a steady state response was based on previous comparisons between responses given immediately after stimulus application (transient response) and responses given at steady state (Coull, 2019; Gerrett et al., 2017; Ouzzahra et al., 2012).

Due to the known 'overshoot' response phenomenon (Hensel, 1982, 1974), whereby an overreaction of a thermal stimulus occurs in the transient stages, a steady state response is arguably more appropriate for the assessment of thermal sensitivity (Gerrett et al., 2017). In support of this, previous studies have reported that the time taken for T_{sk} to stabilise to the stimulus temperature (steady state) was between 7-10 s (Gerrett et al., 2015, 2014; Luo et al., 2020; Ouzzahra et al., 2012) and that this time differs between warm and cold stimuli (Luo et al., 2020). This may help to explain the opposing findings between the present study and Filingeri et al. (2017), in which they asked participants to rate their thermal sensation *immediately* after the thermal stimulus had reached its target temperature. Their approach does not allow sufficient time for T_{sk} to stabilise and thus may potentially be flawed (Gerrett et al., 2017).

Another commonly used definition of thermal sensitivity is threshold detection (Dufour and Candas, 2007; Golja et al., 2003; Inoue et al., 2016; Lautenbacher and Strian, 1991a, 1991b; Takeda et al., 2016; Tochihara et al., 2011). While both techniques (threshold and magnitude) are measures of thermal sensitivity they provide very different outcomes and cannot be directly compared (Harju, 2002).

Other studies have defined thermal sensitivity as the absolute magnitude response divided by the ΔT_{sk} during stimulation (Filingeri et al., 2018; Luo et al., 2020). While in terms of psychophysics this definition makes sense, we have encountered several issues when considering this approach:

1) There can be sharp temperature gradients in the skin, implying that the temperature at the sensor level can differ substantially from the measured skin surface temperature.
2) The sensor measuring T_{sk} tends to be placed between the skin and probe. Given there are temperature gradients between the skin and probe, this measurement does not represent T_{sk} but rather the interface or 'contact' temperature (Jay and Havenith, 2004a; Jay and Havenith, 2004b).
3) West et al. (2019) and West (2019) reported similar magnitude responses after applying the same thermal stimulus to neutral, pre-heated and pre-cooled skin. Taking their data and applying the vote/(ΔT_{sk}) definition, highly different sensitivities are produced between the different thermal conditions, due to the

different starting skin temperatures. In reality, they observed similar absolute sensation votes for the same stimulus across conditions.

Based on the issues highlighted above, we felt that the vote/(ΔT_{sk}) definition in practice is flawed and decided to work with absolute sensations instead.

4.6 Limitations

The order of experimental design with a baseline taken before cold exposure is a limitation, as both conditions (NEUT and COLD) were performed on the same day with the baseline NEUT condition always preceding COLD. Pilot tests showed that when balancing the exposure to NEUT and COLD, participant's physiological and subjective responses were inconsistent (i.e. took longer to stabilise going from COLD to NEUT than vice versa) and so the order of conditions was kept consistent throughout the study and across age groups to maintain stability in responses and allow true comparisons between groups. Furthermore, thermal sensitivity was assessed at eight body regions (Coull, 2019) in order to include the most and least sensitive regions and to ensure all body segments (head, torso, arms and legs) were stimulated. To utilise further body regions, the duration spent in the environmental chamber would increase, dramatically altering thermal state and potentially causing shivering in the COLD condition. Finally, the rapid change in thermal state in the COLD condition could have affected thermal sensitivity responses differently in each participant as cooling occurred progressively over time. To minimise this, the order of conditions were the same for each participant and the order of probe application (both temperature and location) was balanced in each group. Moreover, the majority of thermal responses (physiological and subjective) had reached a plateau prior to the thermal sensitivity test.

4.7 Application

The present findings have health-related and practical applications. Blunting of local cold sensitivity during whole body cooling could increase the risk of cold injuries, especially at the extremities. This may be relevant for cold weather activities or everyday working environments for those in frequent contact with cold objects. Further, it is also important to highlight that the lack of ability within the older group to sense themselves getting colder may be detrimental to health if this results in a failure to initiate an appropriate behavioural response in a cold environment. Future safety guidelines for working in the cold should consider age-related differences in thermoregulatory responses.

4.8 Conclusion

During whole body cooling, local cold sensitivity was blunted but warm sensitivity was maintained in both young and older males. This difference may be explained by the activation of opposing TRP channels during application of a local warm stimulus (no interaction) compared to a local cold stimulus (interaction present). Furthermore, an age-related decline in sensitivity to a warm stimulus was observed in the older group in both NEUT and COLD conditions. Alongside the attenuation in sensitivity, the observed diminished ability to preserve internal body temperature puts older males at an increased risk of cold induced illness and injury during exposure to cold ambient temperatures. These findings highlight the potential thermoregulatory risks associated with ageing, even with short duration (~40 min) exposures to the cold.

Conflicts of interest: None to declare

Word count: 6170

Acknowledgements

The authors would like to thank the participants for taking part in this research.

Author Contributions:

All authors contributed to the study conception, design, data analysis and interpretation. Material preparation and data collection were performed by NAC. The first draft of the manuscript was written by NAC and all authors commented on and edited all versions of the manuscript. All authors read and approved the final manuscript before submission.

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Supplementary Materials

Table 1 Local skin temperature (°C) prior to stimulation in the NEUT condition for all regions tested in both young and older males. Significance level between groups are displayed as *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$ (always lower in the older group). #Significant after Bonferroni correction

	Local Skin Temperature (°C) in the NEUT Condition										Significance between groups
	YOUNG					OLDER					
	Min	Max	Median	Mean	SD	Min	Max	Median	Mean	SD	Absolute
Warm Stimulus											
Hand	31.6	34.1	33.1	33.0	0.8	31.1	33.5	32.5	32.5	0.8	-
Upper back	32.4	34.4	33.4	33.4	0.6	31.1	33.3	32.5	32.5	0.7	**
Knee	30.8	32.5	31.6	31.6	0.6	30.4	32.9	31.3	31.6	0.8	-
Neck	33.2	34.5	34.1	33.9	0.5	31.5	33.9	32.8	32.8	0.7	***§
Medial torso	31.8	34.5	33.2	33.2	0.7	30.9	33.8	32.0	32.2	0.9	*
Foot	27.0	31.7	29.8	29.8	1.7	26.7	31.4	30.4	29.5	1.7	-
Lateral torso	31.3	34.1	33.3	33.2	0.9	30.8	34.2	32.5	32.6	1.0	-
Anterior forearm	32.4	34.3	33.3	33.3	0.6	31.6	33.8	32.7	32.7	0.6	*
Cold Stimulus											
Hand	32.6	33.8	33.4	33.2	0.4	31.4	33.7	32.9	32.7	0.8	-
Upper back	32.3	34.1	33.1	33.2	0.7	31.6	33.7	32.7	32.7	0.7	-
Knee	30.4	32.1	31.5	31.4	0.5	30.7	32.8	31.2	31.6	0.9	-
Neck	33.1	34.8	34.2	34.1	0.6	32.5	34.1	33.4	33.3	0.5	**
Medial torso	32.4	34.7	33.3	33.4	0.7	31.5	33.4	32.2	32.3	0.7	**
Foot	27.2	32.1	29.9	29.7	1.5	26.1	31.2	30.0	29.5	1.8	-
Lateral torso	30.9	34.6	33.5	33.2	1.0	31.4	34.3	33.2	33.0	1.0	-
Anterior forearm	32.5	34.3	33.3	33.4	0.5	31.7	34.1	33.2	33.0	0.7	-

Table 2 Local skin temperature (°C) prior to stimulation in the COLD condition for all regions tested in both young and older males. Significance level between groups are displayed as *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$ (always lower in the older group). §Significant after Bonferroni correction

	Local Skin Temperature (°C) in the COLD Condition										Significance between groups
	YOUNG					OLDER					
	Min	Max	Median	Mean	SD	Min	Max	Median	Mean	SD	Absolute
Warm Stimulus											
Hand	22.7	28.2	24.9	24.9	1.5	21.5	28.8	24.5	24.2	2.2	-
Upper back	26.2	29.9	28.5	28.2	1.3	25.2	34.9	26.5	27.5	2.7	-
Knee	23.1	26.7	24.9	25.0	0.9	22.2	25.7	24.1	24.2	1.2	-
Neck	26.8	30.6	29.2	29.0	1.4	25.7	29.6	27.1	27.3	1.1	**
Medial torso	26.1	30.4	28.7	28.4	1.5	24.6	28.5	25.5	25.8	1.3	**
Foot	20.1	26.3	22.8	22.9	1.9	20.9	25.7	23.8	23.5	1.5	-
Lateral torso	24.1	30.1	28.4	27.9	1.8	25.3	28.6	26.8	26.8	1.2	-
Anterior forearm	25.1	31.5	27.7	27.8	1.9	25.2	28.6	27.3	27.3	1.1	-
Cold Stimulus											
Hand	23.1	34.3	26.0	26.5	3.3	21.2	27.5	24.2	24.0	1.8	-
Upper back	25.9	29.6	28.3	28.1	1.3	24.5	27.9	26.5	26.3	1.0	**
Knee	23.8	26.6	25.1	25.0	0.9	23.1	25.8	24.3	24.4	1.0	-
Neck	26.7	30.8	29.6	29.4	1.3	24.9	29.5	27.5	27.4	1.4	**
Medial torso	27.2	30.6	29.2	28.9	1.2	24.7	27.5	25.6	25.9	1.0	***§
Foot	20.7	26.3	22.7	23.3	1.7	21.6	26.0	23.8	23.8	1.4	-
Lateral torso	24.2	31.9	28.6	28.3	2.1	25.4	30.2	27.2	27.3	1.5	-
Anterior forearm	24.7	31.3	28.0	28.1	1.8	25.0	28.2	27.6	27.2	1.0	-

Author Contributions:

All authors contributed to the study conception, design, data analysis and interpretation. Material preparation and data collection were performed by NAC. The first draft of the manuscript was written by NAC and all authors commented on and edited all versions of the manuscript. All authors read and approved the final manuscript before submission.