CHILLING EFFECTS: OBESITY AND COLD EXPOSURE

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Summary

In individuals living with obesity, adipose tissue aids in reducing (H_{loss}) and also serves as a heat storage compartment. Moreover, lean body mass, which has a higher H_{prod} than adipose tissue plays a crucial role in energy production and thermoregulation. The extent of resistance to the cold remains underexplored in this population, and it is important to understand these responses given the global obesity rise and its health implications. This study aimed to quantify how various body anthropometric variations affected thermal responses in individuals living with obesity during acute compensable cold exposure. A liquid-conditioned suit, connected to a temperature-controlled water circulating bath set at 10°C, was used for 90 min to elicit a compensable cold response in these individuals. Validated methods regarding subjective thermal comfort and sensations, skin temperature (T_{skin}; °C), heat production (H_{prod}; kJ ·min^{-1}), metabolic fuel selection and shivering intensity were recorded to determine the effect of obesity (and muscle and fat mass) on thermogenic and thermal responses. Our study revealed that individuals with obesity, like their lean counterparts, manifest an increased H_{prod} during cold exposure by 1.7 ± 1.3 kJ ·min^{-1}. However, this increase was observed to be lesser in magnitude among individuals living with obesity compared to lean ones. We also explored the source of fuel during cold exposure and found that carbohydrate and lipid oxidation collectively accounted for a significant proportion of H_{prod}, with lipid oxidation dominating at 61%, and carbohydrates at 21%. Regarding muscle activity, it was observed that a decrease in T_{skin} incited an increase in shivering. However, similar to the metabolic responses, shivering in this cohort was much less pronounced than in lean individuals. The study opens avenues for further research, addressing the implications of repeated cold exposure and different lengths, temperatures, or modalities on individuals living with obesity.

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List of Abbreviations

%BF - body fat percentage

BMI – body mass index

BSA – body surface area

CE – cold exposure

CIT – cold induced thermogenesis

T_{core} – core temperature

H_{loss} – heat loss

DEXA – dual-energy x-ray absorptiometry

EMG sensors – electromyography sensors

FFM – fat-free mass

LCS – liquid-conditioned suit

MVC – max voluntary contractions

NST – non-shivering thermogenesis

RMS – root-mean square

SCM – sternocleidomastoid

TEF – thermic effect of feeding

TS – trapezius superior

H_{prod} – heat produced or production

T_{skin} – skin temperature

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Chapter 1 –General Introduction

Homeostasis and Cold Exposure

Homeostasis, as defined by Speakman (2018), is the capacity of an organism to maintain a consistent, stable, and thermoneutral internal environment, irrespective of the changes occurring in the external environment. The body's ability to achieve homeostasis is crucial to ensuring optimal functioning of physiological systems. When exposed to cold temperatures, the body is presented with significant challenges in maintaining homeostasis and as a result, a range of physiological and biological responses are activated to restore the internal environment (Billman, 2020). One such response is cold-induced thermogenesis (CIT), which serves to compensate for the loss of body heat in cold conditions by activating various heat-producing mechanisms. CIT, however, is not always necessary, as primary mechanisms like vasoconstriction and behavioral adjustments can sometimes suffice to maintain homeostasis (Brychta et al., 2019). When these primary mechanisms prove insufficient, secondary mechanisms such as shivering thermogenesis (ST) and non-shivering thermogenesis (NST) come into play. In their study, Brychta et al. (2019) sought to quantify the capacity for CIT in young men with and without obesity. Their main findings revealed that 1) obesity affected the capacity for CIT, in that individuals with obesity did not have a profound increase in CIT, 2) individuals with obesity exhibited less cold-induced H_{prod} compared to lean individuals, and 3) shivering thresholds and patterns differed between the two groups.

It is important to note that homeostasis in the cold is maintained by neural pathways primarily via the hypothalamus (Yang et al., 2023). In response to cold exposure (CE) detection of external temperature changes by cutaneous thermoreceptors (Jänig, 2018), signals are sent to

the central nervous system, primarily to the hypothalamus, which is integral in regulating body temperature. The hypothalamus assimilates this sensory data, managing a series of physiological responses such as ST, cutaneous vasoconstriction, and NST (Osilla, 2023). NST in muscle, the cold-induced increase in H_{prod} not due to muscle activity related to shivering (Himms-Hagen, 1984) is regulated by several factors and mechanisms. The uncoupling protein 1 (UCP1) in brown adipose tissue (BAT) plays a crucial role in this process, allowing for the production of heat instead of ATP. The sarcoplasmic reticulum Ca^{2+}-ATPase (SERCA) is another key player, with its activity being regulated by sarcolipin, a peptide that induces Ca^{2+}-slippage for the purpose of heat generation (Nowack et al., 2017). Sarcolipin, essential for muscle-based thermogenesis, plays a role in regulating SERCA, which is another pathway through which muscle cells contribute to thermogenesis without shivering (Bal et al., 2012). Additionally, non-coding RNAs have been identified as influential in myogenesis and muscle disease, further adding complexity to the regulation of muscle NST (Zhao et al., 2019). Another important aspect of muscle function is nitric oxide (NO) signaling, especially through neuronal nitric oxide synthase (nNOS). nNOS is involved in various muscle functions, including force production, autoregulation of blood flow, and myocyte differentiation. This signaling pathway is crucial for gene expression and muscle growth, as it regulates nucleocytoplasmic transport in skeletal muscle (Hall et al., 2011; Stamler & Meissner, 2001). The hypothalamus sends neural signals to the body's extremities, triggering both vasoconstriction (narrowing of the blood vessels) and shivering as a response to cold. Simultaneously, the sympathetic nervous system, activated by these signals, releases hormones like norepinephrine from the medulla, which rapidly induces vascular contraction throughout the body, aiding in temperature regulation (Arens, 2006).

However, this neural circuity may be altered in individuals living with obesity, although it this has yet to be specifically investigated.

A study by Matsumoto et al. (1999) provided insights into the differences in autonomic nervous system and thermoregulatory responses between young women living with obesity and non-obese women. They found that the women living with obesity had a diminished autonomic response, particularly in the sympathetic nervous system during CE. They found that during acute CE, the very low frequency (VLF) component associated with thermoregulatory sympathetic function was significantly lower in the women living with obesity compared to the non-obese women. Additionally, the responsiveness of this frequency component to cold exposure (indicated by delta changes) was also significantly lower in the women living with obesity group. This suggests that obesity might be associated with impaired sympathetic nervous system function, affecting the body's ability to respond to temperature changes.

In this thesis, the focus will be on compensable CE rather than non-compensable CE. Compensable CE refers to situations where the body can effectively maintain core temperature (T_{core}) through various heat-conserving and heat-generating mechanisms, including thermal responses such as vasoconstriction, ST, and NST (Brychta et al., 2019). In contrast, non-compensable CE occurs when the body is unable to maintain T_{core} due to external factors or limitations in physiological responses, potentially leading to cold-related injuries or hypothermia.

Cold Exposure Methods: Cold Water Immersion, Cold Rooms, and Liquid-Conditioned Suits

There are several methods by which an individual can be exposed to the cold for experimental purposes, including cold water immersion, cold rooms, and liquid-conditioned suits (LCS). The cold-water immersion method involves submerging an individual in cold water,

either partially or completely. Cold water immersion is a highly effective method for inducing rapid heat loss (H_{loss}), as water conducts heat more efficiently than air (the heat specific capacity of water is nearly 4 times greater than that of air; 0.24 kcal/kg °C for air and 1 kcal/kg °C for water). However, cold water immersion can be uncomfortable and potentially dangerous if not closely monitored, as it can lead to hypothermia or cold shock response due to its non-compensable effects (Tipton et al., 2017). Cold rooms are temperature-controlled environments in which an individual is exposed to a specified cold temperature. Cold rooms allow for more controlled exposure to specific temperatures and provide the opportunity to assess the impact of clothing insulation and other behavioral adaptations. However, the rate of H_{loss} is generally slower in cold rooms compared to cold water immersion by up to 20x less (Kempainen and Brunette, 2004), and the overall cold stress experienced by the individual may be less pronounced. Furthermore, the skin functions as a primary interface for the different modalities of heat exchange, involving processes such as radiation, convection, conduction, and evaporation (Gagge and Gonzalez, 1996). This role of the skin in thermoregulation is described by Porter and Gates (1969), who referred to the skin as “a transducer of the environment.” They also went on to describe the process of heat exchange at the skin surface. It typically begins with conduction through clothing. The heat then transfers away from the skin or outer clothing surface through radiation and convection into the surrounding environment. These processes ensure that metabolic heat reaching the skin surface is effectively dissipated. Conduction involves direct heat transfer through solid materials. In contrast, convection is more complex, entailing the mass movement of the medium (such as air or water) that facilitates the transfer of thermal energy from one location to another (Petrone et al., 2003). Evaporation via respiration also plays a role in thermoregulation, particularly in opposing hyperthermia. H_{loss} through the evaporation of

sweat or liquid vapor from the skin surface is a vital biophysical mechanism in both humans and animals. However, this mechanism is not particularly relevant to CE. Thermal radiation is defined as the radiant energy emitted by a medium due to its temperature. This process is integral in the overall heat exchange mechanism of the body. Lastly, the efficiency of skin conduction is influenced by both passive and active regulatory processes. These include the convective heat transfer by blood circulation and the conductive heat transfer from the body's core through tissues to the outer layers of the skin, which will be discussed in later sections. As per Petrone et al. (2014), over 90% of the body's H_{loss} occurs through the skin, with various processes contributing differently: radiation accounts for 55%, evaporation makes up 25% (skin and breathing), conduction is responsible for 15%, and a smaller portion is due to convection. The remaining 5% of H_{loss} happens through the lungs, predominantly via evaporation. LCS are specially designed suits that circulate a temperature-controlled liquid around the participant's body, making direct contact with their skin, providing a highly controlled and adjustable method of cold exposure. In an LCS, CE primarily involves conduction and convection because of the direct contact with the skin. Radiation and evaporation play lesser roles, due to the liquid forming a barrier that limits radiation and impedes the evaporation of sweat. This also lowers the amount of variability in CE responses due to lesser variations in the conduction and convection of the skin being exposed to the stimulus. LCS allow for precise control over the temperature and duration of exposure, making them an ideal tool for studying the physiological effects of CE in a controlled manner. This is important in ensuring that all participants are exposed in a similar manner. Moreover, LCS can be used in conjunction with metabolic carts to assess the effectiveness of various H_{prod} and conservation mechanisms. This is the primary reason that the LCS will be used in this study.

Thermal Responses

Thermal responses involve physiological and behavioral adaptations to maintain T_{core} within a narrow range during temperature fluctuations (Blatteis, 1998). These responses include H_{prod} (e.g., basal H_{prod}, thermogenesis, and shivering) and H_{loss} mechanisms (Mäkinen, 2010). Thermal sensation, the subjective perception of warmth or coldness, also plays a role in triggering behavioral adaptations (Stevens and Choo, 1998). Factors like age, sex, body composition, and acclimatization can influence individual thermal responses. As per the review by Haman et al. (2022), it was deemed that body anthropometrics, body mass, and body composition, including muscle and fat mass, are likely the most crucial factors influencing individual cold tolerance both between and within populations. In the context of obesity, understanding these responses is essential to evaluate the impact of muscle and fat mass differences on an individual's ability to maintain T_{core} during CE so that insights into this population's metabolic health is better understood.

Factors Influencing Thermal Responses

Vasoconstriction and its Effects on Individuals Living with Obesity

One of these aforementioned responses include decreased peripheral blood flow as a result of vasoconstriction (Alba et al., 2019). Vasoconstriction causes blood to be shunted to the core and away from the periphery (Rowell, 1974), which serves to minimize conductive heat transfer and minimizing the exposure of warm blood to the cold environment. This process effectively conserves heat and maintains T_{core} by delaying the cooling of deeper tissues (Jd, 1952), can occur in temperature decreases of just 2°C (Verbraecken et al., 2006) and becomes maximal at T_{skin} of 31°C (Veicsteinas et al., 1982). However, for individuals living with obesity,

the vasoconstriction response is altered, shifting towards a higher temperature threshold (Savastano et al., 2009), i.e., this response occurs at a higher T_{skin}. The distribution and thickness of subcutaneous fat, along with the mass of the individual, can influence the altered vasoconstriction response in individuals living with obesity (Koenen et al., 2021; Savastano et al., 2009). Visceral fat accumulation, associated with impaired flow-mediated vasodilation, is a key factor in this process. Impaired flow-mediated vasodilation refers to the reduced ability of blood vessels to dilate in response to increased blood flow. This impairment, often seen with visceral fat accumulation, leads to an overall tendency towards vasoconstriction, as the blood vessels are less able to counteract narrowing pressures (Hashimoto et al., 1998). In individuals living with obesity, the protective anticontractile properties of perivascular fat are abolished due to local inflammation and hypoxia. Perivascular fat is the fat surrounding blood vessels, which typically releases substances that help to relax and dilate the blood vessels, thus acting as an anticontractile agent. When this function is lost due to local inflammation and hypoxia in obesity, it contributes to increased vasoconstriction (Greenstein et al., 2009). The degree of endothelial dysfunction in obesity is predicted by body fat distribution, particularly the ratio of visceral to subcutaneous fat. Endothelial dysfunction in the context of vasoconstriction refers to the impaired functioning of the endothelium, which fails to regulate vascular tone and balance between vasodilation and vasoconstriction (Arcaro et al., 1999). Severe obesity is linked to structural and functional alterations in subcutaneous small resistance arteries, which can contribute to vasoconstriction (Grassi et al., 2010). Furthermore, O'Brien et al. (1998) and Johnston et al. (1996) both reported that hypohydration and hypoxia, respectively, can impair vasoconstrictor responses to cold, potentially leading to decreased susceptibility to hypothermia.

These changes enable them to dissipate heat for a longer period, maintaining a safe T_{core} and helps hinders H_{loss} (Anderson and Martin, 1994).

Body Mass Index

It is important to consider the mass of the individual, as those with a higher body mass generate more heat and may have a harder time dissipating it (Charkoudian, 2003). Furthermore, the location of cutaneous blood flow relative to the subcutaneous fat also plays a role in heat dissipation. It was previously believed that a greater amount of subcutaneous fat can reduce heat transfer from the body to the environment, as it acts as an insulating layer that impedes the conduction of heat through the tissue (Havenith and Van Middendorp, 1990). This insulation effect would occur because the subcutaneous fat has a lower thermal conductivity compared to other tissues, such as muscle or skin, which slows down the transfer of heat to the external environment (Speakman, 2018). However, current research provides limited support for the idea that white adipose tissue is a significant contributor in preventing H_{loss} in cold conditions in humans (Blix, 2016). Lemire et al. (2008) investigated the cooling rates in males who underwent hyperthermic conditions through exercise in a 40°C environment and then immersed in an 8°C cold bath. The study found no notable difference in cooling rates between individuals with low body fat (approximately 13%) and those with higher body fat (approximately 22%). In a subsequent study by Lemire et al. (2009), they observed that despite higher body fat levels, women cooled nearly twice as quickly compared to men when matched for body surface area to mass ratios. This was attributed to men possessing more lean tissue, which potentially increases thermogenic capacity. However, these findings highlight the complexity in interpreting such studies that focus only on cooling rates without considering H_{prod}, as they can be misleading since thermogenic responses are multi-faceted. Fischer et al. (2016) suggested that in mice, the

lack of observed impact of obesity on insulation could be due to the distribution of fat deposits. Similar to mice, human obesity often involves central fat accumulation rather than peripheral. Increased subcutaneous fat does not necessarily improve insulation. They also noted that analyzing H_{prod} relative to body weight might show an effect of obesity, but this approach can be misleading as it does not account for the overall H_{loss} in obese mice.

Rather than significantly increasing the total body surface area (BSA), body fat contributes to a substantial volume with minimal impact on surface area dimensions (Sardinha et al., 2006). In addition to the factors of individual mass, BSA is a critical element in understanding thermoregulation. BSA refers to the total surface area of the human body and is calculated using the Dubois and Dubois formula below. The concept of BSA with regards to thermoregulation is rooted in the principle that the human body loses heat proportionally (Havenith, 2001) and primarily through its surface and its importance in thermoregulation can be understood through its relationship with heat dissipation mechanisms described above (radiation, convection, conduction, and evaporation). A larger BSA provides a greater area for these heat exchange processes to occur, facilitating more efficient H_{loss} (Petrone et al., 2014). Conversely, a smaller BSA relative to body mass, as often seen in individuals with obesity, means less skin surface area is available for heat exchange (Gonzalez and Sawka, 1988). Therefore, BSA is directly linked to the rate at which the body can dissipate heat (Havenith, 2001). BSA can vary significantly among individuals, influenced by factors such as height, weight, and body composition. This variability means that two individuals with the same body weight might have different BSA values, leading to differences in their thermoregulatory responses. In both humans and other animal species, it's crucial to recognize that the key factors influencing neutral air temperature and the speed of H_{loss} are overall body mass and the total BSA (Haman et al., 2022).

In the context of obesity, BSA becomes a significant factor. Typically, individuals with obesity have a lower BSA relative to their body mass. This altered BSA to mass ratio in obesity impacts heat dissipation efficiency, as a smaller surface area relative to body volume reduces capacity of the skin to lose heat. Fernandes et al. (2012) conducted a study that examined the incidence of hypothermia in individuals living with obesity and individuals not living with obesity undergoing surgery. The researchers found that the incidence of hypothermia was significantly lower in the individuals living with obesity cohort (10%) compared to the individuals living with obesity cohort (60%), suggesting that obesity may provide a protective effect against hypothermia. However, this study has some limitations that should be considered when applying the conclusions. Firstly, the use of a lower body cooling blanket throughout the surgery led to uneven cooling of the body, which may not accurately represent real-world conditions. Additionally, the study only included women, who have been reported to respond to CE more quickly than men, having a 0.3 °C higher T_{core} (Lopez et al., 1994). A study by (Blondin et al., 2011) observed the same participants during the luteal and follicular phases of their menstrual cycle and observed that regardless of the phase, there were no differences in shivering intensity nor in substrate utilization in the cold.

Gagge and Gonzalez (1996) found that individuals with a lower BMI tend to lose more heat when exposed to the cold than others. These findings can be further understood by considering the BSA. Obesity is characterized by an increase in weight without a corresponding increase in height, which leads to a decreased ratio of surface area to body mass (Verbraecken et al., 2006). As cutaneous H_{loss} is generally proportional to skin surface area (Sessler et al., 1991), individuals living with obesity may experience a slower loss of heat compared to those with normal body weight (Kurz et al., 1995).

Lean Individuals and Individuals Living with Obesity

Several studies aimed to compare the differences between lean individuals and individuals living with obesity with regards to H_{prod}. Of these, Quaade (1963) observed that when participants were exposed using two blankets perfused with 4°C liquid for 30 min, there was a considerably higher metabolic increase in lean individuals (BMI of 18.3, with an average increase of 33%) compared to those with normal BMI (21.9, average increase of 11%) and significantly higher than in obese individuals (BMI of 39.8, with an average increase of 2-5%). Brychta et al., (2019) found that when exposed to cool-air temperatures, varying randomly each day between 16°C and 31°C, in a room calorimeter for five hours daily over 13 days, individuals living with obesity experienced a resting H_{prod} increase of 6 ± 7%. In contrast, lean individuals showed a larger increase of 17 ± 11%. Additionally, the study noted that individuals with obesity had a narrower range of tolerability for cooler temperatures. They found that lean individuals shivered more than individuals living with obesity, and that both groups had similar levels of cold perception. However, only young Caucasian men were tested. Cannon and Keatinge (1960) aimed to investigate the impact of body composition on H_{prod} and H_{loss} in cold and warm water. The study found that individuals living with obesity had a higher H_{prod} and H_{loss} in both cold and warm water compared to lean individuals. However, the difference was more significant in cold water, where individuals living with obesity had a 55% higher H_{prod} and 35% higher H_{loss} than lean individuals. In warm water, the difference was 25% and 15% respectively. Limitations of the study include a small sample size and only men were observed. The study also did not measure shivering responses using sensors; shivering was measured visually. Wijers et al. (2010) also sought to explore the differences in cold-induced adaptive thermogenesis between lean individuals and individuals living with obesity. They exposed participants to a mildly cold

temperature (16°C in a cold chamber) for 2 days and found that although both lean and participants living with obesity experienced an increase in H_{prod} during CE, the increase was only significantly greater in lean participants (increase of 0.30 MJ/day for lean individuals, no change for individuals living with obesity). In lean individuals, the decrease in distal T_{skin} was more pronounced than in participants living with obesity, while individuals living with obesity experienced a more significant reduction in proximal T_{skin} compared to their lean counterparts.

H_{loss} is prevented more effectively in individuals living with obesity, which is one theory as to why there is little increase in H_{prod}, and so a more intense CE is required to increase their H_{prod} to a similar percentage as that of lean individuals. This may be due to several factors, a higher resting H_{prod} at baseline, or differences in muscle mass and metabolic activity. Ooijen et al. (2006) conducted a study that confirmed the difference in H_{prod} between lean and overweight individuals during CE. After being exposed to mild cold (15°C in a cold chamber) for one hour, there was a noticeable contrast in metabolic response between lean and overweight individuals. The lean subjects experienced a 17.2% increase in mean H_{prod}, while the overweight subjects only experienced a 6.4% increase. The researchers did not find any difference in mean T_{skin} between the two groups, although mean T_{skin} did drop significantly during CE. The findings suggest that overweight subjects were more efficient at preserving heat due to a reduced H_{loss} relative to their body size. They also reported that trunk temperature was negatively correlated to body fat percentage during CE ($r^2 = 0.40$).

Another factor that could contribute to the lower relative increase in H_{prod} in individuals living with obesity is their higher resting H_{prod} at baseline, as a result of their higher body mass (Ravussin et al., 1988). This higher resting H_{prod} may reduce the need for additional H_{prod} during CE. The authors found that the total H_{prod} of subjects was found to be positively correlated with

their fat-free mass (FFM) or lean body mass, but not with their body weight or body fat percentage (%BF). This indicates that FFM is a major determinant of H_{prod} in humans. They also found that age and sex were significant predictors of 24-hour H_{prod}. Men had a higher H_{prod} than women, and younger subjects had a higher H_{prod} than older subjects, even after adjusting for differences in FFM.

Increased muscle mass present in individuals living with obesity could also play a role in the increased H_{prod} observed during CE, relative to lean individuals. Muscle mass contributes to H_{prod} through muscle metabolism and contractile activity (Zurlo et al., 1990). However, the study only investigated non-obese, healthy individuals. Therefore, the findings may not be generalizable to other populations such as individuals living with obesity or those with metabolic disorders. Additionally, the study only investigated the contribution of skeletal muscle metabolism to resting H_{prod} and did not consider other factors that may contribute to resting H_{prod}, such as whole-body composition or hormonal factors. The effect of subcutaneous fat thickness on T_{skin} is mainly due to its biophysical properties. Thicker subcutaneous fat diminishes H_{loss} from the tissue underneath and, as the thickness of this fat layer increases, the T_{skin} drops due to decreased internal conduction. This decrease in T_{skin} reduces the thermal gradient between the skin and the surrounding environment. Since body H_{loss} rate is dependent on this gradient's magnitude, a lower T_{skin} effectively means less overall body H_{loss}, which helps maintain T_{core} (Castellani and Young, 2016).

Skeletal Muscle Mass in Lean Individuals and Individuals Living with Obesity

Skeletal muscle mass (SMM), a component that is increased with a larger amount of subcutaneous fat, provides the single largest source of heat, which is measured as H_{prod} (Blondin et al., 2014; Park et al., 1984). It is important to note that individuals living with obesity tend to

have a high body heat content (Donahoo et al., 2004). While their resting H_{prod} is often higher compared to lean individuals, this is not largely due to their larger proportion of FFM as previously suggested (Prentice et al., 1986). However, when exposed to the cold, their relative increase is not as great as lean individuals, although their absolute heat produced during CE remains higher. At the same time, the higher absolute muscle mass may contribute to a greater H_{prod} capacity when needed. Furthermore, given that skeletal muscle is more vascularized than adipose tissue, vasoconstriction significantly impacts heat retention in these tissues. In individuals living with obesity, greater vasoconstriction in skeletal muscles during CE further reduces the amount of warm blood reaching these highly vascularized tissues, effectively lowering H_{loss} through internal convection. Resistance to heat conduction is significantly increased by unperfused muscle tissue in resting individuals. According to Ducharme et al. (1991), this insulation plays a major role in the capacity of the body to retain heat. This dissipates heat from the outer layers, reducing the insulative properties of the muscles. However, the exact change in H_{prod} for individuals living with obesity under the same cold stress would depend on various factors, including the distribution of adipose tissue, individual metabolic responses, and the severity of the CE. Uncovering this uncertainty and determining what anthropometric measurement is most closely associated with insulation against cold is one of the aims of this thesis.

Shivering as a Heat-Generating Mechanism

Shivering is used to maintain thermoneutrality and is an involuntary response driven primarily by skeletal muscle (Haman and Blondin, 2017). As per Haman (2006), CE leads to an increase in H_{prod} through the activation of ST and NST, with the former being the main contributor to compensatory H_{prod} in non-acclimatized humans. The main physiological

mechanisms of cold adaptation in humans, including the increase in H_{prod}, are driven by decreasing contractions in skeletal muscle and an increasing proportion of NST (Saltykova, 2018). One concern to be aware of with depending on ST as the main contributor to compensatory H_{prod} is that it can interfere with motor control and performance (Meigal, 2002).

Despite an overarching trend, there is considerable variability in muscle recruitment patterns, evident even among individuals with similar body morphology, including both men and women (Bell et al., 1992; Haman, 2006). For example, Haman et al., (2006) observed that the activity of burst shivering was not synchronized across different muscles, diverging from the findings by Bawa et al. (1987). As per Hohtola and Stevens (1986), muscles more suited for aerobic activities tend to exhibit continuous shivering (rich in type I fibers), whereas muscles reliant on anaerobic metabolism (rich in type II fibers) are inclined to shiver in bursts. Additionally, it was found that muscle fiber composition varies significantly among individuals (Simoneau & Bouchard, 1989). This may be one reason as to why large variability exists with regards to ST, as skeletal muscle is made up of different types of fibers.

CE response also varies greatly between individuals, and most of this variability is due to body composition differences (Castellani and Young, 2016). It has also been shown that using a LCS with lean individuals and inducing a 3°C decrease in T_{skin} led to an increase of about 2% of maximum voluntary contraction (MVC), whereas a 9°C decrease led to shivering increases of about 10% of MVC. (Blondin, Tingelstad, et al., 2014). Previous research by Haman et al. (2007) and Tikuisis and Giesbrecht (1999) done in lean individuals determined that maximal H_{prod} during CE can only increase about five times above baseline values. Another study by Haman et al., (2006) showed that a ~25% T_{skin} (down to ~26°C) decrease due to a 5°C LCS perfusion for 90 min in lean individuals showed a 3.3-fold increase in H_{prod}. The relative

contributions of plasma glucose, muscle glycogen, and lipids to total H_{prod} during shivering are well-documented, with muscle glycogen becoming dominant as shivering intensifies (Haman, 2005; Haman, 2002). In lean individuals, lipids and muscle glycogen were the primary sources of energy for H_{prod}, contributing 50% and 30%, respectively. However, research on how individuals living with obesity have their metabolic fuel selection impacted by acute CE is limited. Although this has yet to be investigated, once shivering starts, individuals living with obesity may experience similar or even greater H_{prod} due to their larger muscle mass, as shivering involves involuntary muscle contractions.

Sex Differences in Thermal Responses to the Cold

According to Tikuisis et al. (2000), women with an average %BF of ~22.4% immersed in 18°C water cooled at a rate approximately half as fast as men with an average %BF of ~10.6%. However, when comparing with similar %BF, there were no sex differences. The variance in cooling rates can be attributed to differences in surface area and %BF%BF. These findings suggest that while there were some differences in T_{skin} and vasoconstriction responses between men and women during cold-water immersion, the overall thermoregulatory responses, including the rate of T_{core} decrease and shivering intensity, were similar between the sexes in cooler water temperatures (between 15-20°C). The increased %BF in women may have contributed to a slightly lower rate of H_{loss} during the early stages of cold-water exposure. Building on previous research by Lopez et al., (1994), Kaikaew et al. (2018) found that the onset of shivering as a means of H_{prod} occurs earlier in women than in men, although this was due to the women having a slightly higher BSA to mass ratio than men, which was a significant determinant for shivering in this study. Controlling for lean body mass and fat mass revealed sex differences but controlling for body surface area (BSA) eliminated these differences. No sex differences were

observed in CIT. Variability in H_{prod} and shivering intensity therefore suggests that morphological and body composition differences influence thermogenesis and shivering (Dumont et al., 2022). It appears that there is a lack of sex differences with regards to the physiological response to CE. However, it has been suggested that there may be differences between men and women with regards to their thermal sensitivity to the cold (Graham, 1988; Kingma and Van Marken Lichtenbelt, 2015). This may have important implications with regards to survival in extreme environments, physical performance, and health outcomes. Recognizing these differences can help inform guidelines and interventions related to CE such as clothing, training programs, or occupational safety protocols for men and women. Additionally, a deeper understanding of these differences may contribute to the development of more personalized medical treatments and preventative strategies for cold-related injuries and illnesses.

The Importance of Understanding Cold Exposure Response in Individuals Living with Obesity

Numerous studies investigating metabolic and T_{core} responses to water cooling in humans clearly show that obesity serves a thermoregulatory purpose. Individuals living with obesity are more resistant to cold temperatures, but they are more vulnerable to heat stress (Speakman, 2018). However, the degree to which they are resistant has yet to be explored in detail. As can be seen above, very few studies, if any, have looked at how individuals living with obesity react to CE in a standardized manner. With the increasing number of individuals living with obesity, this health crisis is now being classified as a global pandemic per the World Health Organization. This is impactful in many ways, as obesity is linked to metabolic diseases (Martin-Rodriguez et al., 2015), cancer (Calle and Thun, 2004), and being a financial burden (Finkelstein et al., 2009). Furthermore, there are contradictory findings between studies; shivering is seldom measured

with instrumentation (usually measured visually), and women are rarely involved as participants. Whether CE can be used as another mechanism by which to increase H_{prod} after individuals lose weight (Rosenbaum et al., 2008) to ensure they do not regain weight has not been tested in individuals living with obesity, although it has been shown to work in lean individuals (Brychta et al., 2019). This is one of the reasons why it is extremely important to test how individuals living with obesity respond to CE, especially as minor differences in H_{prod} can lead to substantial long-term changes in body weight levels, and understanding the significant interindividual variations in H_{prod} increase can help develop CE treatments specifically designed for individuals living with obesity.

Objective

The objective was to quantify the effects of variance in total body mass (kg), lean body mass (kg), body mass index (kg/m^2), body fat %, fat mass (kg), fat-free mass (kg), body surface area (m^2) and skeletal muscle mass (kg) on thermogenic and thermal responses in individuals living with obesity during acute compensable CE. Sex differences will also be explored in the context of their thermogenic and thermal responses.

Hypotheses

Individuals with larger body anthropometric measurements (body mass, LBM, BMI, %BF, FM, FFM, BSA, SMM) will exhibit significantly greater H_{prod} and shivering in response to acute compensable CE relative to their resting state. Participants will have a significantly decreased T_{skin} than at rest, decreased carbohydrate oxidation and greater fat oxidation during the CE and will have lower thermal comfort and sensation ratings.

Outcomes

Primary outcomes include T_{skin} and H_{prod} changes when exposed to the cold, and shivering intensity as related to anthropometric measurements. Secondary outcomes include metabolic fuel selection changes, and subjective thermal comfort and thermal sensation ratings.

Chapter 2 – Methods

The study population consisted of a minimum of 13 men and 13 women living with obesity (BMI between 27 and 40 kg/m^2). Participants took part in the study throughout the entirety of the year, including the winter months.

Inclusion criteria

Individuals that were 18-55 years old, have had no significant weight fluctuations over the past 6 months (±2 kg), were sedentary (<2 sessions/week of 30 min exercise) and, in the case of women, were premenopausal were selected.

Exclusion criteria

Individuals with psychiatric disorders, on medications that impacted appetite, had a history of cardiac problems, were diabetic, had 2 or more servings of alcohol per day (14 servings/week), any hard drug intake, or were pregnant or planned to become pregnant over the duration of the trial were excluded.

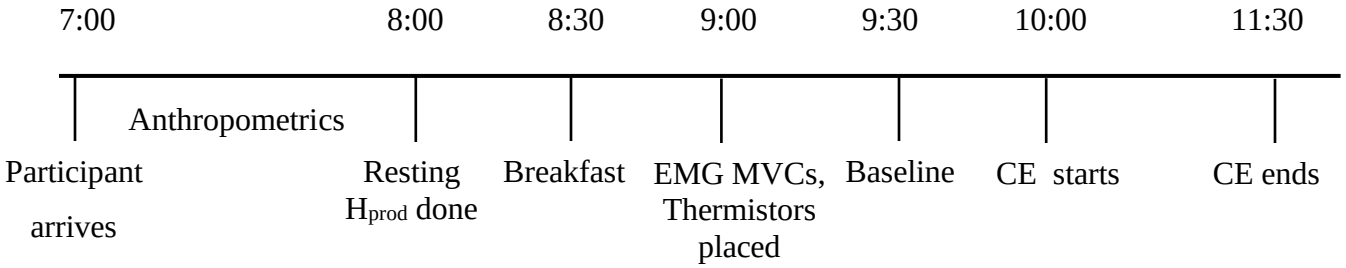
A body mass index (BMI) of 27 was used instead of 30, due to difficulties in recruiting individuals in the target population. BMI was used instead of %BF due to it being a less invasive method to assess obesity. Using %BF required participants to undergo a dual x-ray absorptiometry (DEXA; DXA, Lunar Prodigy, GE Healthcare, Madison, WI) scan, while using BMI ensured participants were not exposed to unnecessary radiation as part of the screening process.

Experimental Procedures

1. Participants underwent one CE session.

1.1. Participants underwent a DEXA scan and other anthropometric measurements such as height (m), Body mass (kg), lean body mass (kg), body fat (%) and BMI (kg/m^2). Body surface area (m^2) was calculated using the Dubois and Dubois formula. Resting $H_{prod}$was taken for 30 min, followed by a standardized breakfast of 464 kcal to standardize the thermic effect of feeding (TEF). Participants had 4 electromyography sensors (EMG sensors) placed for the CE and completed 3 isometric maximum voluntary contractions (MVCs) (see below). They were then fitted with 12 iButton thermistors at various sites on their body (see below). For the control session, participants rested at a thermoneutral state while their H_{prod} and T_{skin} data was collected. For the CE, participants laid down while the liquid cooled at 10 °C was circulated throughout the LCS. Metabolic, T_{skin}, and EMG data continued to be collected.

Experimental timeline



Anthropometric measurements

Body surface area was calculated using the Dubois and Dubois formula [Formula (1), Supplementary Data], one of the most validated formulas for this measurement (Burton, 2008). FFM [Formula (2), Supplementary Data] was calculated using the formula developed by Loenneke et al. (2012). After participants were scanned with the DEXA, subsequent body composition analysis was conducted using GE Encore version 17.0. This analysis provided

quantification of whole-body FFM (kg), FM (kg) and %BF. The total SMM (kg) was estimated using the predictive models proposed by Kim et al. (2002) [Formula (3), Supplementary Data]. These models utilize the measurement of appendicular lean soft tissue mass, which is the combined lean soft tissue mass of the right and left arms and legs. Height was taken with a wall-mounted height rod (HR-200 Tanita).

There was no significant difference for total body mass measured with the DEXA and measured with the Tanita BWB-800 scale (mean difference of 0.9 ± 4.5 kg, p = 0.837). Due to there not being a significant difference with body weight measured with the DEXA or the scale, the body weight with the scale was used in all calculations in this thesis.

Table 2.1. *Participant anthropometric characteristics*

Anthropometric	**Mean ± SD**	**N**	**Mean ± SD (Men)**	**N**	**Mean ± SD (Women)**	**N**	**Sig.**
Age (years)	30.0 ± 10.7	25	31.4 ± 8.6	11	28.9 ± 12.3	14	0.574
Height (m)	1.7 ± 0.1	25	1.8 ± 0.1**	11	1.7 ± 0.1	14	0.005
Body mass (kg)	99.3 ± 18.0	25	105.7 ± 16.8	11	94.4 ± 17.8	14	0.119
Lean body mass (kg)	55.9 ± 11.2	23	64.7 ± 9.4**	10	49.1 ± 6.9	13	<0.001
Body mass index (kg/m^2)	33.1 ± 4.5	25	33.5 ± 4.8	11	32.7 ± 4.3	14	0.671
Body fat (%)	42.1 ±6.4	21	36.5 ± 5.8	8	45.6 ± 3.8**	13	<0.001
Fat mass (kg)	41.7 ± 10.4	23	38.7 ± 10.3	10	43.9 ± 10.2	13	0.243
Fat-free mass (kg)	58.1 ± 11.0	21	67.8 ± 9.5**	8	52.2 ± 6.8	13	<0.001
Body surface area (m^2)	2.1 ± 0.2	25	2.2 ± 0.2**	11	2.0 ± 0.2	14	0.040
Skeletal muscle mass (kg)	29.8 ± 9.1	6	33.5 ± 8.9	4	22.4 ± 3.1	2	0.179

* Indicates significance at the $p < 0.05$ level
** Indicates significance at the $p < 0.001$ level

Temperature Measures

Twelve iButtons (DS1921H High-Resolution Thermochron iButton Devices, Maxim Integrated) were placed on the right side of the body at various sites: forehead, hand, bicep, forearm, pectoralis, abdomen, quad, hamstring, front calf, back calf, upper back, and lower back to measure T_{skin}. Mean T_{skin} was calculated using a mean-weighted formula (Hardy et al., 1938) - equation (4):

(4) $(Mean\ T_{skin}\ (°C) = (T_{Abdomen} \times 0.095) + (T_{Back\ calf} \times 0.075) + (T_{Biceps} \times 0.090) + (T_{Chest} \times 0.095) + (T_{Forearm} \times 0.070) + (T_{Forehead} \times 0.070) + (T_{Front\ calf} \times 0.085) + (T_{Hamstring} \times 0.095) + (T_{Hand} \times 0.040) + (T_{Low\ back} \times 0.095) + (T_{Quad} \times 0.095) + (T_{Upper\ back} \times 0.095)$

Equation (4) was used to determine the T_{skin} rate of cooling (°C) during CE, which was calculated with equation (5):

(5) $T_{Skin} Rate\ of\ Cooling\ (\frac{^{\circ}C}{min}) = \frac{T_{Skin90} - T_{Skin0}}{90-0}$

Metabolic Measures

Metabolic measures such as VO_2 and VCO_2 were collected and then analyzed to determine metabolic fuel selection and impact of body mass on these measures. Equipment used consisted of a ventilated hood and the Vmax system (SensorMedics Corporation, Yorba Linda, CA, USA).

Resting metabolic data was collected for 30 min to serve as a baseline while fasting, and then again after breakfast over a 120-min period during the session, in 15-min intervals. There was 30 min where the participant rested before starting the 90 min of CE for baseline measurements. Ninety min of CE was chosen based on previous studies (Dumont et al., 2022).

H_{prod} (kJ ·min^{-1}) was calculated using the following equation:

(6) $Heat_{prod}(\text{kJ} \cdot min^{-1}) = CHO_{ox}(\text{kJ} \cdot min^{-1}) + FAT_{ox}(\text{kJ} \cdot min^{-1}) + PROT_{ox}(\text{kJ} \cdot min^{-1})$

To determine the contribution of each metabolic fuel source for a participant's $Heat_{prod}(\text{kJ} \cdot min^{-1})$, the following equations developed by Livesey and Elia (1988) were used:

(7) $CHO_{ox}\left(\frac{g}{min}\right) = 4.59V_{CO_2}\left(\frac{l}{min}\right) - 3.23V_{O_2}\left(\frac{l}{min}\right)$

(8) $FAT_{ox}\left(\frac{g}{min}\right) = -1.70V_{CO_2}\left(\frac{l}{min}\right) + 1.70V_{O_2}\left(\frac{l}{min}\right)$

V_{CO_2}(l ·min^{-1}) and V_{O_2}(l ·min^{-1}) values were adjusted to account for the volumes of O_2 (1.010 l ·g^{-1}) and CO_2 (0.843 l ·g^{-1}) related to protein oxidation.

Energy equivalents of 16.3 and40.8kJ per gram were utilized to calculate the oxidation rate (kJ/min) of each metabolic fuel source, as shown in equations (9) – (10):

(9) $CHO_{ox}(\text{kJ} \cdot min^{-1}) = CHO_{ox}\left(\frac{g}{min}\right)x16.3\left(\frac{kJ}{gram}\right)$

(10) $FAT_{ox}(\text{kJ} \cdot min^{-1}) = FAT_{ox}\left(\frac{g}{min}\right)x40.8\left(\frac{kJ}{gram}\right)$

This was then used to calculate the relative proportions of carbohydrates (CHO%) and lipids (FAT%) respectively, oxidized during CE as a total percentage of 100 (Péronnet and Massicotte, 1991). This is shown in equations (11) – (12):

(11) $CHO\ \%_{ox} = \frac{CHO_{ox}(\text{kJ} \cdot min^{-1})}{Heat_{prod}\ (\text{kJ} \cdot min^{-1})}x100\%$

(12) $FAT\ \%_{ox} = \frac{FAT_{ox}(\text{kJ} \cdot min^{-1})}{Heat_{prod}\ (\text{kJ} \cdot min^{-1})}x100\%$

The standardized breakfast consisted of 60 g of whole wheat toast, 20 g of strawberry jam, 20 g of creamy peanut butter and 250 g of orange juice. Following breakfast, participants had their H_{prod} measured again. The interindividual change in H_{prod} was graphed below. There was no

significant difference between H_{prod} pre- and post-feeding (5.8 ± 1.0 vs. 6.4 ± 1.6 kJ ·min^{-1}, p = 0.119).

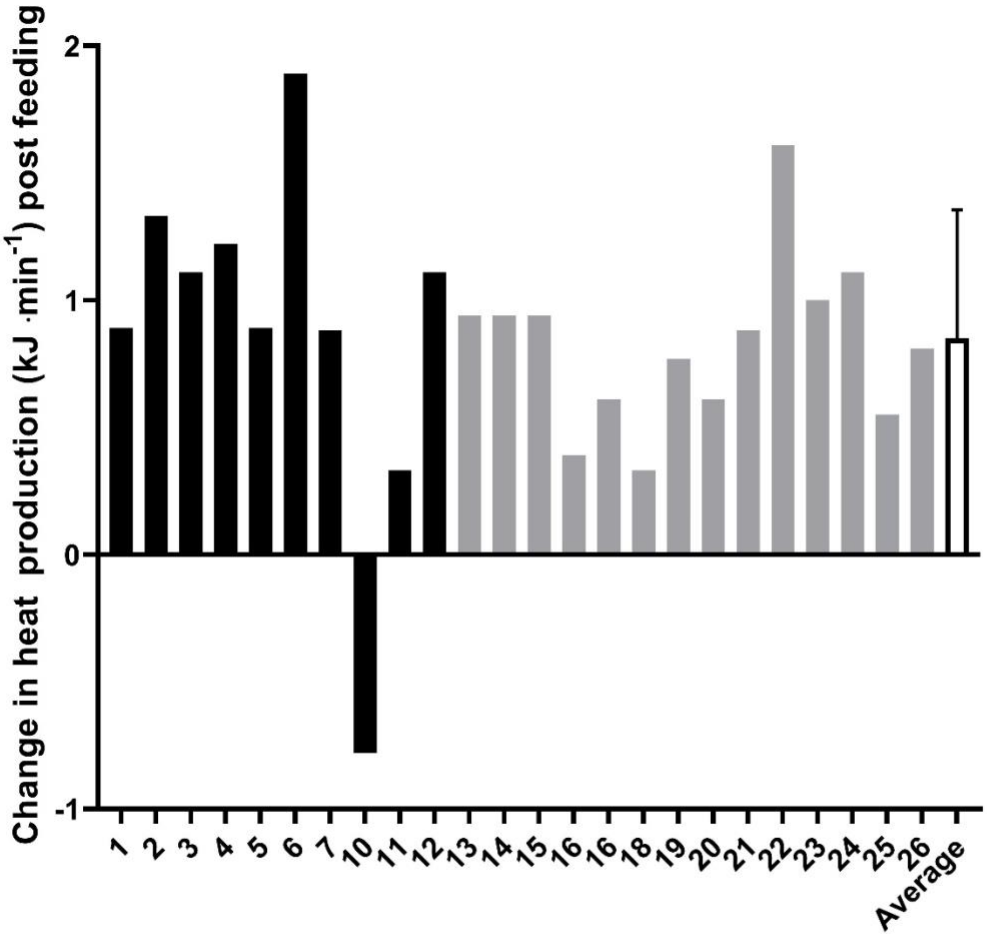


Figure 2-1: Changes in in heat production (kJ ·min^{-1}) after participants were fed a standardized breakfast, pre cold exposure. Missing participants: M009, M010

However, this could be due to the individual variability that the TEF could have. A correlation analysis was conducted to investigate the relationship between TEF and H_{prod} during CE. The results of the correlation analysis, showing a correlation coefficient of 0.22 and a p-value of 0.286, indicated that there was no significant relationship between TEF and H_{prod} during

CE. Based on this outcome, it was concluded that TEF did not influence H_{prod} changes during cold exposure and, therefore, was not factored into subsequent calculations.

To assess the changes in H_{prod} due to CE, the pre-feeding H_{prod} value was subtracted from the CE H_{prod} value. This method was chosen over using the control session for relative comparisons because, although the TEF is similar in both sessions, its presence influences the CIT when examining relative changes. By focusing solely on the CE session and subtracting the pre-feeding H_{prod}, the analysis effectively removed the influence of TEF from CIT. This approach acknowledges that while TEF may be similar in both sessions, it is not a constant value and is part of a broader physiological system that interacts with the heat produced during cold exposure. Thus, this method provides a more accurate representation of the specific effects of cold exposure on H_{prod}, unconfounded by the metabolic responses to feeding.

Shivering Activity

Skin site preparation for EMG placement involved shaving and using 3M Red Dot Trace Prep (3M Canada, London, ON, Canada) along with ethanol swabs (Alcohol Prep Pad, Dukal Corporation). Throughout the CE session, muscle activity was recorded at 15-min intervals, ranging from 15-min prior to CE (baseline) to 90-min. Fifteen min of EMG activity was measured prior to the start of CE, to determine participant baseline muscle activity levels. Raw EMG signals were collected at a rate of 1926 Hz, and the signal underwent filtration to eliminate spectral components below 20 Hz and above 450 Hz, including 60 Hz contamination and related harmonics.

EMG sensors were placed on 4 muscle bellies on the left side of the body: *trapezius superior* (TS), *pectoralis major* (PEC), *rectus femoris* (RF) and *sternocleidomastoid* (SCM)

following recommendations from Hermens et al., 2000. These 4 muscles were chosen to represent both large proximal and distal muscle groups, known to account for over 90% of all shivering muscles (Bell et al., 1992). MVCs were used to determine the maximum contraction that the target muscles can produce so that shivering from CE can be normalized. Participants were instructed to perform shoulder shrugs for the TS, chest flies for the PEC, leg extensions for the RF, and resisted neck rotations for the SCM for 3 isometric repetitions of 5 seconds each, with a 1-min break between each repetition. Participants were verbally encouraged to produce their maximum effort. Voluntary muscle activity was minimized as much as possible to prevent contamination of the results due to non-shivering movements. Area under the curve (AUC) was used to represent total muscle shivering intensity (Gosselin and Haman, 2012).

All EMG signal analyses were performed using a custom-made MATLAB algorithm (Mathworks, Natick, MA). To quantify the shivering intensity of each muscle, root-mean-square (RMS) values were calculated from the raw EMG signals via a 50-ms overlapping window (50%). Baseline RMS values ($RMS_{baseline}$: the 15 min RMS average measured prior to CE) were subtracted from shivering RMS (RMS_{shiv}) values and RMS values derived from individual muscle MVCs (RMS_{MVC}). The normalization of shivering intensity to RMS_{MVC} was achieved using the equation provided by Haman et al. (2004):

(13) $$EMG_{shiv}\ (\%\ MVC) = \frac{RMS_{shiv} - RMS_{baseline}\ x\ 100}{RMS_{MVC} - RMS_{baseline}}$$

The AUC of shivering intensity per muscle was calculated using the Riemann sum:

(14) $$EMG_{shiv}\ (\%\ MVC) = \sum EMG_{shiv} \Delta t$$

Thermal Comfort and Sensation

Ten min before the CE period and every 10 min afterwards, participants were asked to provide their subjective TC and TS using their right hand to minimize effects on the muscles being measured by the EMG sensors. The questions were provided directly above the participants, so they did not have to move their neck and therefore contaminate the EMG data. The TC Likert scale ranges from -3 ("very uncomfortable") to +3 ("very comfortable") with no neutral option, and the TS Likert scale ranges from -5 ("coldest I've ever felt") to +5 ("warmest I've ever felt"), with a "thermoneutral" option at 0. Average TC and TS were measured as the last 20 min for each condition. These TC and TS Likert scales have been previously validated by Haman, Péronnet, Kenny, et al. (2004). The scales are presented in the supplementary data section.

Statistical Analyses

The results are depicted as the mean ± standard deviation (SD). To examine the changes in T_{skin}, H_{prod}, TC, TS, and EMG shivering intensity between the baseline and CE, a one-way ANOVA was utilized. To determine any sex differences between the T_{skin}, H_{prod}, TC, TS, and shivering intensity between sexes for the baseline and CE, a two-way ANOVA was done. Statistical differences were deemed significant at a p-value of less than or equal to 0.05. Bivariate correlations were done to determine which variables were related to each other, and Bonferroni corrections were applied. A multiple linear regression analysis was done as well to determine predictor effects on the outcomes during CE. An ANCOVA was done to isolate the effects of body anthropometrics from sex for the outcomes during CE. All statistical analyses were done in SPSS for Mac version 24.0, Chicago, IL. Graphs were created using GraphPad

Prism version 9.5.1 for Mac (GraphPad Software, San Diego, California USA, www.graphpad.com).

Chapter 3 – Results

Anthropometric variations

Even for similar total body mass, large variations in body composition exists as shown in Figure 3-2.

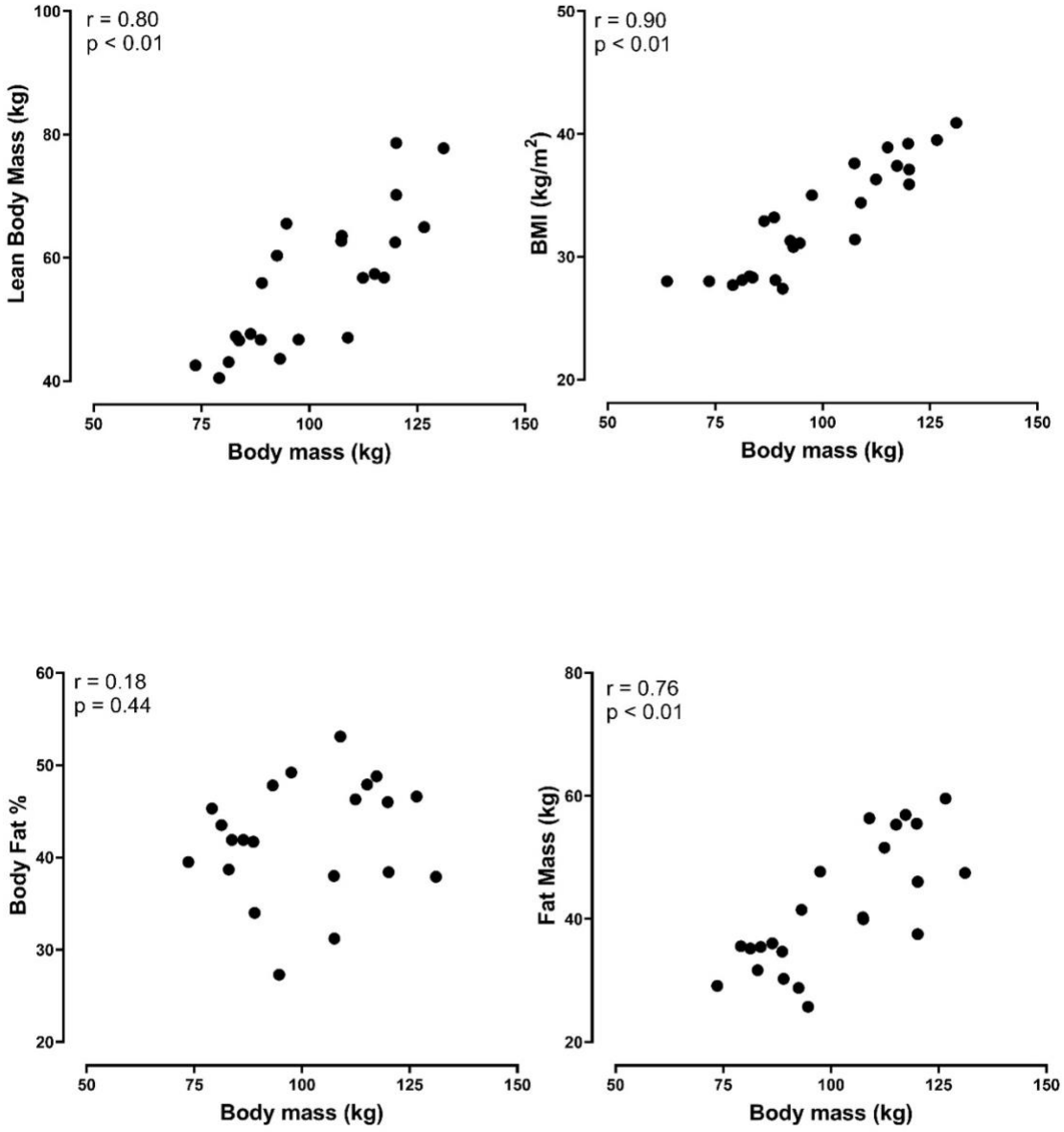


Figure 3-2: Participant body composition anthropometrics for their given body mass (kg)

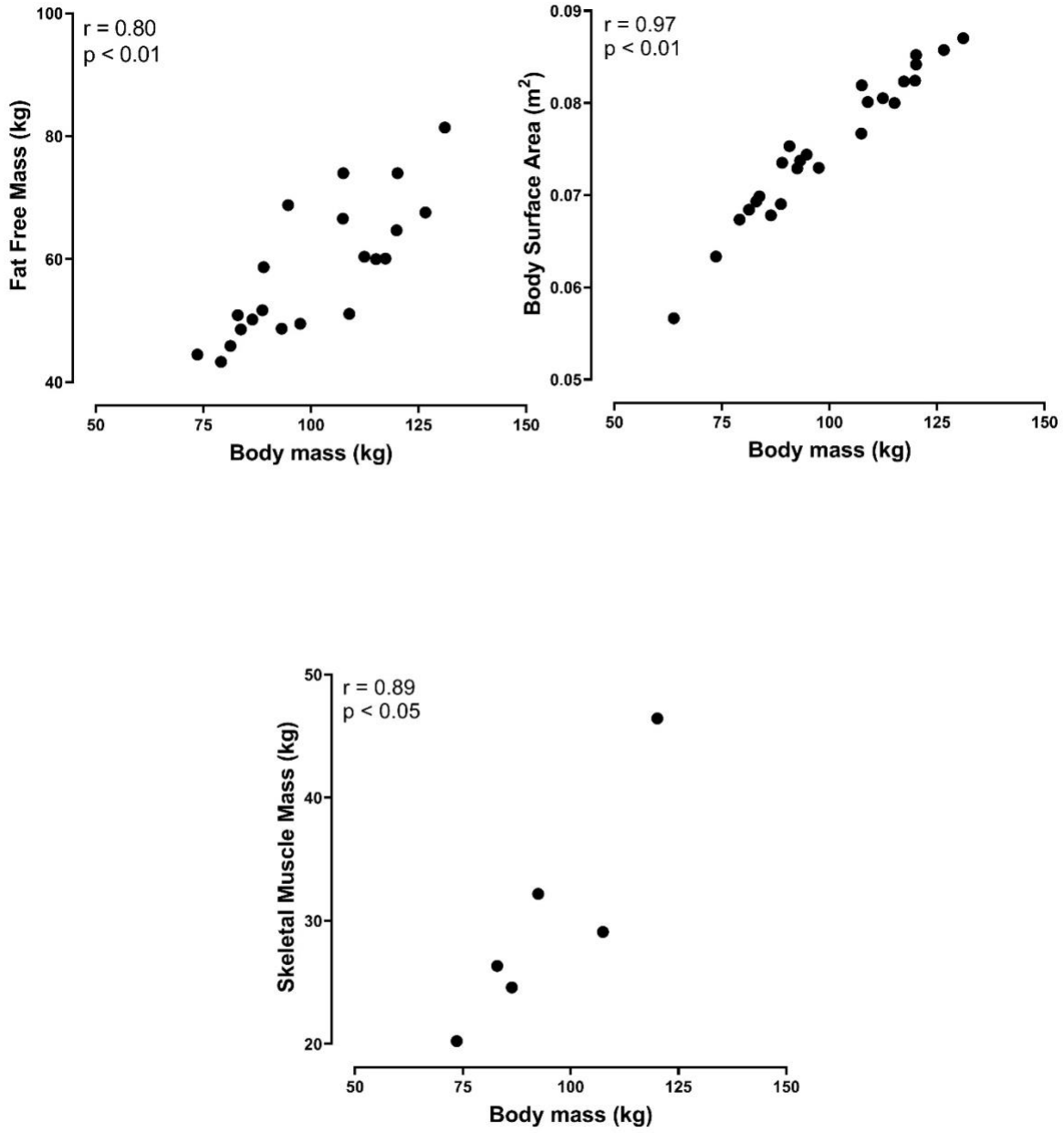


Figure 3-2: Participant body composition anthropometrics for their given body mass (kg)

These graphs show the amount of variability present within participants, even when they have the same total body mass. With an average BMI of 33.1 ± 4.5 (with a range from 27.4 to 40.9 kg/m^2), our study population was sufficiently classified as individuals living with obesity. Our

cohort consisted of 12 men and 14 women. Overall, men measured significantly higher for LBM, BSA, and FFM, whereas women had a significantly higher %BF. Furthermore, although there was a small sample count due to participants having to cross their arms to fit into the DEXA, men (n=4) had higher muscle mass (33.5 ± 8.9 vs. 22.4 ± 3.1 kg) for SMM than women (n=2). Due to the study population, participants could not have their entire body reliably placed on the DEXA. Furthermore, specific body anthropometrics varies among individuals.

Temperature Measures

The average T_{skin} over time is shown in Figure 3-3 across all participants. There was no significant difference between men and women across both control and 10 °C conditions for their final T_{skin} value ($p = 0.436$), shown in Figure 3-4. The final T_{skin} of each participant is shown in Figure 3-5.

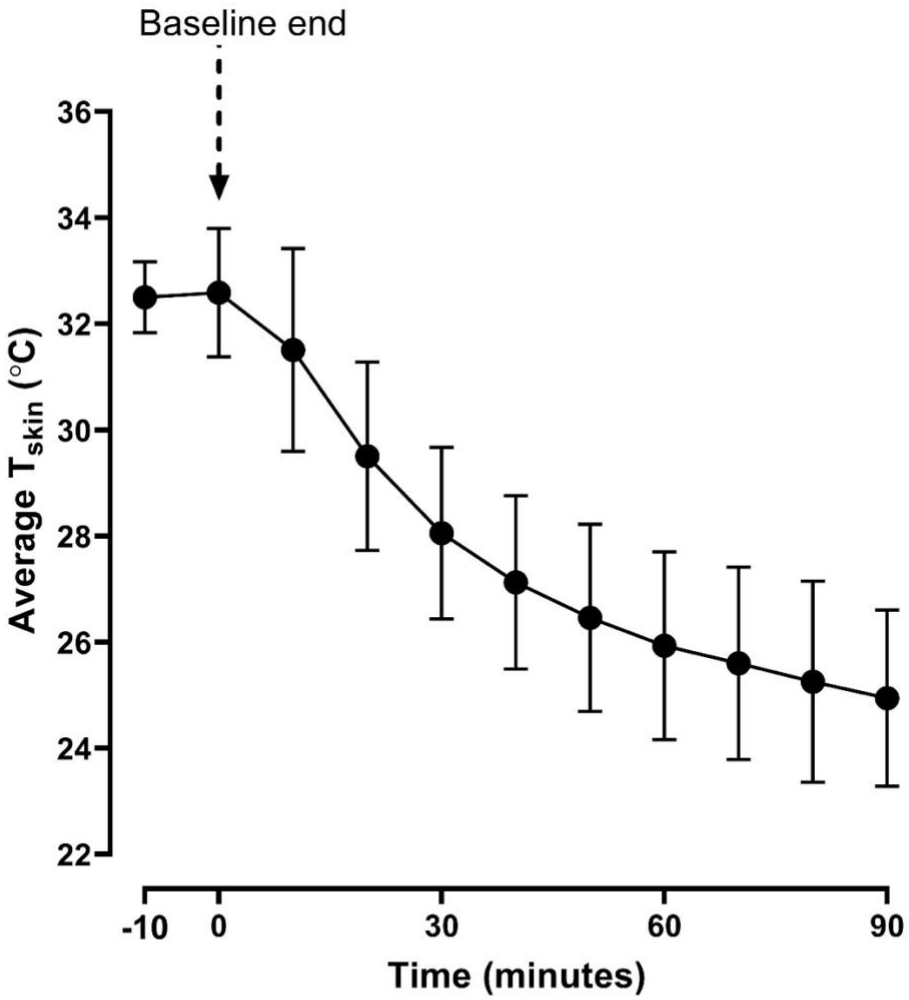


Figure 3-3: Average T_{skin} (°C) of participants over time during 10°C cold exposure. Missing participants: M009

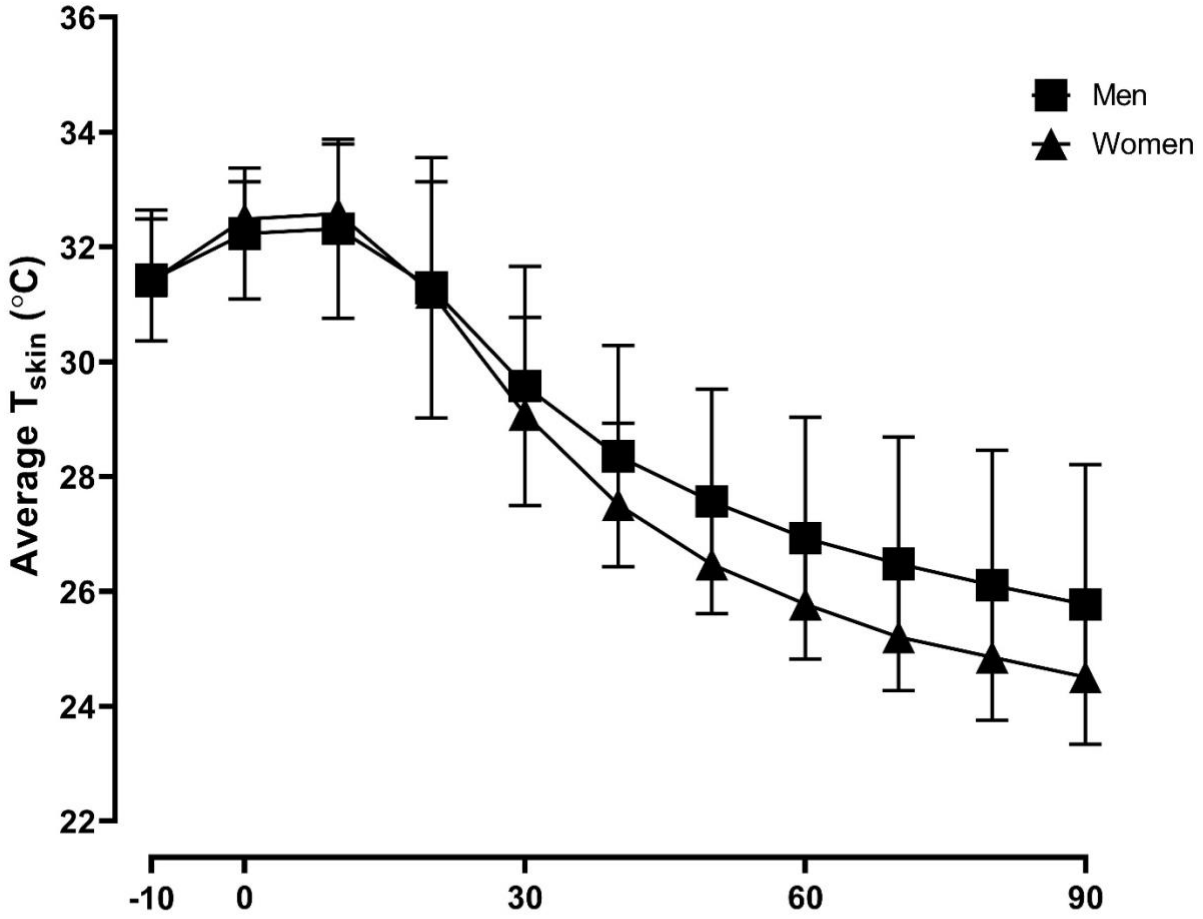


Figure 3-4: Average T_{skin} (°C) of participants, separated by sex, over time during 10°C cold exposure. Missing participants: M009

On average, participants started the CE with a T_{skin} of 32.5 ± 0.7 °C and ended the CE at 24.2 ± 1.1 °C, indicating an average of 8.3 ± 1.5 °C drop in T_{skin}. There was no significant difference between men and women for their final T_{skin} ($p = 0.256$). There was also no significant difference between men and women with regards to their T_{skin} rate of cooling during CE ($p = 0.108$).

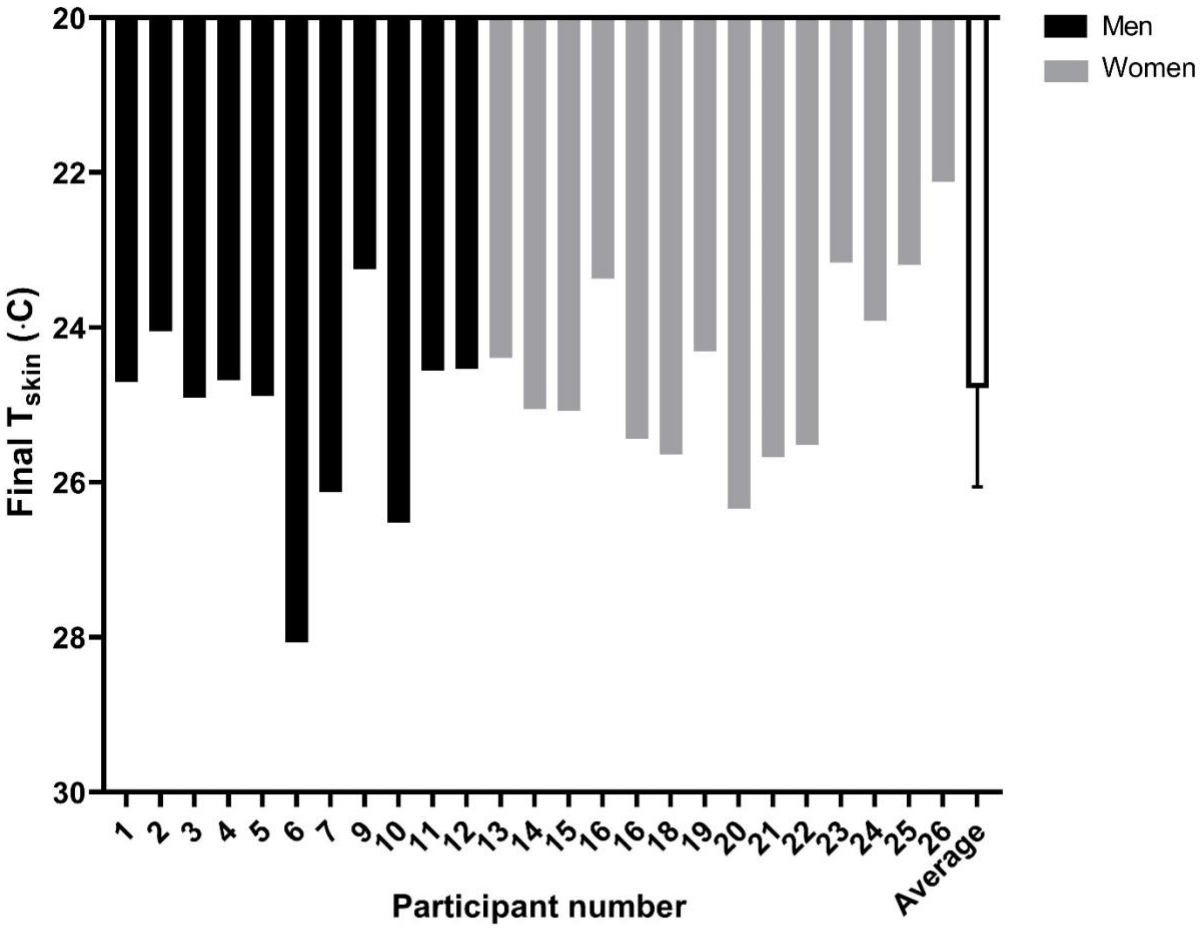


Figure 3-5: Final T_{skin} (·C) for participants after 90 mins of 10 ·C of cold exposure.
Missing participants: M009

To assess whether anthropometric measurements had a relationship with T_{skin} rate of cooling during CE, a bivariate correlation analysis was done in Table 3.2. Several relationships were found Table 3.2.

Table 3.2. *Correlations between participant anthropometrics and T_{skin} rate of cooling ($\frac{^{\circ}C}{min}$) and final T_{skin} (° C) during cold exposure (CE).*

Anthropometric	**T_{skin} rate of cooling**	**N**	**Sig.**	**Final T_{skin}**	**N**	**Sig.**
Body mass (kg)	0.25	24	0.242	0.27	24	0.209
LBM (kg)	0.36	23	0.090	0.41	23	0.052
BMI (kg/m^2)	0.21	24	0.331	0.15	24	0.477
BF %	0.33	21	0.428	-0.28	21	0.219
FM (kg)	-0.18	23	0.904	-0.09	23	0.701
FFM (kg)	0.03	21	0.350	0.20	21	0.377
BSA (m^2)	0.22	24	0.233	0.31	23	0.137
SMM (kg)	0.25	6	0.112	0.87	6	0.024

* Indicates significance at the $p < 0.05$ level
** Indicates significance at the $p < 0.001$ level

Table 3.3. *Correlations between participant anthropometrics, separated by sex and T_{skin} rate of cooling ($\frac{^{\circ}C}{min}$) and final T_{skin} (° C) during cold exposure (CE).*

	T_{skin} rate of cooling				**Final T_{skin}**			
Anthropometric	**Men**	**Sig.**	**Women**	**Sig.**	**Men**	**Sig.**	**Women**	**Sig.**
Body mass (kg)	0.07	0.85	0.21	0.47	0.04	0.92	0.27	0.36
LBM (kg)	0.19	0.61	0.32	0.29	0.37	0.30	0.27	0.38
BMI (kg/m^2)	0.02	0.95	0.26	0.38	-0.06	0.88	0.23	0.42
BF %	-0.17	0.69	0.02	0.94	-0.68	0.06	0.04	0.90
FM (kg)	-0.05	0.89	0.19	0.54	-0.26	0.46	0.18	0.56
FFM (kg)	-0.14	0.74	0.21	0.48	0.04	0.92	0.16	0.61
BSA (m^2)	0.09	0.81	0.18	0.55	0.10	0.78	0.27	0.35
SMM (kg)	0.65	0.35			0.89	0.11		

* Indicates significance at the $p < 0.05$ level
** Indicates significance at the $p < 0.001$ level

To assess whether T_{skin} measurements had a relationship with other dependent variables such as H_{prod} and % MVC during CE, a bivariate correlation analysis was done. Relationships are presented in Table 3.4.

Table 3.4. *Correlations between T_{skin} rate of cooling (°C·min^{-1}) and final T_{skin} (° C) with* H_{prod} *(kJ ·min^{-1}) and % max voluntary contraction (MVC) during cold exposure (CE) for the last 15 min.*

Variable	***H*$_{prod}$ baseline**	**N**	**Sig.**	***H*$_{prod}$ CE**	**N**	**Sig.**	**% MVC**	**N**	**Sig.**
T_{skin} rate of cooling	0.19	25	0.397	0.06	24	0.792	-0.01	23	0.951
Final T_{skin}	0.34	25	0.103	0.36	24	0.077	0.24	23	0.258

* Indicates significance at the $p < 0.05$ level
** Indicates significance at the $p < 0.001$ level

There were no correlations between H_{prod} during baseline and final T_{skin}, CE and % MVC, and T_{skin} rate of cooling and final T_{skin}.

Metabolic Measures

The H_{prod} over time across all participants during CE is shown in Figure 3-6.

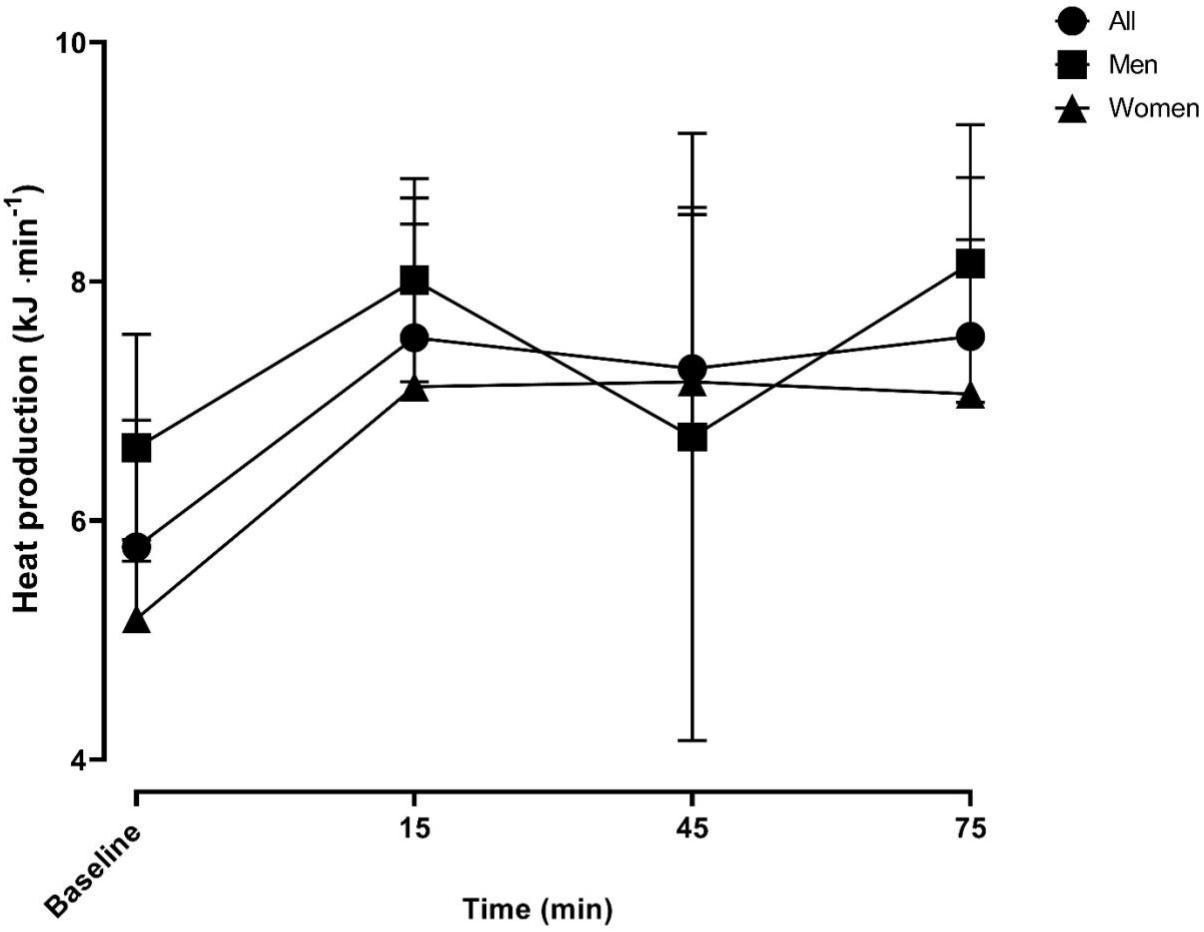


Figure 3-6: Heat production (kJ ·min^{-1}) across all participants over time when exposed to 10°C cold exposure conditions. Missing participants: M009

There was a significant difference in H_{prod} for all participants between the baseline and CE conditions (5.8 ± 1.0 kJ ·min^{-1} vs. 7.5 ± 1.3 kJ ·min^{-1}, $p < 0.001$). The individual variability and the average H_{prod} during CE are shown in Figure 3-7. Men had a significantly higher average H_{prod} than women during baseline conditions (6.6 ± 0.9 vs. 5.2 ± 0.6, $p = 0.004$), and during CE (8.2 ± 1.2 vs. 7.1 ± 1.3, $p = 0.037$).

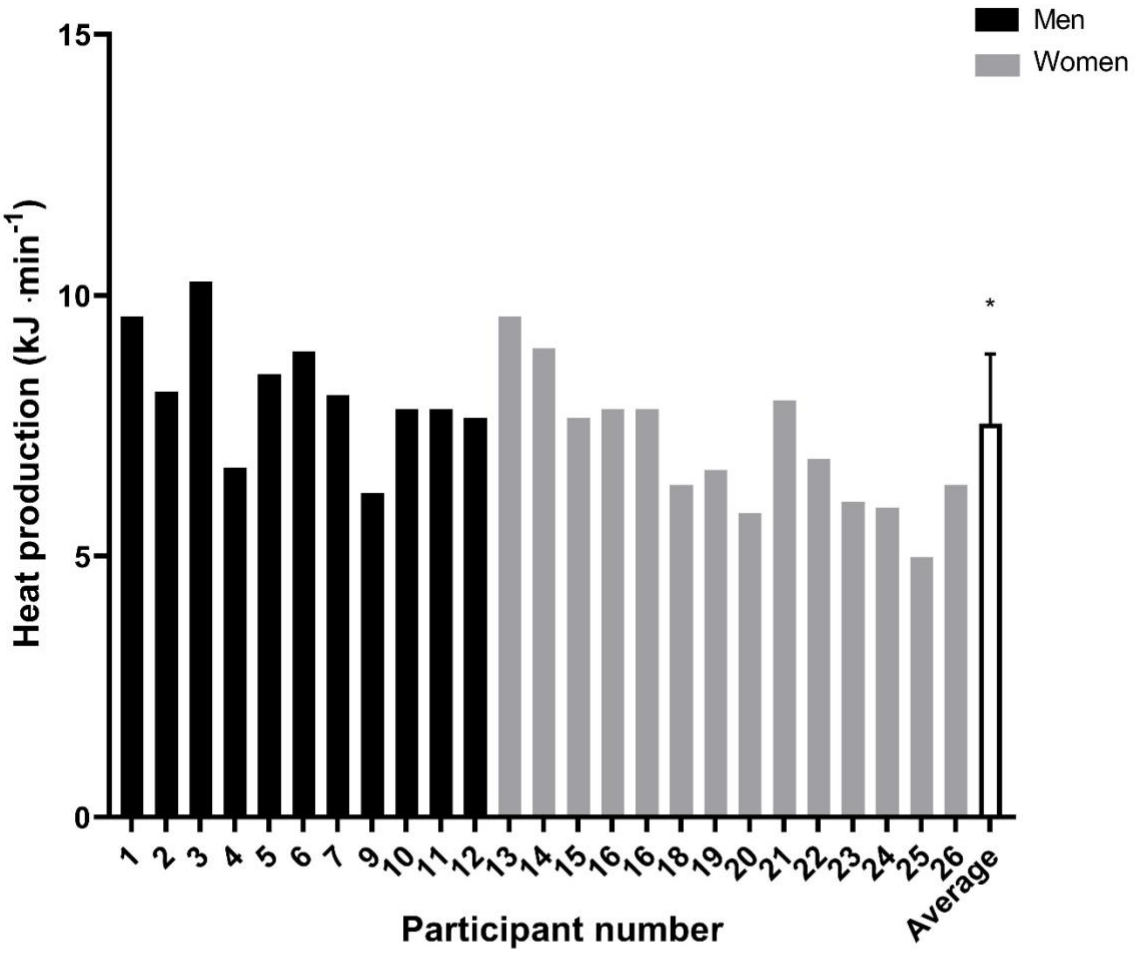


Figure 3-7: Heat production (kJ ·min^{-1}) per participant when exposed to 10°C cold exposure conditions during the final 15 min.
Missing participants: M009

The individual variability and the average of all participants for the total H_{prod} AUC during CE is shown in Figure 3-8.

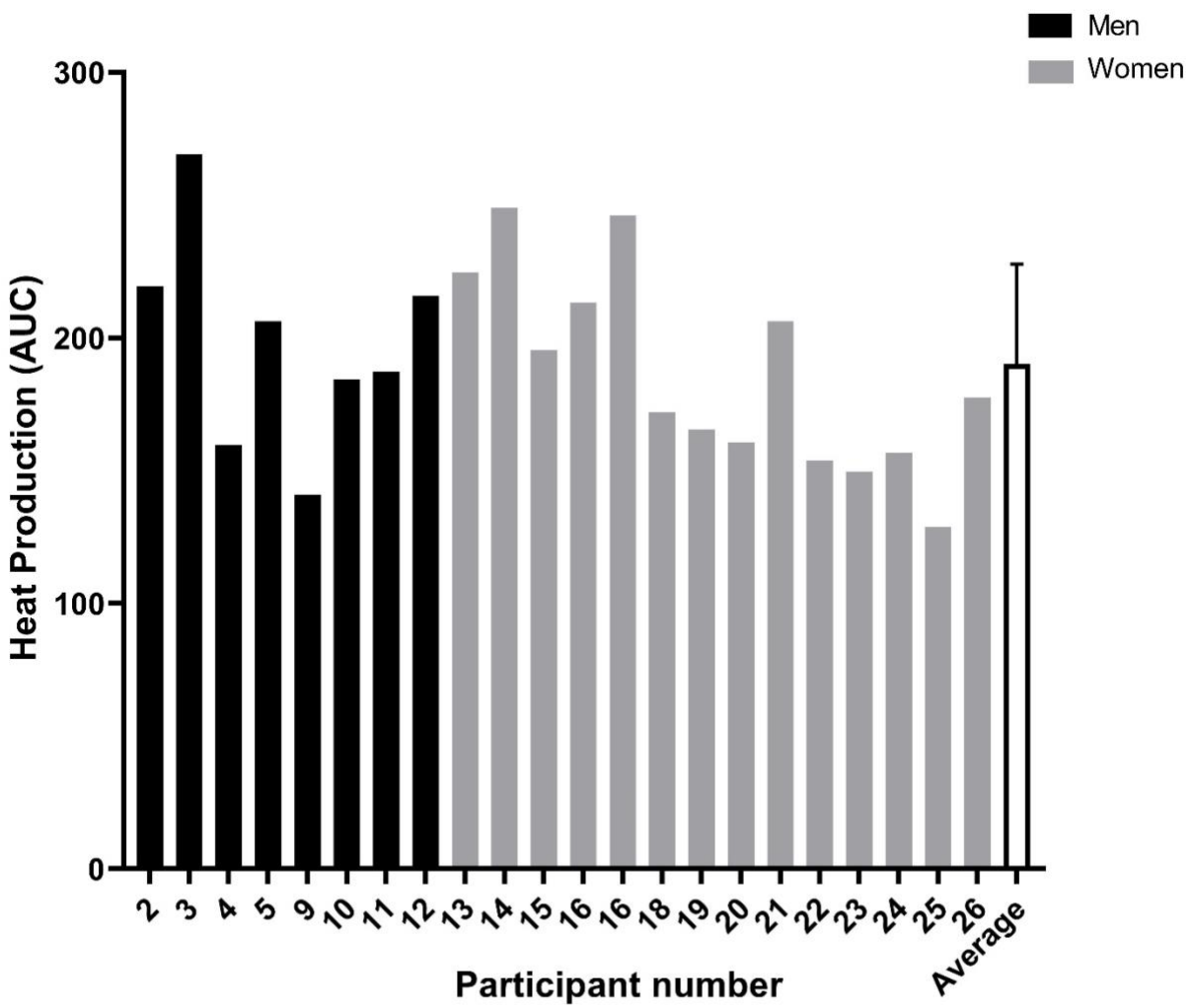


Figure 3-8: Total heat production (AUC) per participant when exposed to 10°C cold exposure conditions. Missing participants: M001, M007, M008, M009

There were no significant differences between men and women for the AUC for H_{prod} (kJ) during the CE condition (197.8 ± 36.9 vs. 185.6 ± 35.9 kJ, p = 0.481). If any participant has missing data blocks or incomplete data at any point during the cold exposure sessions, it would render their AUC calculation inaccurate, and so they were excluded.

The individual variability for CHO_{ox} (kJ ·min^{-1}) during CE is shown in Figure 3-9, and, there was a significant difference between baseline and CE conditions (0.62 ± 0.8 vs. 1.6 ± 1.3, p = 0.003) for all participants.

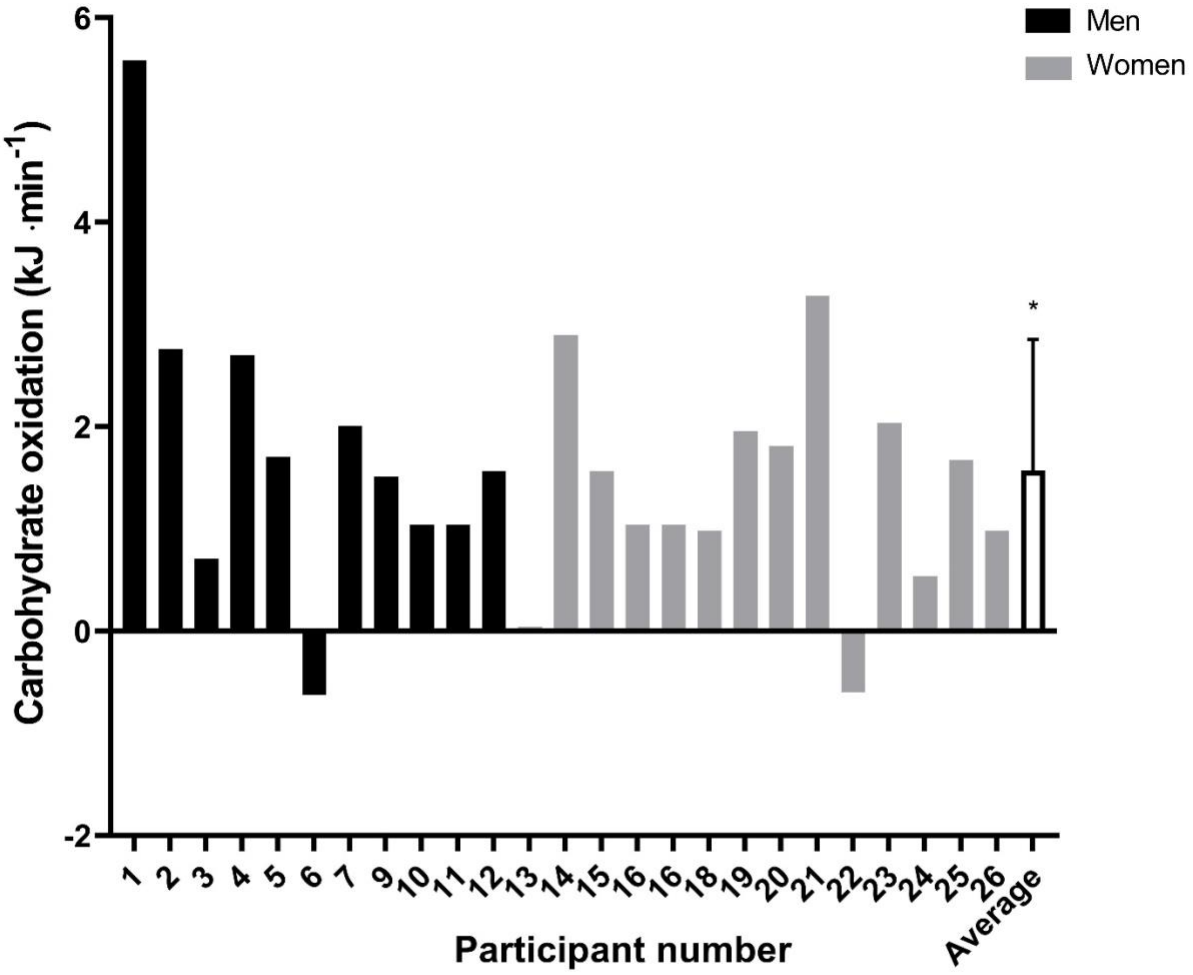


Figure 3-9: Carbohydrate oxidation (kJ ·min^{-1}) per participant when exposed to 10°C cold exposure conditions. Missing participants: M009

The individual variability for FAT_{ox} (kJ ·min^{-1}) is shown in Figure 3-10, and FAT_{ox} was no significant difference between baseline and CE conditions (3.6 ± 1.4 vs. 4.5 ± 1.8, p =0.0569) for all participants.

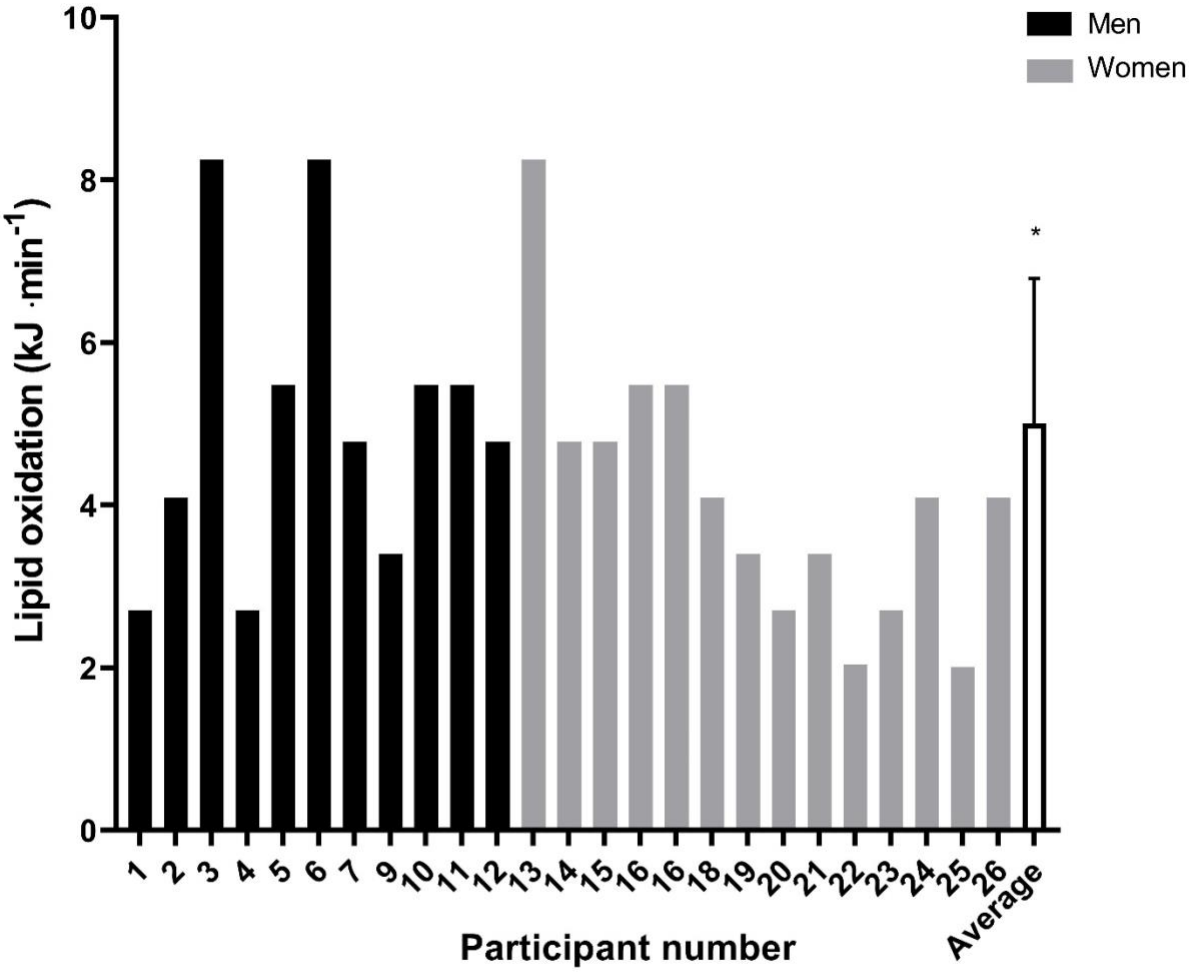


Figure 3-10: Lipid oxidation (kJ ·min^{-1}) per participant when exposed to 10°C cold exposure conditions. Missing participants: M009

Between men and women, there were no significant differences when it came to CHO_{ox} across both baseline (p = 0.554) and CE conditions (p = 0.405). There was no significant difference between men and women for FAT_{ox} for both baseline (p = 0.282, and CE conditions (p = 0.196). The metabolic fuel selection as a total percentage (total %) per participant when exposed to CE conditions CHO_{ox} and FAT_{ox}, was graphed in Figure 3-11 and Figure 3-12, respectively.

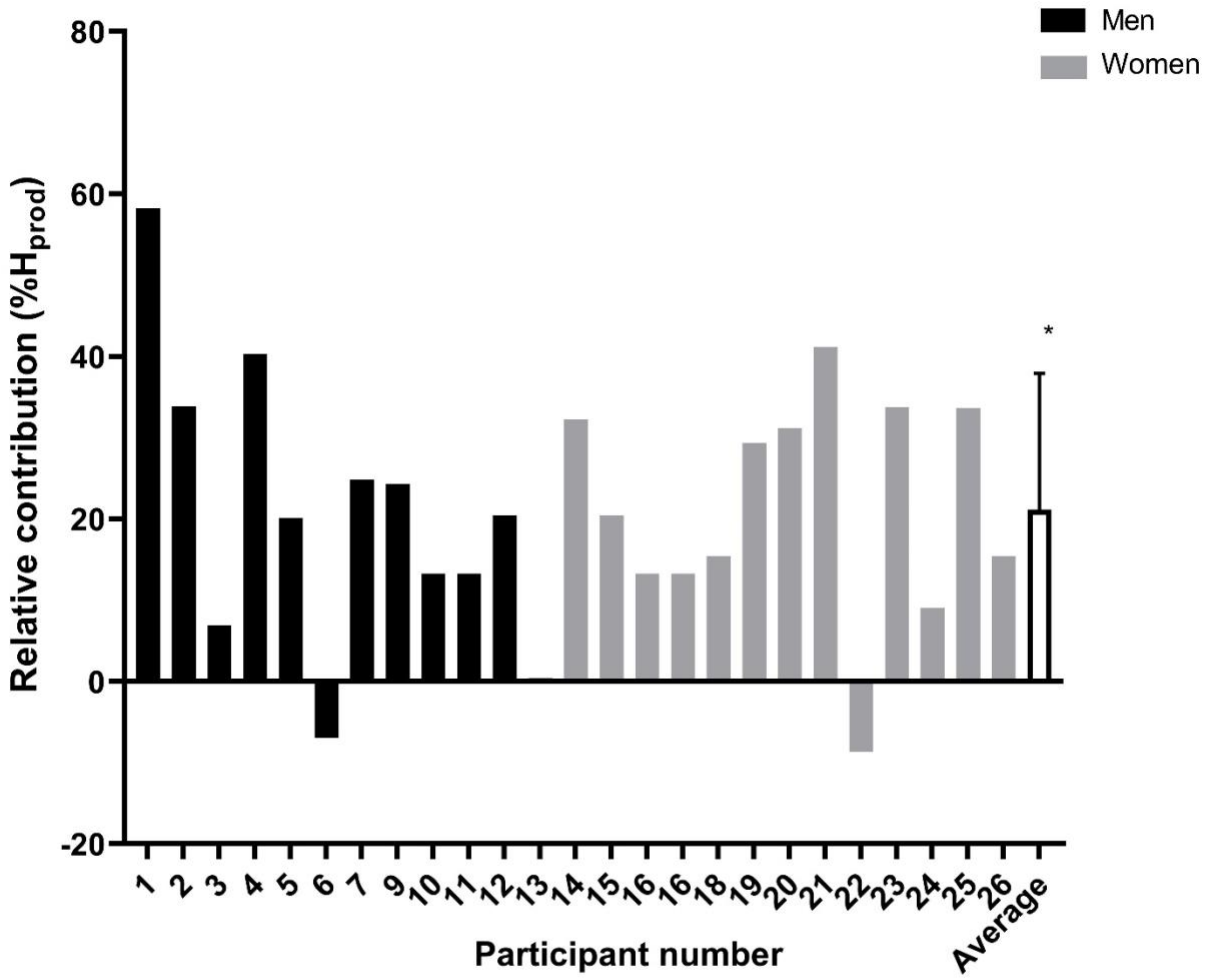


Figure 3-11: Relative contribution of carbohydrates to total heat production (%H_{prod}) per participant when exposed to 10°C cold exposure conditions during the final 15 min. Missing participants: M009

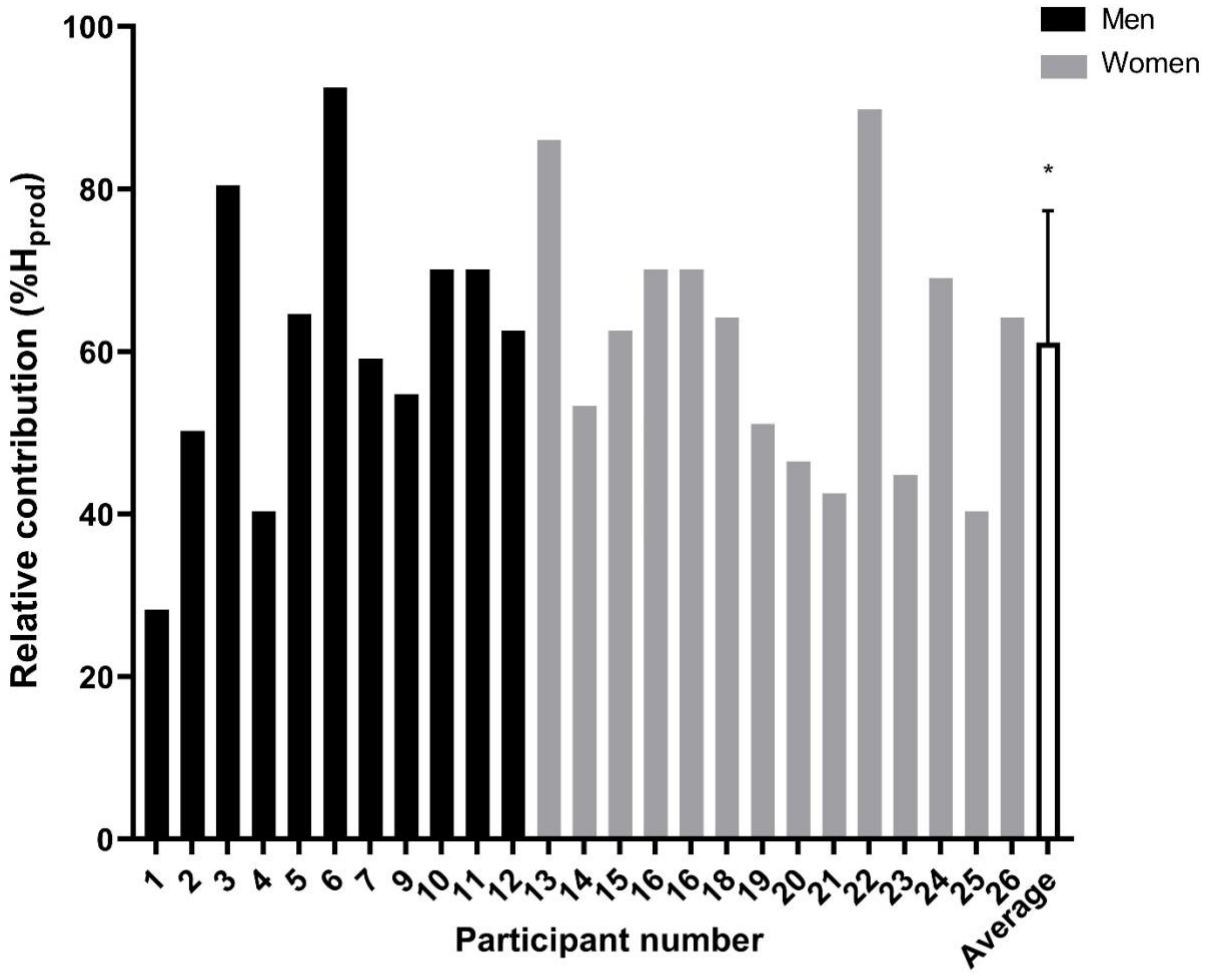


Figure 3-12: Relative contribution of lipids to total heat production (%H_{prod}) per participant when exposed to 10°C cold exposure conditions during the final 15 min. Missing participants: M009

Across all participants $CHO\ \%_{ox}$ was significantly lower during baseline than during CE (10.9 ± 12.8 % vs. 21.1 ± 15.1%, p = 0.017). $FAT\ \%_{ox}$, was significantly lower during baseline than during CE (37.4 ± 21.8% vs. 61.1 ± 17.1%, p < 0.001).

With regards to metabolic fuel differences between men and women, $CHO\ \%_{ox}$ during baseline (p = 0.698) and CE conditions (p = 0.685) had no significant differences between men

and women. $FAT\ \%_{ox}$ during baseline was significantly higher for men than for women (p = 0.048), but there was no significant difference for the CE condition (p = 0.984). Specific values are given in Table 3.5, Supplementary Data.

To assess whether anthropometric measurements had an influence with rate of H_{prod}, a bivariate correlation analysis was done. Several significant relationships were found Table 3.6.

Table 3.6. *Correlations between participant anthropometrics and heat produced (kJ ·min^{-1}) during fasting (pre-cold exposure), post-feeding and during the final 15 min of cold exposure (CE).*

Anthropometric	**Baseline**	**N**	**Sig.**	**Post-Feeding**	**N**	**Sig.**	**CE**	**N**	**Sig.**
Body mass (kg)	0.76**	24	< 0.001	0.72**	24	< 0.001	0.45	24	0.029
LBM (kg)	0.88**	22	< 0.001	0.76**	22	< 0.001	0.49	23	0.016
BMI (kg/m^2)	0.65**	24	< 0.001	0.68**	24	< 0.001	0.39	24	0.054
BF %	-0.29	20	0.197	-0.03	20	0.885	-0.08	21	0.721
FM (kg)	0.25	22	0.252	0.36	22	0.097	0.13	23	0.571
FFM (kg)	0.85**	20	< 0.001	0.71**	20	< 0.001	0.45	21	0.042
BSA (m^2)	0.76**	24	< 0.001	0.69**	24	< 0.001	0.45	24	0.027
SMM (kg)	0.94	6	< 0.005	0.94*	5	0.005	0.61	6	0.195

* Indicates significance at the p < 0.05 level
** Indicates significance at the p < 0.001 level

To assess whether anthropometric measurements had an influence with the change in rate of H_{prod}, a bivariate correlation analysis was done. Relationships that were found are shown in Table 3.7.

Table 3.7. *Correlations between participant anthropometrics and changes in metabolic measurements during the final 15 min of cold exposure (CE) from baseline*

Anthropometric	**Δ H_{prod}**	**N**	**Sig.**
Body mass (kg)	-0.26	22	0.219
LBM (kg)	-0.37	21	0.079
BMI (kg/m^2)	-0.15	22	0.494
BF %	0.22	19	0.323
FM (kg)	-0.07	21	0.744
FFM (kg)	-0.35	19	0.109
BSA (m^2)	-0.28	22	0.187
SMM (kg)	-0.56	5	0.251

* Indicates significance at the $p < 0.05$ level
** Indicates significance at the $p < 0.001$ level

When looking at relationships between body anthropometrics and the relative change in H_{prod} from baseline, there were no significant correlations. One thing to note is that in Table 3.6 with the exception of %BF, all body anthropometrics had a negative correlation (although not significant) with the relative change in H_{prod}. This may indicate that their increased body anthropometrics confer a protective effect in resisting a higher relative change in H_{prod}. However, without further testing with more samples to determine whether there truly is no significance, this interpretation remains unfounded.

Shivering Activity

The % MVC over time for all participants is shown in Figure 3-13.

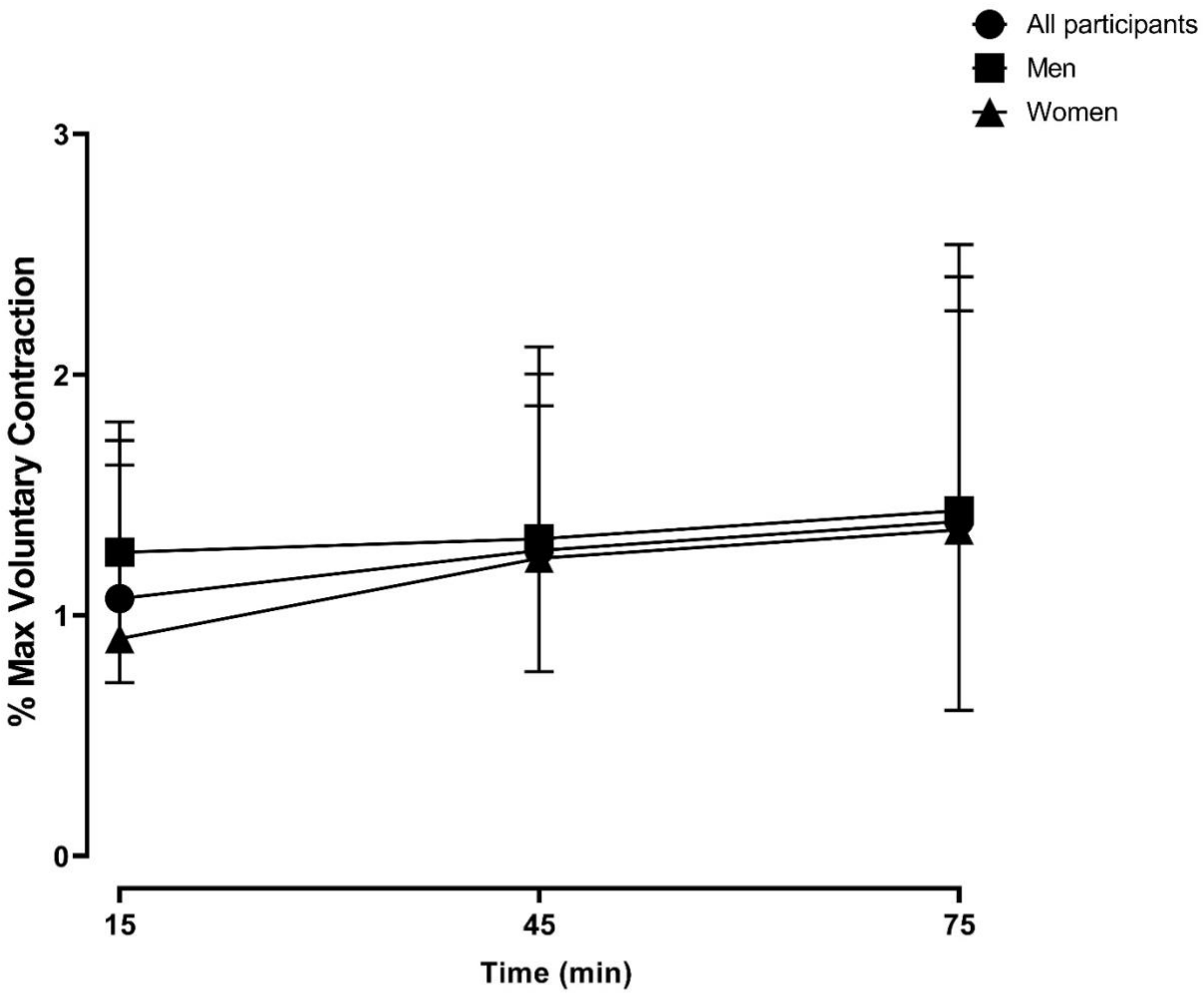


Figure 3-13: Changes in shivering (% max voluntary contraction) across all participants when exposed to 10°C cold exposure conditions over 90 min.
Missing participants: M009

The % MVC (% shivering intensity) for each participant was graphed in Figure 3-1 to show the variability in their responses when exposed to CE.

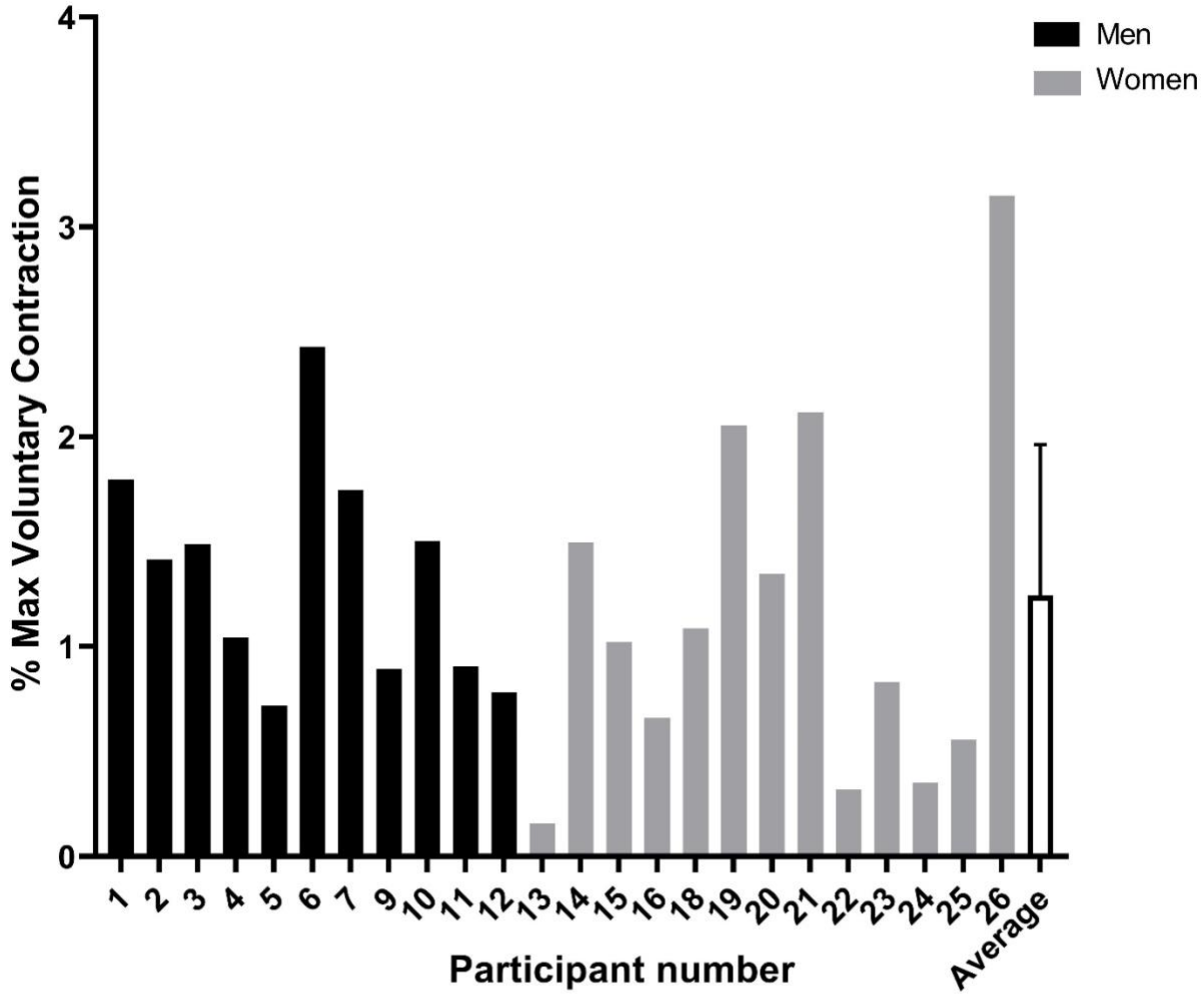


Figure 3-14: Changes in shivering (% max voluntary contraction) per participant when exposed to 10°C cold exposure conditions over 90 min.
Missing participants: M009, W006

This reaction wasn't localized to specific muscle groups; rather, it was generalized and did not significantly differ between sexes. This implies a universal, non-selective activation of muscle groups in response to CE.

The average % MVC AUC (% shivering intensity AUC) across all muscles for each participant was graphed in Figure 3-15 to show the variability in their responses when exposed to CE.

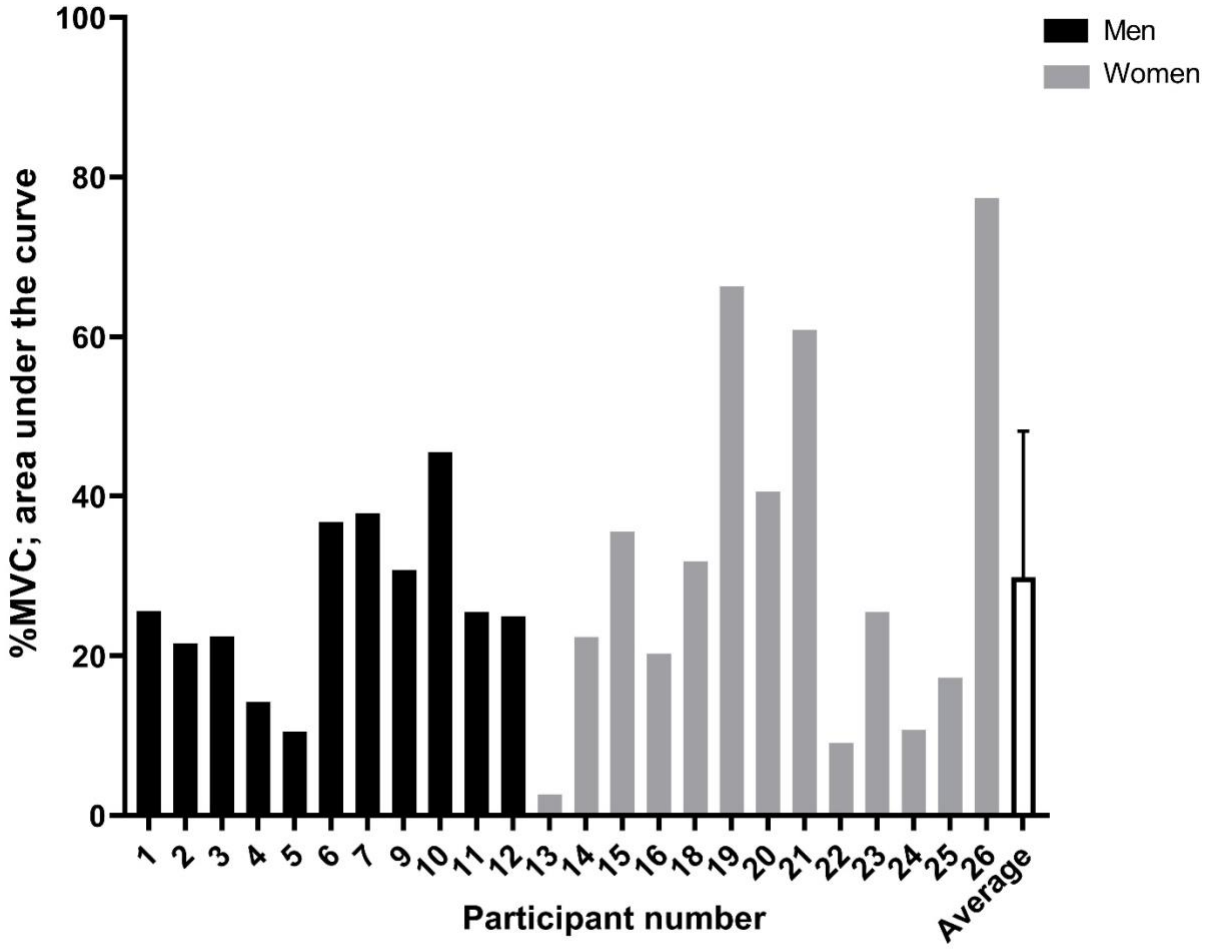


Figure 3-15: Shivering (%MVC; area under the curve) per participant when exposed to 10°C cold exposure conditions over 90 min.
Missing participants: M009, W006

There was no significant difference for average % EMG MVC activation between men and women (1.4 ± 0.7 vs. 1.2 ± 0.9, p = 0.407). There was no significant difference for average MVC AUC between men and women (26.9 ± 10.3 vs. 32.3 ± 23.2, p = 0.481).

To determine whether anthropometric measurements had a relationship with % average MVC or average MVC AUC, a bivariate correlation analysis was done. The results are shown in Table 3.8.

Table 3.8. *Correlations between participant anthropometrics and % average max voluntary contraction (MVC) during cold exposure (CE).*

Anthropometric	**% MVC**	**N**	**Sig.**	**AUC**	**N**	**Sig.**
Body mass (kg)	-0.01	23	0.954	-0.26	23	0.232
LBM (kg)	0.23	22	0.302	-0.07	22	0.767
BMI (kg/m^2)	0.13	23	0.562	-0.14	23	0.518
BF %	-0.44	20	0.054	-0.38	20	0.098
FM (kg)	-0.39	22	0.074	-0.43	22	0.046
FFM (kg)	0.13	20	0.582	-0.09	20	0.699
BSA (m^2)	-0.08	23	0.758	-0.29	23	0.174
SMM (kg)	0.37	6	0.473	-0.39	6	0.444

* Indicates significance at the $p < 0.05$ level
** Indicates significance at the $p < 0.001$ level

To determine whether there was a relationship between the % MVC and H_{prod} for each participant, a bivariate correlation analysis was done. The result is shown below in Figure 3-16. There was no correlation.

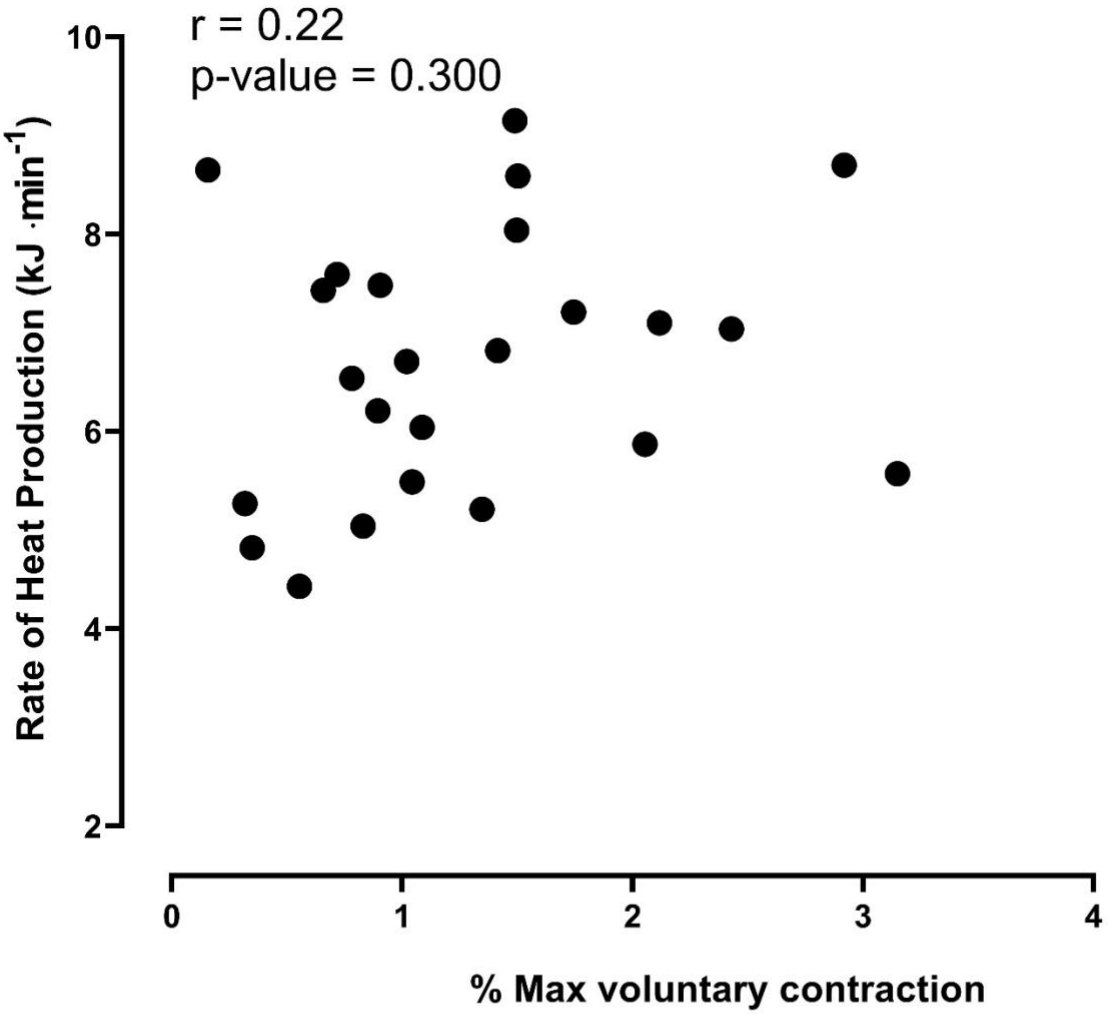


Figure 3-16: Relationship between the shivering (%MVC) and rate of heat production (kJ ·min^{-1}) when exposed to 10°C cold exposure conditions during the final 15 min.

Thermal Comfort and Sensation

The change in TC and TS ratings per participant when exposed to CE relative to baseline conditions is shown in Figure 3-17 and Figure 3-18, respectively. There was a significant difference for both the average TC and TS ratings between both the baseline and CE conditions ($p < 0.05$) across all participants. Specifically, TC values decreased by 2.4, going from +1.2 ± 1.6 to -1.2 ± 1.5. Similarly, TS values decreased by 3.6, from +0.7 ± 1.4 to -2.9 ±1.3.

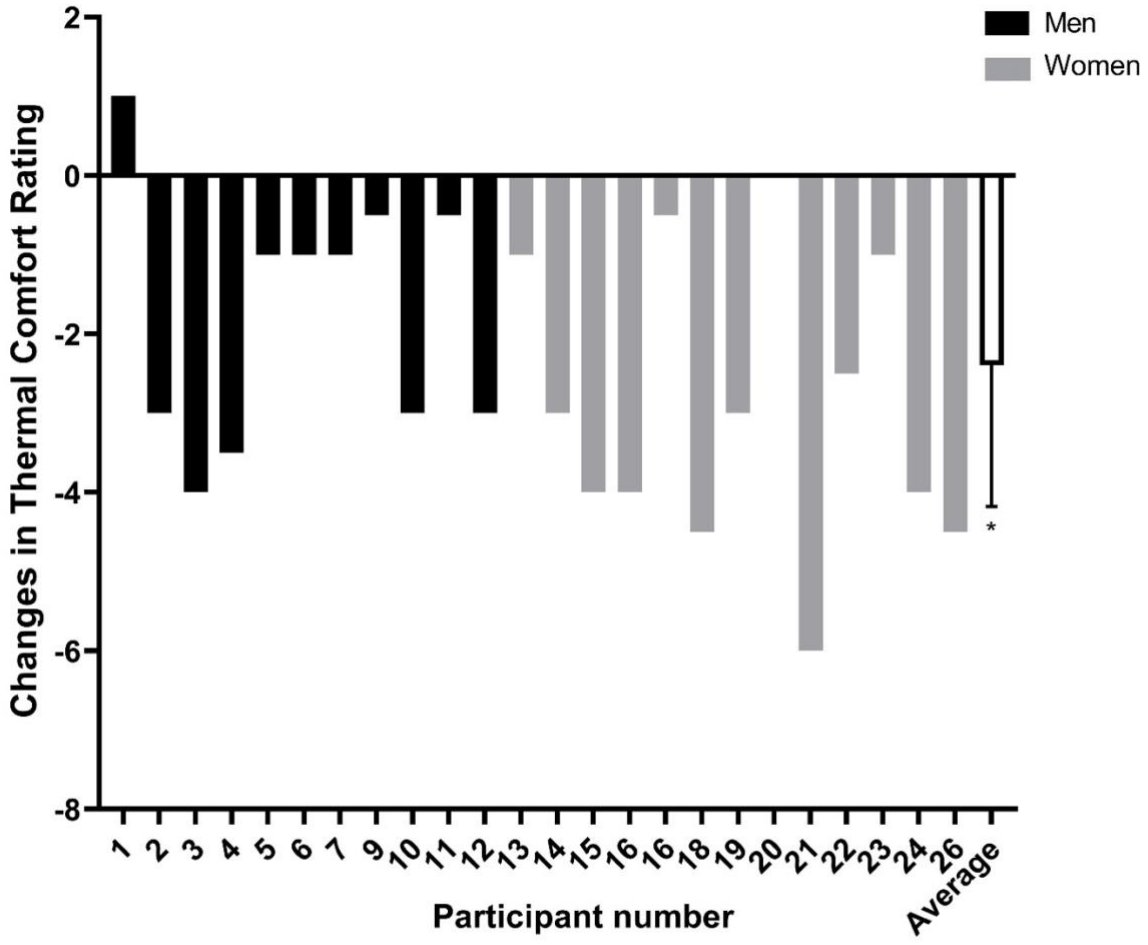


Figure 3-17: Changes in thermal comfort rating per participant when exposed to 10°C cold exposure conditions during the final 20 min from baseline.
Missing participants: M009, W014

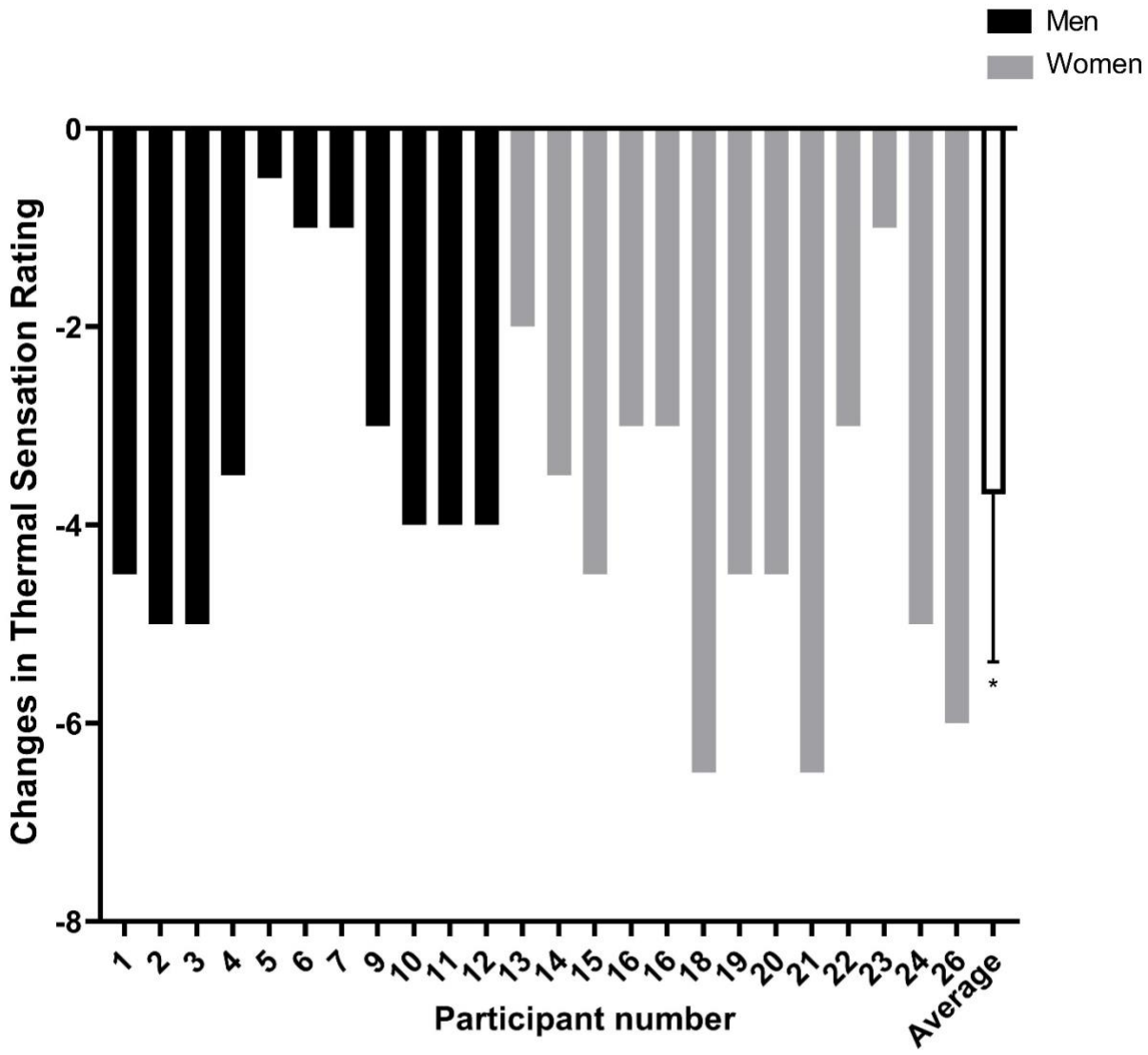


Figure 3-18: Changes in thermal sensation rating per participant when exposed to 10°C cold exposure conditions during the final 20 min from baseline.
Missing participants: M009, W014

There were no significant differences between men and women for TC or TS across both the baseline and CE conditions ($p > 0.05$ for all) Table 3.9, Supplementary Data. For TC in men, there was a decrease in TC from +0.5 ± 1.7 to -1.3 ± 1.1 and for women, a decrease in TC from

+1.7 ± 1.2 to -1.1 ± 1.9. For TS in men, there was decrease from +0.3 ± 1.8 to -3.0 ± 1.1 and for women a decrease in TS from +1.1 ± 0.9 to -2.9 ± 1.4. There were no significant differences between men and women across all conditions.

To assess whether anthropometric measurements had a relationship between TC or TS, a bivariate correlation analysis was done. Results are presented in Table 3.10.

Table 3.10. *Correlations between participant anthropometrics and changes in thermal comfort (TC) and thermal sensation (TS) ratings during cold exposure (CE) during the final 20 min from baseline.*

Anthropometric	**Δ TC**	**N**	**Sig.**	**Δ TS**	**N**	**Sig.**
Body mass (kg)	0.196	23	0.371	0.228	22	0.307
LBM (kg)	0.281	22	0.206	0.341	21	0.131
BMI (kg/m^2)	0.152	23	0.489	0.150	22	0.505
BF %	-0.090	20	0.707	0.083	19	0.737
FM (kg)	0.180	22	0.422	0.365	21	0.104
FFM (kg)	0.277	20	0.237	0.284	19	0.239
BSA (m^2)	0.203	23	0.354	0.237	22	0.287
SMM (kg)	0.540	6	0.269	0.608	6	0.200

* Indicates significance at the $p < 0.05$ level
** Indicates significance at the $p < 0.001$ level

To assess whether TC or TS had a relationship with other dependent variables such as H_{prod} and % MVC during CE, a bivariate correlation analysis was done. Results are presented in Table 3.10. The average final TC and TS rating was used to determine the correlation, as it was also the average final as H_{prod} and MVC measurements used.

Table 3.11. *Correlations between thermal comfort (TC) and thermal sensation (TS) ratings during cold exposure (CE) during the final 20 min with* H_{prod} *(% max voluntary contraction (MVC) and average max voluntary contraction area under the curve (MVC AUC)*

Rating	***H*_{prod} Baseline**	**N**	**Sig.**	***H*_{prod} CE**	**N**	**Sig.**	**% MVC**	**N**	**Sig.**	**MVC AUC**	**N**	**Sig.**
TC	-0.08	23	0.694	-0.02	24	0.913	-0.37	23	0.075	-0.34	23	0.119
TS	0.02	24	0.921	0.06	24	0.760	-0.59*	23	0.003	-0.06	23	0.791

* Indicates significance at the $p < 0.05$ level
** Indicates significance at the $p < 0.001$ level

Chapter 4 – Discussion

The purpose of my thesis was to determine how variances in body anthropometrics relate to an individual's thermogenic and thermal responses in acute compensable CE. This was done by exposing participants to 90 min of 10°C of circulating cold water while they lay supine in an LCS and changes in T_{skin}, H_{prod}, muscle activity, and TC and TS ratings were recorded. Results showed significant decreases in final T_{skin}, but, relative to lean individuals, a lessened metabolic and shivering response. Participants still showed strong, negative TC and TS ratings. I hypothesized that participants with greater mass and larger body anthropometric measurements would exhibit greater thermal responses to the CE. As per the results, these hypotheses were refuted.

Anthropometric variations

This difference in body weight and composition between individuals living with obesity and lean individuals is influenced by factors such as genetics, age, sex, and energy balance. These anthropometric differences between men and women may have played a role in how individuals reacted during both baseline and the CE conditions, which will be explored in each section below. Furthermore, although some individuals have a similar total body mass, the distribution and proportion of various body anthropometrics varies between them, and so that total body mass should not be used as the sole determinant when it comes to determining how they react in CE – it may be their specific variable body composition that also plays a role in how they react in CE. Each anthropometric measure is investigated below to determine its effects on dependent variables like T_{skin}, H_{prod}, shivering activity, and TC and TS ratings. However, it is

unclear how these variations in anthropometric measurements can influence H_{prod} and other metabolic responses during mild CE.

Temperature Measures

A decrease in T_{skin} determines H_{loss} due to a cascading effect of physiological reactions so therefore subsequent interpretations of primary and secondary outcomes will be based on effects of T_{skin} cooling. This cascade begins with thermal receptors in the skin detecting the drop in temperature, which sends neural signals to the hypothalamus. The hypothalamus then activates various thermoregulatory mechanisms, discussed above, including vasoconstriction to minimize heat loss through the skin and potentially triggering processes such as ST. This results in an increase in H_{prod} to generate more internal heat.

How anthropometric measures influence the variability within participant temperature measures will be explored in this section, whereas later sections will explore how this variability influences other factors. While there remained a decrease in T_{skin}, this decrease was not the primary driver behind the increased H_{prod} as expected.

It is generally agreed that T_{skin} at rest is decreased with increased body fat percentage (Salamunes et al., 2017; Savastano et al., 2009), and a greater body fat percentage and a greater skinfold thickness are associated with delayed and lower increases in T_{skin} following exercise (Weigert et al., 2018). On average, participants started the CE with a T_{skin} of 32.5 ± 0.7 °C and ended the CE at 24.2 ± 1.1 °C, indicating an average of 8.3 °C drop in T_{skin} when subjected to the 10 °C cold stimulus for 90 min. None of the correlations between T_{skin} rate of cooling and body anthropometrics were significant, which indicates that body composition factors do not have a substantial impact on the T_{skin} rate of cooling during CE within participants. Similarly, between

final T_{skin} and body anthropometrics. This suggests that factors other than body composition might play a more critical role in T_{skin} variability in response to CE.

Metabolic Measures

This section aims to explore how H_{prod} and fuel selection may have been influenced by body anthropometrics, and the variability in H_{prod} and fuel selection within participants. As per Table 3.6, when exposed to cold, all participants displayed a greater variability in their physiological responses. Given these observations, CE accentuates physiological differences within individuals, irrespective of their body anthropometric measures. CE acts a stressor that heightens the unique physiological characteristics of each individual, making these differences more pronounced than under normal conditions, and this occurs irrespective of body anthropometric factors.

During CE, there were no correlations with H_{prod}. This is dissimilar to what was expected, as evidenced in the study by Ravussin et al. (1988), who observed that H_{prod} was positively correlated with LBM and FFM, but not by body mass or %BF at room temperature. Furthermore, when looking at relationships between body anthropometrics and the relative change in H_{prod} from baseline, there were no significant correlations.

As expected, there was an observed average increase in H_{prod} (1.7 ± 1.3 kJ $\cdot min^{-1}$) during CE. However, this increase in H_{prod} is much less pronounced than in lean individuals when exposed to a similar stimulus (cold exposed by an LCS) (7.0 ± 1.8 kJ $\cdot min^{-1}$as per Dumont et al. (2022)). Furthermore, although participants in the study expressed a warmer T_{skin} (27°C vs. an average of 25°C), they expressed a higher H_{prod}.

There was a significant amount of interindividual variability in H_{prod}, with some participants seeing no increase when CE, whereas others saw an increase almost as high as 3.4 kJ

·min^{-1}. Although there was a sex difference with regards to H_{prod}, when controlling for body anthropometrics, this sex difference disappeared. This is in line with what Admiraal et al. (2013), Castellani and Young (2016) and Tikuisis et al. (2000) found, but not in line with the sex differences regarding H_{prod} after controlling for %BF that S. E. Pettit et al. (1999) found. This implies that the differences in H_{prod} during CE between men and women were linked to anthropometric differences [height (m), body mass (kg), LBM (kg), BMI (kg/m^2), %BF, fat mass (kg), FFM (kg) and BSA (m^2)], rather than sex differences (while controlling for their menstrual cycle). SMM (kg) was not used as a covariate in the ANCOVA due to the low sample size (n=6). However, the correlation between LBM (kg) and SMM (kg) was 0.951, p = 0.004. %BF

On average, there was only a 22% increase in H_{prod} during CE, calculated with the Weir (1949) equation. As a point of comparison, young women walking at a moderate speed (around 3 km/h) on level ground has an H_{prod} increase of around 112% (Haveman-Nies et al., 1996) while Sato and Yamada (2018) found a 112% increase when walking at 4.2 km/h. With regards to individuals living with obesity specifically, it was found that having individuals walking while working led to a 90% increase in H_{prod} per hour compared to just sitting (Levine and Miller, 2007).

With regards to metabolic fuel selection during CE, a study by Haman, Legault, and Weber (2004) found that CIT led to an increase in CHO_{ox} ranging anywhere from 2-8 times higher than a participants' resting state in lean individuals. This CHO_{ox} % then represented 33-78% of H_{prod} during CE, whereas FAT_{ox} accounted for 14-60% of H_{prod} during CE. Our results differed with all 3 respects. On average, there was no significant increasein CHO_{ox} when exposed to the cold, which accounted for 21% of H_{prod} during CE, whereas lipids accounted for 61% of H_{prod} during CE. There was also a wide range in responses to CHO_{ox} (0.4% - 58.2%) and

FAT_{ox} (28.2% - 92.4%). The only anthropometric measure to significantly correlate with CHO_{ox} and FAT_{ox} was SMM. However, due to the low sample count of 6 participants, further research is necessary.

Previous studies (Haman et al., 2002; Haman et al., 2005; Pettit et al., 1999) have shown that $FAT\ \%_{ox}$ contributes 25% more of the total H_{prod} for women than for men (vice versa for $CHO\ \%_{ox}$, there is a greater contribution to H_{prod} for men than for women) under the same CE conditions. However, as per Table 3.5, Supplementary Data, there were no significant differences between men and women in our cohort between $FAT\ \%_{ox}$ and $CHO\ \%_{ox}$ when exposed to the cold. Although the differences were not significant, women had both a lower $FAT\ \%_{ox}$ (-0.3%) and $CHO\ \%_{ox}$ (-13.8%) than men. However, use of the LCS in a lean population also presented no significant differences in fuel selection between sexes in the Dumont et al. (2022) study. Due to the contradictory findings, further studies should be done to isolate whether sex differences in fuel selection is dependent on what type of CE (compensable vs. non-compensable) is administered, or whether there are anthropometric factors involved as well.

Variations in shivering activity

This section aims to investigate how anthropometric variations relate to shivering activity. As per Table 3.8, no significant correlations found, which indicates that the relationships between anthropometric measurements and shivering intensity during CE in individuals living with obesity is little influenced by an individual's body composition. One reason this may be because of the level of heterogeneity in the participant group. Daniels and Baker (1961) identified a significant negative correlation in men between %BF and shivering (measured by levels of H_{prod}, shivering was measured on a 5-point scale) when subjecting

participants to 15 °C cold air for two hours. Specifically, they found that for men with an average %BF of 18.2%, the correlation between %BF and H_{prod} was marked (r= -0.60). This suggests that as body fat percentage increases, the H_{prod} during shivering decreases. An important note to make is that shivering was rated subjectively on a 5-point scale. However, this relationship appears to differ in populations with higher body fat percentages. In this thesis, the average %BF was 42.1%, and the correlation was notably weaker (r= -0.08). This minimal correlation implies that in individuals with higher body fat, the expected decrease in H_{prod} with increasing %BF during shivering is not as pronounced. This could be indicative of a threshold effect where beyond a certain level of body fat, the impact on H_{prod} and, consequently, shivering response, becomes less significant.

A previous study by Blondin, Tingelstad, et al., (2014) found that a 9 °C decrease in T_{skin} (°C) lead to shivering increases of about 10% MVC in lean individuals. However, in our cohort, an 8.3 °C decrease in T_{skin} lead to a shivering increase of only about 1.4% across sexes. There were no significant sex differences in overall muscle activation, which indicates that despite differences in body composition and other physiological parameters between men and women, sex does not significantly influence the muscle activity response to CE in obesity. This suggests that in the context of obesity, both sexes recruit similar levels of muscle activity to generate heat during CE. This is similar to what previous studies have found (Dumont et al., 2022), and doing this allows us to present thorough knowledge of shivering intensity in individuals living with obesity in a standardized manner. This would be in line with what van Marken Lichtenbelt et al., (2009) stated, that individuals with higher adiposity don't experience as significant an increase in H_{prod} as lean individuals. It is important to remember that H_{prod} is primarily driven by muscle metabolism and contractile activity (Zurlo et al., 1990). This phenomenon of lower H_{prod} could

be attributed to the decreased blood flow to skeletal muscle due to vasoconstriction. Consequently, this delays the need for increased H_{prod} from skeletal muscle. Furthermore, previous studies have indicated a significantly reduced mitochondrial content in the SMM of individuals living with obesity (Bouchard, 1995; He et al., 2001) which may also be a reason as to why individuals living with obesity demonstrate low levels of shivering.

Thermal Comfort and Sensation

TC and TS are subjective measures that participants record based on what they are exposed to. In day-to-day life, achieving neutral TC and TS is ideal as it can influence productivity, health and well-being and physiological reactions. In the study of thermal comfort and sensation, varied findings have emerged regarding the impact of body fat on perceived thermal responses. Daniels and Baker (1961) highlighted that individuals with higher body fat, particularly men, reported reduced discomfort in cold conditions compared to their leaner counterparts. However, this observation wasn't uniformly supported across other studies. For instance, Buskirk et al., (1991) noted minimal or no significant link between body fatness and sensations of cold. After subjecting participants to two hours of whole-body cooling at 10 °C, Budd et al. (1991) discovered that participants with higher body fat did not experience less discomfort or strain compared to leaner individuals. Despite lower T_{skin} these individuals tended to feel warmer. As expected, participants experienced a drop in TC and TS during the CE condition, although there was not any significant difference between men and women. This lack of sex differences is in line with what Dumont et al., (2022) found, but contradictory according to suggestions from Graham (1988) and Kingma and Van Marken Lichtenbelt (2015). With the average TC being -1.2 ± 1.5 and TS being -2.9 ± 1.3, participants still perceived the cold response somewhat strongly. However, this notable decrease in T_{skin} (average drop of 8.3 °C)

and TC ratings – indicating a physiological response that is still activated – was accompanied by only a modest increase in H_{prod}, with an average increase of 1.7 ± 1.3 kJ ·min^{-1} during CE. This disparity suggests a potential disconnect between the body's sensory perception of cold and its metabolic response, particularly when compared to lean individuals in other studies. In rats, Cabanac and Serres (1976) reported that the sensation of cold discomfort can exist independently of the shivering response. While shivering typically contributes to the perception of cold in normal conditions, this research highlights the potential for other sensory or neurological mechanisms to influence the sensation of cold discomfort. Furthermore, no correlations were found between body anthropometrics and changes in TC and TS, implying that none of the assessed anthropometric measures were correlated with the perception of TC and TS in the cold. Taking the results from the studies above and the results in this thesis suggest that body fat and the other body anthropometric factors may not significantly alter discomfort or strain levels in cold conditions. There appears to have been a stabilization in how participants were feeling with regards to their TC and TS after the initial drop within 30 min. As per the Dumont et al., (2022) study, a ~6 °C decrease in T_{skin} lead to an average TS value of -2.0. Coupled with the H_{prod} and muscle activity results above, it poses questions regarding their sensitivity to acute CE while lacking the associated physiological benefits that leaner individuals gain. There were no correlations between TC and TS to outcomes such as H_{prod} during baseline or CE. There was a significant correlation between TS and % MVC during CE, which indicates that individuals who feel colder tend to exhibit higher shivering intensities. This relationship aligns with the body's natural response to CE, where shivering is a thermogenic response triggered to generate heat and counteract the cold sensation.

Implications

Our findings present several implications for obesity and CE. Firstly, the general metabolic response of individuals living with obesity to CE, characterized by increased H_{prod}, confirms the body's adaptive mechanism of thermogenesis in response to cold stress, regardless of obesity. The smaller degree of increase compared to lean individuals, as noted previous studies , indicates a dampened thermogenic response in individuals with obesity, consist with previous observations. While our findings suggest that CE can increase H_{prod} and therefore might offer a supplementary method for caloric deficit, it's important to understand the multifaceted nature of weight loss. Effective and sustainable weight loss, traditionally linked to dietary management and physical activity, faces challenges due to individual differences in genetics, metabolism, and lifestyle. The effectiveness of these strategies is not uniform, and adherence over the long term is complex. Thus, while CE may augment the total H_{prod}, it needs to be combined with other strategies to result in meaningful weight loss. It is important to remember that the increased H_{prod} is much less pronounced than in lean individuals and the impact on overall weight loss might be modest.

Furthermore, when conducting a multiple linear regression analysis on the participant anthropometric data mentioned above, all variables (except for SMM (kg) due to its low sample size), were found to be statistically non-significant ($p > 0.05$), indicating that none of these variables, in the presence of others, serve as statistically significant predictors of T_{skin} (°C), H_{prod}, shivering intensity, TC or TS.

Future Research

The relatively consistent shivering observed across our study's duration suggests that the thermogenic response in obesity might be steady over time. However, this needs to be confirmed

with longer durations of CE. It may be possible that due to our cohort's body mass, 90-min of CE is not enough to induce more marked changes in H_{prod}. Furthermore, the temperature of the cold stimulus could significantly impact the thermogenic response. Our study employed a mild cold stimulus (10°C), but further investigations could explore the impact of even lower temperatures on the thermogenic response. It is possible that such a change could incite a more robust response or, alternatively, the response could plateau beyond a certain temperature. There is also a likelihood that a milder cold stimulus could be sufficient to trigger a thermogenic response in obesity, potentially providing a safer or more tolerable intervention method. While our study used whole-body CE, alternative modalities such as cold-water immersion or localized CE may elicit different responses. For instance, due to the higher thermal conductivity of water, cold water immersion is recognized for instigating a stronger thermogenic response. It is important to note however, that cold water immersion carries its own set of risks like hypothermia, and as such, may not be the most effective strategy in increasing H_{prod} outside of a clinical setting. On the other hand, localized CE could be a more practical and comfortable option for some individuals. However, the capacity of this modality to induce a substantial thermogenic response necessitates further research. Future studies could also look at the interplay between all these factors. As the global prevalence of obesity continues to rise, it is crucial to fill the research gap that currently exists in studying individuals living with obesity. Such investigations can provide significant insights and contribute to the ongoing efforts to address this global health issue.

Limitations

A limitation present in this study is the low number of SMM (kg) measurements that could be recorded. Due to the study population and the equipment being used, most of the

participants could not be scanned with a DEXA lying completely supine. They had to have their arms crossed to fit into the machine, which resulted in the inability to calculate the SMM (kg) for these individuals. This underscores the need for better measurement methodologies for SMM in individuals living with obesity. Additionally, our cohort's average BMI (33.07 ± 4.45 kg/m^2) was on the lower end of the obesity range, which limits the extrapolation of our findings to a population of individuals living with more severe obesity. Standardizing what clothes participants were wearing (a set Clo value) would also a consideration for future studies so that participants could have a similar amount of skin contact with the LCS during CE. Finally, the use of surface EMG for this cohort may not be the best choice due to its low signal-to-noise ratio and the relatively low number of motor units recruited. Increased subcutaneous tissue has been shown to reduce the signal quality in individuals living with obesity (Kuiken et al., 2003), and the subcutaneous thickness significantly lower the amplitude and mean frequency estimates of EMG signals (Minetto et al., 2013). Furthermore, another limitation of our study is the absence of lean individuals in our experimental cohort. To address this gap, our study had to rely on comparisons with findings from other studies that included lean individuals under similar stimuli. While this approach allows for some level of comparative analysis, it does not offer the direct, controlled comparison that could be achieved with a concurrent lean cohort. This reliance on external data sources may introduce variables that are not accounted for in our study design, such as differences in experimental conditions or participant characteristics. In addition to these considerations, another limitation of our study involves the confounding effect of feeding participants. The TEF can produce physiological responses similar to those elicited by CE, making it challenging to isolate the effects of CIT and determine the absolute magnitude of H_{prod} solely from CE. This similarity in response complicates our ability to discern the distinct

contributions of TEF and CIT to overall thermogenesis. As both feeding and CE can independently stimulate H_{prod}, our study's protocol, which included feeding participants, may have influenced the thermogenic responses attributed to CE. This overlap in physiological effects emphasizes the importance of controlling dietary factors in future studies to more accurately isolate and assess the specific impact of CIT in the context of metabolic research.

Chapter 5 – General Conclusion

With the number of individuals living with obesity rising, and the multifaceted impact of obesity on an individual's health, understanding how this cohort physiologically reacts to CE serves to fill the existing gap in the literature. This thesis provides a detailed exploration of the physiological responses to compensable CE in individuals living with obesity. In one of our key findings, we discovered that, similar to lean individuals, those with obesity do increase their H_{prod} during CE by about 1.7 kJ $\cdot min^{-1}$ as an adaptive thermogenic response to cold stress. However, this increase was less pronounced in individuals living with obesity compared to their lean counterparts, as per previous studies. Furthermore, they demonstrated lower levels of shivering, but still experienced thermal comfort and sensation sensitivity to the cold stimulus. Sex differences emerged during our study, with men initially showing a greater metabolic response to CE than women but this was attributed to the anthropometric differences between them. There are several areas that warrant further investigation, such as the impact of repeated CE and the effects of different durations, temperatures, or modalities of CE on individuals living with obesity. Furthermore, the large range in interindividual responses can be further investigated with better measurement techniques (i.e., a larger DEXA bed so participants do not cross their arms). This study faced limitations due to the low number of SMM measurements and the average BMI of the cohort being on the lower end of the obesity range, limiting the generalizability of the findings. Additionally, challenges like the use of surface EMG in obese individuals, the absence of lean individuals in the cohort, and the confounding effects of feeding participants on thermogenesis assessments underscore the need for improved methodologies in obesity research. Despite these limitations, the results of our study add significantly to the

existing body of knowledge about obesity and thermogenesis and can contribute to more accurate weight management strategies and interventions for obesity.

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Supplementary Data

Thermal comfort scale:

-5	Hottest I’ve ever felt
-4	Very hot
-3	Hot
-2	Warm
-1	Slightly warm
0	neutral
1	Slightly cool
2	Cool
3	Cold
4	Very cold
5	Coldest I’ve ever felt

Thermal sensation scale:

-3	Very comfortable
-2	Comfortable
-1	Just comfortable
1	Just uncomfortable
2	Uncomfortable
3	Very uncomfortable

Dubois and Dubois formula:

(1) BSA (m^2) = $0.007184 * (height^{0.725}) * (weight^{0.425})$, where height is in meters and weight is in kg

FFM (kg) formula:

(2) FFM (kg) = $weight - (\frac{weight * BF\%}{100})$

SMM (kg) formula:

(3) SMM (kg) = $1.13 * ALST - (0.02 \times \text{age}) + (0.61 \times \text{sex}) + 0.97$, where ALST stands for appendicular lean soft tissue mass (legs and arms), and male sex is 1, female sex is 0.

Table 3.5. *Participant metabolic fuel source differences by percentage between men and women*

Fuel source	Baseline		Cold Exposure	
	Men	**Women**	**Men**	**Women**
$CHO\ \%_{oxidation}$	12.2 ± 12.9	10.1± 13.7	22.6 ± 17.4	20.0 ± 14.3
$FAT\ \%_{oxidation}$	47.2 ± 19.4	29.7 ± 21.9	61.2 ± 17.9	61.0 ± 15.5

* Indicates significant difference at $p < 0.05$

Table 3.9. *Average thermal comfort (TC) and thermal sensation (TS) rating significance between men and women*

Scale / Condition	Sig.
TC / CE	0.809
TC / CON	0.895
TS / CE	0.056
TS / CON	0.152